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THE STATE OF READINESS FOR THE 2005-2006 FLU SEASON

HEARING

BEFORE THE

SUBCOMMITTEE ON
OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND
COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDRED NINTH CONGRESS

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THE STATE OF READINESS FOR THE 2005-2006 FLU SEASON

WEDNESDAY, MAY 4, 2005

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

The subcommittee met, pursuant to notice, at 2:21 p.m., in room 2123, Rayburn House Office Building, Hon. Ed Whitfield (chairman) presiding.

Members present: Representatives Whitfield, Stearns, Ferguson, Burgess, Blackburn, Barton (ex officio), Stupak, DeGette, Schakowsky, Inslee, and Baldwin.

Staff present: Anthony Cooke, majority counsel; Alan Slobodin, majority counsel; Mark Paoletta, chief counsel; Clayton Matheson, research assistant; Chad Grant, clerk; Edith Holleman, minority counsel; Voncille Hines, minority research assistant; and Chris Knauer, minority investigator.

Mr. WHITFIELD. I would like to bring this hearing to order, and I would like to apologize in advance to the witnesses that we were a little late. We had a vote on the floor. But we are excited about your being here today. We look forward to your testimony on the state of readiness for the 2005-2006 flu season.

At this time, as chairman, I will do my opening statement, and we will go through the subcommittee, and then we will get right to your testimony.

On October 5 of last year, one of our Nation's two largest suppliers of influenza vaccine informed the American public that it would be unable to provide any of the 46 to 48 million doses it had planned. Overnight, the expected supply of flu vaccine in the U.S. was cut nearly in half. Almost immediately there were news reports of imminent delays and shortages that could deprive millions of Americans who needed and wanted flu shots from getting them. Elderly people, parents of young children, adults with chronic illnesses, and countless other Americans panicked and flocked to local doctors' offices, healthcare clinics, and pharmacies to obtain the vaccine before it ran out. Fortunately, the flu season proved to be a relatively mild one, and coordination among HHS, the remaining manufacturers and the public turned the concern of a national shortage into a matter of some local and regional surpluses.

In light of last year, this committee must carefully monitor preparations for the 2005-2006 flu season.

First, we need to look closely at the goals and strategies behind our preparations for this season. We need a realistic assessment of

the manufacturers' capabilities and the vaccine doses they should produce, and we must then plan accordingly. Specifically, we must ensure FDA's focus on efforts to confirm the entry, or reentry, of all available manufacturers into the vaccine market; and we must be certain the U.S. is prepared for all contingencies in which one or more of the producers of flu vaccine fail to achieve the necessary license or suffer from sterility or quality control problems that prevent distribution of their vaccine.

Second, we must take advantage of this opportunity to consider the manner in which we communicate important flu and vaccination information to the public. This past year, the American people listened to the media's troubling portrayals of the shortage, and they panicked. Everywhere in the U.S., including my home district as well as others throughout the country, worried people rushed to their doctors, rushed to their pharmacists, where they all too often were either forced to linger in long lines or were even turned away. It is essential that our Nation's vaccine policymakers persistently endeavor to communicate clearly and concisely accurate and up-to-date information to the American people so that flu seasons are never characterized by unnecessary concern or confusion.

I welcome today's witnesses and look forward to their testimony. I hope this hearing will leave all of us with a more complete understanding of what to expect for the 2005-2006 flu season and more confidence in how our Nation's public health stakeholders will manage the flu manufacture and vaccination process.

With that, at this time I would like to welcome and introduce Mr. Bart Stupak, the ranking minority member, for his opening statement.

Mr. STUPAK. Thank you, Mr. Chairman; and thank you for holding this hearing.

Last year we had a very difficult flu season. In October, just as most people were thinking about getting their flu vaccine, the Centers for Disease Control was gearing up for their vaccine education program, and the Nation learned that it would only receive one-half of the 80 to 85 million doses of flu vaccine that it was counting on. Because of sterility problems in the manufacturing process, Chiron was not able to produce any of the 46 million doses it had promised. If you were not elderly, not very young, not disabled, or not with a compromised immune system, you were asked to step aside and let the more medically needy have their vaccine.

Americans did step aside, but the distribution to the medically needy was haphazard. Some nursing homes, for example, had trouble getting vaccine doses. Elderly persons lined up in the morning at clinics only to find there were not enough doses to go around. Health care providers struggled to make value judgments about who in the high-risk populations, including themselves, should get the limited number of vaccines. In Michigan, for example, there were only 2 million doses of flu vaccine available for 3.4 million high-risk individuals.

There are many questions about why the United States had so few suppliers. By January, however, after one manufacturer produced extra vaccine, there were available doses but not enough customers. Approximately 3.5 million doses out of the 60 million were discarded.

We are now preparing for the next flu season. At this point we have no more suppliers than we did a year ago. Sanofi is planning to produce 50 to 60 million doses, and MedImmune will produce another 3 million of the FluMist. Chiron hopes to produce 25 to 30 million doses but has not yet been approved to do so. Glaxo may enter the market with 10 million doses but has not yet filed for a license. If all goes well, that would provide 93 to 103 million doses, or 9 to 21 percent more doses than this country has ever used. If these vaccine promises are not fulfilled, we will have approximately the same amount that we had last year or maybe even less.

Today I am interested in knowing what changes have been made in the distribution and education system so that this year the medically needy are served quickly and efficiently and there is no waste of vaccine because populations have been discouraged to receive their flu vaccine.

I also want to know why the drug companies are raising their prices by 17 percent, citing market demand, and whether this increased cost will discourage use.

In addition, I remain concerned that the Department of Health and Human Services now seems to be relying on only one domestic manufacturer to produce extra vaccine and to develop new methods to manufacture flu vaccine. If anything goes wrong with this domestic supplier, like it did at Chiron, America will be in serious trouble.

There has been concern about our flu vaccine policy for some time. Two years ago, several members of this committee sent a letter asking for a hearing on our flu vaccine policy. Flu kills 35,000 people per year even without a shortage. I look forward to hearing from the witnesses today about their agency's plan to ensure an adequate supply and appropriate distribution of this life-saving vaccine.

In addition, Mr. Chairman, I am sorry drug companies are not here to answer the questions about their intent and interests in meeting this Nation's needs. To get a complete picture of the situation, we need to hear directly from the manufacturers of the flu vaccine, and I look forward to such a hearing.

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

Mr. WHITFIELD. Thank you very much.

We will be calling on opening statements in order of appearance at the committee. So at this time I would like to call on Mrs. Blackburn of Tennessee for her opening statement.

Mrs. BLACKBURN. Thank you, Mr. Chairman; and I want to thank our guests who are with us today for taking the time to be here. I will waive my statement and reserve the time for questions.

Mr. WHITFIELD. Mrs. Blackburn waives her opening statement.

At this time, I recognize Ms. DeGette of Colorado.

Ms. DEGETTE. Thank you very much, Mr. Chairman, for holding this hearing. I would ask unanimous consent to put my full statement in the record.

Mr. WHITFIELD. Without objection.

Ms. DEGETTE. I commend the chairman for having the hearing. I also think we need some follow-up hearings on an issue that has been of great concern to me, and that is the avian flu, which isn't really the topic for today, but I think it is the kind of the elephant

in the room, if you will, because—and I see our witnesses nodding in agreement. So I hope we can do that.

But, with respect to today's topic, I am concerned, like my colleagues, about our system for flu vaccine production. We have three manufacturers committed to supplying the U.S. with flu vaccine, but there have been concerns for many years that our system doesn't adequately support these manufacturers; and, also, the danger exists that the yearly destruction of unused flu vaccine creates a disincentive for innovation and adequate supply.

Last year, Colorado, my State, was among the first States hit by the flu strain known as Fujian A, which was not included in the 2004 flu vaccine. This flu strain for unknown reasons disproportionately affected children and caused at least 11 deaths last year. We need to do better, and I hope that the witnesses today can improve our understanding of the public health issues and also describe the technological advances in virus identification and antiviral production, because, as we all know, the flu vaccine for any given year may not actually cover all the viruses that go around. And, finally, I would like the witnesses to talk about how prepared the U.S. is for a flu pandemic, not just avian flu but any flu.

In late 2002, the SARS virus disrupted travel and tourism and claimed the lives of many people. Now, I know the World Health Organization has established a global monitoring system to track influenza outbreaks, but the cost of complying with this system is certainly too much for the world's poorer nations where some of these viruses originate. I hope the witnesses will talk about the adequacy of the surveillance system and also our Nation's ability to cope with the pandemic.

It is my understanding that countries like Japan, Finland, and Australia are stockpiling antiviral treatments against pandemic flu for about a quarter of their population. Our stockpile in the U.S. is only about 1 percent of the population. So I would hope that we can talk about that as well as the other issues raised by the ranking member, the chairman, and others.

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

[The prepared statement of Hon. Diana DeGette follows:]

PREPARED STATEMENT OF HON. DIANA DEGETTE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF WYOMING

Flu related spending by the Department of Health and Human Services has risen almost sevenfold over the past 5 years. While for some individuals a flu infection is merely a few days sick in bed, for other more vulnerable populations, the flu can cause serious illness and even death. Even with all the advances of 21st century medicine, 30,000 Americans die from flu or flu-related illnesses each year. In some studies, vaccination against flu has shown to provide protection to between 70 and 90 percent of healthy adults. Unfortunately, some of our vulnerable populations, including health workers, have dismal rates of vaccination. We must do better.

I commend the Chairman for holding this hearing and agree that we need to examine this important issue now, before the next crisis. It is my understanding that many of the flu vaccine manufacturing has begun this month in preparation for next year's flu season. I hope that today's hearing will provide insights that will improve our readiness.

Like many of my colleagues, I remain concerned about the United States system for flu vaccine production. We have at least 3 manufacturers committed to supplying the U.S. with flu vaccine, but there have been concerns for many years that our system does not adequately support these manufacturers. Additionally, the danger ex-

ists that the yearly destruction of unused flu vaccine creates a disincentive for innovation and adequate supply.

Last year, Colorado was among the first states hit by the flu strain known as Fujian A, which was not included in the 2004 flu vaccine. This flu strain, for unknown reasons, disproportionately affected children, and caused at least 11 deaths of children last year. We clearly need to do better. I hope that the three witnesses here with us today will improve our understanding of this public health issue and describe the technological advances in virus identification and antiviral production.

In addition to concerns about flu vaccine supply, I hope that our three expert witnesses will also comment on how prepared the U.S. is for a flu pandemic.

In late 2002, the SARS virus disrupted travel and tourism and claimed the lives of many people. I know that the World Health Organization has established a global monitoring system to track influenza outbreaks, but the cost of complying with the system is certainly too much for the world's poorer nations. I hope that the witnesses will comment about the adequacy of this surveillance system and our nation's ability to cope with an outbreak. It is my understanding that countries such as Japan, Finland and Australia are stockpiling antiviral treatments against pandemic flu for up to one quarter of their nations' population. The U.S. stockpile is maintained for only 1 percent of our population. We may need to reexamine this strategy.

Many experts have stated that in addition to surveillance, we need a reliable and flexible vaccine production system. Last year, the license suspension of the Chiron company's vaccine manufacturing plant in the U.K. was a wake up call to all of us. In addition to a "shortage" of supply, we also were faced with educating the public about appropriate distribution and recipients. I hope that the witnesses will help us understand what went wrong last year and what lessons were learned.

This hearing continues this Committee's examination of FDA's ability to protect the public's health. It is my understanding that there may be inadequate funding for FDA inspectors to travel overseas and scrutinize manufacturing facilities. I hope that Dr. Goodman from FDA's Center for Biologics Evaluation and Research will describe these current challenges. Drug safety has been of great interest to me and this Committee for a number of years, and the situation at the Chiron plant is only one example of our concerns being realized. We clearly must take steps to ensure that history is not repeated.

Mr. WHITFIELD. Thank you very much.

At this time, I would recognize Dr. Burgess for his opening statement.

Mr. BURGESS. Mr. Chairman, thank you for calling this important hearing on public health readiness and how it relates to influenza outbreaks. You know, we have to work with our public health agencies to ensure access to adequate supplies of vaccines are present but at the same time work with the manufacturers to make certain that they have the ability to produce flu vaccine.

Some of the concerns I have regarding the vaccine availability aren't with today's focus on the flu vaccine supply. Many people have forgotten that since 2000 we have also had shortages of vaccine that protect against eight childhood diseases. The flu vaccine shortage was only symptomatic of the broader vaccine supply problem: There are only a handful of manufacturers making vaccines for Americans. Three manufacturers had licensed products for flu vaccines last year, many childhood vaccines have only one manufacturer, and none have more than two manufacturers, increasing the risk of shortages.

The question comes up as to why there are so few manufacturers. Certainly the vaccine business is complex in its development, complex in its manufacturing, and certainly complex because of the regulatory challenges, many of which Congress has imposed upon it. Obviously, that all adds to the cost. Vaccines, however, are a fairly low-margin business, and again that may be partly our responsibility as well because there are some price controls on vaccines.

Then, finally, vaccines have one of the greatest liability burdens of any medical product; and the statute of limitations, particularly for childhood vaccines, is incredibly long. We need to address the overall issue of vaccines supply in this country, and I encourage the country to take up the broader issue of ensuring a stable supply for all vaccines this year.

I yield back.

Mr. WHITFIELD. Thank you very much.

At this time, I recognize Ms. Schakowsky for her opening statement.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman.

Thirty thousand people die annually from the flu virus, hundreds of thousands of others end up in the hospital, and no American should again be asked to compromise their health because of the failures of the Bush administration to provide sufficient doses of the flu vaccine.

Last October, we learned that we would have only half the expected supply of influenza vaccine for the fall and winter flu season. When the Food and Drug Administration was told of contamination at the Chiron facility, one the largest flu vaccine producers, it failed to act in a meaningful way to address the problem, which was secure additional vaccine supplies elsewhere. We saw price gouges appear out of the woodwork to profit from a public health crisis; and we saw many who would normally seek a vaccination, those at greater risks of contracting the flu, foregoing shots.

Had the FDA taken the appropriate course of action, last year's vaccine shortage and perhaps unnecessary sickness and loss of lives in the United States may have been avoided. None of these problems occurred in other countries where the government plays a far greater role in assuring affordable access to health care. In fact, in Canada there was adequate flu vaccine supply to sell to those Americans who were close enough to the border to go across for a shot.

Last fall, Illinois Governor Rod Blagojevich, a leader in the fight for affordable prescription drugs, including prescription drug reimportation, acted to secure additional vaccine supplies for the most vulnerable people in our State. Although in a hearing we held last November the FDA indicated to me that it planned to provide a decision within 2 or 3 weeks of that time as to whether Illinois would be allowed to bring vaccines into the country, Governor Blagojevich is still awaiting FDA authorization.

So I want to know why, 5 months later, Illinois still has not received a response from the FDA; and I want to know why, given the fact that we are still entirely relying on foreign sources to meet our flu vaccine needs, the Bush administration is still adamantly blocking Illinois' reimportation efforts of other life-saving medications. The FDA allowed politics to trump personal health when it undermined Governor Blagojevich's effort to address a serious health crisis. Why would a Federal agency stall an emergency situation like the one we faced last fall? The answer can only be because of their fear that Governor Blagojevich's success in importing flu vaccine would provide validation for his efforts to import prescription drugs for the people of Illinois.

Today, the Wall Street Journal highlights how many doctors, pharmacists, and hospitals across the U.S. already fear another major shortage of flu shots. The Vice President of Amerinet, Inc., a health care purchasing group of St. Louis, termed the shortage in order of, "a feeding frenzy." Manufacturers are already charging at least 17 percent more for the flu shots, reflecting this rush for advanced orders. According to the Wall Street Journal, this, "shows that the vaccine production infrastructure remains nearly as fragile and outdated as it was before last year's crisis."

We should learn from mistakes made last year. I would like to hear from the witnesses today what concrete actions the administration is taking to ensure that this same fiasco will not happen again. I want to hear what changes have been made to our flu vaccine infrastructure since last year.

It is clear that we need better cooperation and information sharing not only between the manufacturers and distributors but also with the regulatory agencies of other countries where the manufacturing plants are located. Because we are still clearly relying on foreign sources to meet our flu vaccine needs, we need to improve monitoring of and communication with those sources. I would like to see how the FDA and CDC will work with the State and local health officials, manufacturers, and the public to improve distribution of available supply; and I want to hear how it is that, after news of massive shortages, we actually ended up with regional surpluses of the flu vaccine. That fact is especially troubling because it means that many of those who needed the vaccine but couldn't get it could have avoided unnecessary illness.

At last year's hearing I questioned the Bush administration's attitude toward vaccine accessibility. I was disturbed by Vice President Cheney's explanation that vaccine production just isn't profitable enough for private companies, and I will ask the same question: Are the administration's concerns for the high profits of the pharmaceutical companies to take precedence over the health of the American people?

I want to be able to assure my constituents that there will not be a shortage of flu vaccine in Illinois this fall, and I hope this committee will be made aware in advance and in real time of the status of flu vaccine production at the labs with which we contract so that the 2005-2006 flu season will not be a relapse of last year's problems.

Thank you, Mr. Chairman.

Mr. WHITFIELD. Thank you.

At this time, I will recognize the chairman of the Energy and Commerce Committee, Mr. Barton of Texas, for his opening statement.

Chairman BARTON. Thank you, Mr. Chairman; and I am going to submit my formal statement for the record.

I just want to briefly say I appreciate you holding this hearing. I look forward to our panelists. We don't want to have happen next year what happened this year. It was very disconcerting to go from there was a big shortage and we were rationing flu vaccinations to, later in the season, if you wanted one, come in and get it. So we have a lot of issues.

But I guess the bottom line issue is going to be, are we prepared for next year and will every American who wants a flu vaccination next year be able to get one? I hope we get an answer to that in the hearing today.

With that, Mr. Chairman, I would yield back.

[The prepared statement of Hon. Joe Barton follows:]

PREPARED STATEMENT OF HON. JOE BARTON, CHAIRMAN, COMMITTEE ON ENERGY AND COMMERCE

It's hardly seems like the flu season is past. But it is and it was one of the most publicized ever. In just six months, it all starts again. Millions of Americans will want a flu vaccination come this fall and I think I can promise you that many are wondering right now whether their vaccine will be available.

Last year, men and women in this country, many of them elderly, stood in long December lines to get a flu vaccination when production problems shut down the Chiron plant in Liverpool, England.

Almost immediately after the supply was interrupted, this Committee held a hearing to try to determine what happened and how it could be prevented in future seasons. Well, the future is upon us—vaccine manufacture for the 2005-2006 flu season is well underway. We've invited here today three representatives from the Department of Health and Human Services to answer some simple questions: Are we ready? How are we doing?

Let me be more specific. How many doses of flu vaccine do we expect to need for the coming season and how many do we anticipate from the companies manufacturing for the American market? When have we last checked the progress of these manufacturers and what issues are outstanding?

Looking back to the problems of last year, what are the specific changes made to our flu vaccine policy and practice? Has FDA cleared up its communication problems with the MHRA? What is the status of efforts to introduce more vaccine manufacturers into the U.S. market? What plans and contingencies do we have in place so we aren't caught flat-footed in the event of another production failure like we experienced last year?

Finally, while I recognize the complexities and uncertainties of flu vaccine manufacture and distribution, I hope HHS can better communicate to the American people the important information about influenza and immunization. Last year, people heard warnings about shortages then news of surplus. And each day more stories appear in the press about the threats of deadly flu strains. People are worried about the flu and whether their shots will be there in the fall. HHS must keep them up to date with straightforward, clear, and measured information.

I want to thank Mr. Whitfield for holding this important hearing. And I look forward to today's testimony on the state of preparedness for flu.

Mr. WHITFIELD. Thank you, Mr. Chairman.

At this time I would recognize Ms. Baldwin for her opening statement.

Ms. BALDWIN. Thank you, Mr. Chairman; and thank you to the witnesses who are testifying before us today.

Like many of my colleagues, I was distressed by the series of events last fall that led to the U.S. Having a severe vaccine shortage. We ended up being pretty lucky, but we certainly shouldn't have to be relying on luck to ensure the health and well-being of Americans.

Preparing a flu vaccination strategy certainly seems to be as much an art as it is a science. I understand the challenges that we face in predicting which flu strains will be most prevalent during the upcoming flu season and needing to prepare the necessary vaccines months and months in advance, but I am also interested in ways that we can strengthen this line of defense for the health of Americans, either through changing the actual vaccine production methods or changing the way that we communicate and coordinate with other countries and vaccine makers.

I am interested in hearing from our panel of experts today, and specifically I am interested in knowing what are the lessons learned from last year's experiences and how their various agencies are moving forward to ensure that we have a reliable flu vaccine supply. As Dr. Burgess mentioned in his opening statement, I also share his interest in ensuring that we have a reliable supply of other vital childhood vaccinations. Thank you for being here today.

Mr. Chairman, thank you for holding this hearing, and I look forward to our discussion.

Mr. WHITFIELD. Thank you.

At this time, I will recognize the gentleman from New Jersey, Mr. Ferguson, for his opening statement.

Mr. FERGUSON. Thank you, Mr. Chairman.

I appreciate our panelists for being here today. We thank you very much.

We certainly have seen some major problems in the supply of flu vaccine; and we certainly, as others have already said, don't want a repeat of last year's problem. We know from history that when we have seen severe flu problems literally hundreds of thousands, millions of people can lose their lives. Tens of thousands of people die in a typical flu season when there is no vaccine problem, so certainly if there is a shortage that exacerbates that problem. I am certainly interested in the avian flu and some of the other issues that have been described here, and I look forward to getting into some of those issues when we have time for questioning.

I would only say it has been raised here in our opening statements the topic of bringing in vaccines from Canada, and perhaps that might be a model for bringing in drugs from Canada or other countries on a broader scale. I would only suggest that if we want to see similar problems that we have seen with the flu vaccine, if we want to see similar problems in the broader drug supply, let us start bringing in drugs from all sorts of other countries.

Some have suggested, well, let us only bring in—why don't we only import drugs from Canada and forget the health and safety standards, the very high standards that we have here in this country? Of course, that is a bit of a red herring. Canada can't possibly make and manufacture and supply all the drugs that they use and supply all the Americans who want to get their drugs from Canada as well, whether it is the State of Illinois or anybody else. Canada has simply become a post office, not a manufacturer of drugs; and it has become common knowledge that if you go across the border into Canada you are not necessarily buying Canadian drugs, you are buying drugs from South Africa or China or India or the Czech Republic or any one of a host of other countries that don't have close to the health and safety standards that we have in our country or even that Canada has in their own country.

So I would suggest that if we want to cripple the companies and the industry that are making these drugs, these life-saving cures and medications in the first place, let us not use the vaccine situation as the example of where we should go.

One of the problems, certainly one of the reasons we are seeing such severe problems with the vaccine situation is because we have driven manufacturers out of the business. We have created an environment through our action in the Congress and through other cir-

cumstances whereby companies just don't find it sensible any longer to be in the business. If we want to go that route for all medications, I would suggest, great, let us just start importing drugs from other countries and not worry about the health and safety standards, because that is exactly where it is going to lead.

Thank you, Mr. Chairman. I yield back.

Mr. WHITFIELD. Thank you.

As you all are aware, this is an oversight investigation subcommittee, and it is our custom to take testimony under oath. And I would like to ask each of you—and before I ask you, I do want to introduce all of you.

First of all, we have with us today Dr. Julie Gerberding, who is the Director for the Centers for Disease Control and Prevention; and we welcome you. In addition, we have Dr. Bruce Gellin, who is the Director of the National Vaccine Program Office at the Department of Health and Human Services; and then we have Dr. Jesse Goodman, the Director of the Center for Biologics, Evaluation and Research at the Food and Drug Administration.

We do welcome all of you. We look forward to your testimony, your expertise.

As I stated, we do take testimony under oath; and I would ask you, do you have any objection to testifying under oath this afternoon?

I would also advise you that, under the rules of the House and the rules of the committee, you are entitled to be advised by counsel at these hearings. Do you desire today to be advised by counsel during your testimony?

Okay, in that case, if you would please rise and raise your right hand, I would like to swear you in.

[Witnesses sworn.]

Mr. WHITFIELD. You are now under oath, and we look forward to your testimony.

Dr. Gerberding, we will start with your testimony.

TESTIMONY OF JULIE LOUISE GERBERDING, DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION; BRUCE G. GELLIN, DIRECTOR, NATIONAL VACCINE PROGRAM, DEPARTMENT OF HEALTH AND HUMAN SERVICES; AND JESSE L. GOODMAN, DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION

Ms. GERBERDING. Thank you.

I thank the subcommittee for having this hearing. I think this is a critical time for us to keep a strong focus on influenza, and I appreciate your helping us do that from the congressional perspective. I can assure you we are doing that at the Department of Health and Human Services. Secretary Leavitt is having the Department leaders meet every day on this subject, so we are looking forward to giving you a perspective on how we are preparing for the fall.

I wanted to start with a graphic that I think illustrates one of the most important principles about influenza—on the next graphic, please—and that is the fact that the virus itself is so unbelievably unpredictable. This is kind of a time line of influenza as it has evolved over the last century. Each one of those arrows is the be-

ginning of the appearance of a new strain of flu, and each circle represents a pandemic that started when a new strain appeared. So, in the last 100 years, three times we have had major international pandemics as H1, H2, and H3 appeared in the world and caused devastating outbreaks. That is a very difficult event to predict.

Up in the right-hand corner of this graphic are the little mini appearances of the avian isolates. And, of course, as you mentioned, right now we are very concerned about avian influenza in Asia, and we would look forward to being able to update you on that topic.

But the point of all of this is that we don't know in any given flu season whether this will be a pandemic year, a mild season, when it will start, how long it will go, when it will peak, how severe it will be, how many people will be affected, will it be worse in adults or children. There is absolutely no certainty about the strain or the characteristics of the flu season on any given year, and that is a challenge for all of us, even if we didn't have to face additional challenges.

But on my second graphic I have illustrated the outcome of this past season. In the yellow bars here, the figures for the coverage of the high-risk populations are presented. In the far left graph is the comparison from this past year to the year before and the number of young infants that were immunized. And you can see that, despite our vaccine shortage, we were able to achieve about a 50 percent immunization of that age group. This is the first year that recommendation was made for those children.

In the high-risk adults, those adults who have other medical conditions, our immunization rates were not quite as good as they were the year before. Among adults over 65, they were very close to the year before but not quite the same. Among health care workers, they were not quite the same. But, overall, despite having 50 percent of the vaccine we predicted, we came pretty close to achieving the immunization coverage rates that we would have normally achieved in a year where we had plenty of vaccine.

That is not a success, but it represents an effort of hundreds and hundreds of people around the country as well as the government and the private sector to really at a late date make the doses that we did have available to as many of the high-risk people as we can. And of course this illustrates that it is not just the virus that is unpredictable, it is the vaccine supply that is unpredictable, and it is the demand for vaccine that is unpredictable as well.

So what are we doing about the vaccine supply? Well, the first thing we are doing is buying lots of vaccine. Since 2004, CDC's dollar investment in vaccines for flu has gone up by $118 million. In the President's proposed budget for fiscal year 2006, that would include $30 million for an insurance policy to buy monovalent vaccine as a reserve if something goes awry with one of the other manufacturers as well as the 20 million purchase of vaccine for distribution to the States on top of what is included in the Vaccines for Children program.

We are also providing a fair purchase price for this vaccine. We think it is a good thing that over the last decade the price paid for flu has gone from pennies to a price that allows manufacturers to receive a fair reimbursement; and, also, our government, through

our Medicare and Medicaid services, are reimbursing providers appropriately for providing vaccine.

We are also planning scenarios. We will start the flu season with a focus on high-risk people because we want the flu shot in their arms first. Then, if the supply comes forward as we are hopeful it will, we will be able to expand in to people who have less risk from flu complications and ultimately into healthy people as the season unfolds. But we will start the season this way, with a clear message that that is the CDC's priority. But people will have to understand, just as is true in any year, the communication about flu does change as the season progresses. We find out where it is peaking, we find out if it is severe, we find out where vaccine supplies are short, and we have to adjust our message as we go forward. We want people to anticipate that and to expect that they will have to pay attention, because the message will evolve.

I see there are many other steps and progress that I will let my colleagues present to you, but, again, I just wanted to say that we are very pleased that the committee is interested, and we will do everything we can to keep you updated on all of these unpredictabilities as we go forward and do as much as we can to take the uncertainty out of the system. Thank you.

[The prepared statement of Julie L. Gerberding follows:]

PREPARED STATEMENT OF JULIE L. GERBERDING, DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. Chairman and members of the Committee, I am pleased to be here today to update you on the Centers for Disease Control and Prevention's (CDC) efforts to address the influenza vaccine supply status and our planning for the 2005-06 influenza season. We faced unprecedented challenges during the 2004-2005 influenza season. Due to tremendous collaboration among our public health and private sector partners, our collective ability to modify and enhance our response strategy as circumstances changed, and the cooperation of the public, I am pleased to report that we have been successful in our effort to promote and protect the public's health. We learned valuable lessons from the 2004-2005 influenza season that are enhancing our planning efforts for the upcoming influenza season.

Vaccination is the primary strategy for protecting people who are at greatest risk of serious complications and death from influenza. In the face of this season's influenza vaccine supply shortage, CDC, state and local public health officials, vaccine manufacturers and distributors initiated extraordinary partnership activities to address this public health challenge. For example, sanofi pasteur (formerly Aventis Pasteur) provided access to vaccine distribution information to aid in the allocation of the available vaccine supply to those people most in need this season. State and local public health officials also worked closely with CDC to ensure equitable distribution of vaccine to those areas with the greatest need And we must not forget the important service of immunization providers on the front lines in doctors' offices, health clinics, grocery stores, and pharmacies working to prioritize, deliver, and administer vaccine so that it reaches high-risk individuals. Together, we found new and effective ways to address the sudden, late emergence of a substantial influenza vaccine shortage that had never before occurred.

Despite the challenges presented by the unexpected shortage of influenza vaccine, CDC immediately responded by changing recommendations to focus vaccine efforts and then began monitoring the results of those changes. State specific flu vaccination data for adults and children were rapidly collected and reported on an ongoing basis from November 2004 through February 2005. CDC's Behavioral Risk Factor Surveillance System reported that 62.7 percent of Americans 65 years of age and older reported being vaccinated for influenza between September 2004 and January 2005. This coverage is comparable to the percentage of older Americans vaccinated in previous years without supply shortages. So, many at-risk older Americans were vaccinated as a result of effective work of state and local health departments and the cooperation of younger, healthier Americans who "stepped aside" to allow the older and more vulnerable populations to receive vaccine. In addition, through January of 2005, 48.4 percent of young children (between 6 and 23 months of age) were

vaccinated. This marked the highest vaccination coverage rate in response to a first-time recommendation of a new vaccine for children.

PREPARATIONS FOR THE 2005-06 INFLUENZA SEASON

As we prepare for the 2005-2006 influenza season, we are incorporating into the planning process successful strategies used this past year. For example, our budget request reflects the need to strengthen the influenza vaccine supply. Another example is the inclusion of our state and local public health partners and the vaccine manufacturers in the planning process for the next influenza season. Another partnership is the National Influenza Summit, which is cosponsored by the American Medical Association (AMA) and CDC and has been meeting annually since 2001. The Summit brings together stakeholders to discuss issues of concern regarding the annual influenza season, including vaccine supply. Additionally, throughout the year Summit partners continue to collaborate to address barriers to increased influenza vaccinations. This year the Summit will be held May 10-11 in Chicago.

The best strategy for influenza prevention and control both during annual outbreaks and during a pandemic is vaccination. However, the vaccine manufacturing system in the United States is fragile. Currently, there are only three influenza vaccine manufacturers producing vaccines for the US market, and only one of those manufacturers produces its vaccine entirely in the United States.

Anticipating and planning for the next influenza season is an enormous and complex challenge, involving numerous public health and private sector entities. The production of influenza vaccine is a lengthy and complicated process. Six to nine months before the influenza season begins, manufacturers must predict demand and decide the amount of the vaccine to produce. Moreover, the onset of the influenza season, its severity and duration, as well as the potential public demand for vaccine are highly unpredictable from year to year.

CDC has already begun its planning efforts for the 2005-06 influenza season in anticipation of continued challenges in meeting the nation's vaccine supply needs. We have established a planning team that meets almost weekly. The team consists of staff from across CDC, as well representatives from state and local public health agencies with input from the National Vaccine Program Office and the Food and Drug Administration.

To date, CDC has:

- Developed possible scenarios for vaccine supply for the coming season, including the possible disruption of production among the current influenza vaccine manufacturers for the U.S. market, the re-entry of Chiron into the market, and the entry of additional influenza vaccine manufacturers into the U.S. market;
- Worked with the Advisory Committee on Immunization Practices (ACIP) to develop more refined vaccination priority plans that can be used should there be another critical vaccine shortage;
- Met with U.S.-licensed and other vaccine manufacturers to discuss their plans for the next season, including production estimates, and distribution strategies and anticipated time lines for vaccine availability; and
- Worked with sanofi pasteur and other prospective manufacturers and distributors so that, during the prebooking process, customers indicate both the total amount of vaccine they need, assuming an adequate supply, and the number of doses needed to vaccinate high priority groups in the event of supply limitations.

In addition, CDC is:

- Pursuing a vaccine contracting strategy that addresses routine influenza vaccine purchase and stockpile purchase. We recently signed contracts for 3.5 million doses maximum of sanofi pasteur thimerosal-free vaccine, three million doses maximum of sanofi pasteur multi-dose vials and one million doses of MedImmune's FluMist. The stockpile doses are being negotiated now that we have the contracts. The bulk purchase solicitation is pending.
- Monitoring antigen-sparing studies designed to determine if reduced vaccine dosages can provide sufficient immunity against influenza, thereby allowing for the protection of more persons with fewer doses of vaccine.
- Developing infection control strategies to prevent the spread of influenza.
- Drafting a written plan highlighting key activities that state and local public health agencies should consider to prepare for the upcoming season. This plan is currently being reviewed by our partners, and we hope to have it finalized before the end of summer 2005. This will be complemented with a list of key activities CDC will undertake.
- Preparing communication strategies with appropriate messages to respond to the fluctuations in supply and demand anticipated throughout the season.

• Developing and implementing a plan to evaluate the season.

These comprehensive planning efforts are intended to support the achievement of important public health objectives, including increasing the domestic production of influenza vaccine, increasing demand for vaccine among persons indicated for annual influenza vaccination, and increasing vaccination coverage, particularly among persons in high-risk groups, so that we can protect and improve the public's health.

CONCLUSION

Influenza is a serious public health threat, taking the lives of about 36,000 Americans each year and hospitalizing on average more than 200,000 each year. For this reason, it is imperative that we continue to refine and improve our capacity to meet any challenges that arise in terms of vaccine supply, seasonal severity, or other unusual circumstances. We are applying the lessons learned from the challenging experiences of the 2004-05 influenza season for this upcoming season and have established a mechanism to continue to improve and learn in an effort to assure our nation's citizens are protected from this disease.

Thank you for focusing attention on this important public health issue and for the opportunity to provide an update on our current efforts. CDC is committed to protecting and promoting health for all Americans, preventing disease and disability through public health research and public outreach, and supporting important public health interventions, including vaccination. We appreciate your interest in this issue and your support of CDC's efforts to protect the public's health.

I will be happy to answer any questions.

Mr. WHITFIELD. Thank you, Dr. Gerberding.

At this time we recognize Dr. Gellin for his opening statement.

TESTIMONY OF BRUCE G. GELLIN

Mr. GELLIN. Thank you very much, Mr. Chairman and members of the committee.

I am Dr. Bruce Gellin. I'm the Director of the National Vaccine Program Office of the Department of Health and Human Services. I am glad to have the opportunity to speak to you today about the U.S. influenza vaccination program and the role of the National Vaccine Program Office, NVPO, in strengthening the U.S. Influenza vaccine supply.

The NVPO was established in 1988 and has responsibility for coordinating and ensuring collaboration among the many Federal agencies involved in vaccine and immunization activities. We accomplish this by communicating and coordinating with our HHS agencies as well as with the Department of Defense and the U.S. International Agency for International Development, and through our National Vaccine Advisory Committee The development, production, and delivery of influenza vaccine every year underscores the complexities of vaccine production itself. Because they involve living organisms, developing and producing vaccines poses different challenges than the development and manufacture of drugs.

In the United States, as with many other countries, the protection of the population through vaccination depends on vaccines produced by private companies for profit as well as for public good. U.S. vaccine manufacturers are faced with substantial challenges, including the costs and uncertainties of developing new products, limited returns on investment for vaccines compared with pharmaceutical products, a regulatory environment that has very high standards for safety and effectiveness, concerns about liability issues and, for influenza vaccine, variable demands from one season to the next.

Consequently, the number of companies that produce licensed vaccines for the U.S. Market is small. Each type of vaccine is made

by a limited number of suppliers, as you have already commented upon; and, in many cases, a single manufacturer supplies vaccines that we rely on.

Producing the flu vaccine has additional challenges. It is a vaccine that has to be redesigned and produced every year and delivered on time to tens of millions of people who desire it over a several month period in the fall in advance of the annual flu season. We all witnessed the fragility of the system last year when one of our two large manufacturers could not supply vaccine to the market. In recent years, we have also seen both surges in demand and delays in the delivery of influenza vaccine creating mismatches between vaccine availability and enhanced demand, resulting in these de facto shortages.

While we are optimistic that an increased number of manufacturers are now interested in the U.S. influenza vaccine market, presently only three companies are licensed to sell flu vaccine in the U.S. Two produce an inactivated influenza vaccine, and a third produces a live-attenuated vaccine that is delivered by nasal spray.

All U.S.-licensed vaccines are developed from viruses that are grown in eggs in a process that is unique for influenza vaccine. In a collaborative effort, both CDC and FDA contribute to the influenza vaccine manufacturing every year by providing the vaccine companies with vaccine reference strains, the so-called seed viruses, as the starting point for a large-scale manufacturing.

In addition, FDA supplies reagents that set standards for the manufacturers that determine the vaccine's potency. The number of vaccine doses produced is limited by the capacity of the manufacturers' production facilities, the availability of eggs, the yield of virus growth in the eggs, and the length of time the manufacturing continues into the season. Although it is possible for production to continue beyond the summer and into the fall, there is a substantial risk that late-season vaccine will go unused since the later vaccine is produced, the later it will be available to clinics.

Companies need to plan the amount of vaccine that they will produce well in advance of the flu season so they can secure the needed egg supply in which the vaccine viruses are grown. Production of annual flu vaccines takes about 6 to 9 months, and any disruption in the production schedule for any reason may lead to a delay in the availability of the vaccine.

Influenza vaccine supply issues are also critical for pandemic influenza preparedness since the pandemic vaccine supply is directly related to existing influenza vaccine manufacturing capacity. Many experts believe that the risk of a flu pandemic or a global epidemic is higher now than it has been in the past because of the spread of avian influenza in wild and domestic bird species across Asia. Since January 2004, 89 people, mostly young and otherwise healthy, have been confirmed by the World Health Organization to have been infected with the H5N1 virus, and 52 of them have died. And we heard of a new case reporting a death from Cambodia just this morning from the World Health Organization. The people who died were known to have died of this infection. We are concerned that should this virus develop the capacity to be easily transmitted among humans, either through a mutation or mixing genes with a human flu virus, a pandemic could result.

Ensuring the ability to meet current annual demand for flu vaccine, to improve prevention of influenza disease, and to prepare for a pandemic all require strengthening the flu vaccine supply in the U.S. Building on the response to the flu vaccine shortage last year, NIH and FDA have worked to facilitate the clinical evaluation of a flu vaccine produced by GlaxoSmithKline and to expeditiously develop the data base necessary to allow the company to apply for FDA approval in the coming influenza season.

Several additional HHS flu vaccine initiatives have been put in place to address our pandemic preparedness needs and will also help to achieve our annual influenza prevention goal. The objective of these initiatives are to secure and expand the U.S. influenza vaccine supply, diversify production methods, and establish emergency surge capacity. To support these activities, HHS received $50 million in fiscal year 2004 and $99 million in fiscal year 2005. The President's fiscal year 2006 budget includes an additional $120 million to further strengthen this component of overall pandemic influenza vaccine preparedness.

To enhance our Nation's ability to produce influenza vaccine at any time during the year, we issued a contract with Sanofi-Pasteur of Swiftwater, Pennsylvania, for $41 million. This has allowed the company to change the way it manages eggs, and they have already begun to change its flock management strategy to ensure that eggs are available year-round for the vaccine.

Diversification of flu vaccine production methods will also help to strengthen our system. Cell culture technology is a well-established vaccine production method for other vaccines such as the inactivated poliovirus, and two companies have registered their cell culture flu technology in Europe. This technology does not require eggs as a substrate, thereby avoiding the vulnerabilities associated with an egg-based production system.

Secretary Leavitt announced last month that HHS issued a 5-year contract to Sanofi-Pasteur for $97.1 million to develop cell culture influenza vaccine technology and conduct clinical trials with the goal of obtaining an FDA license for such a vaccine. Under this advanced development contract, the company has also committed to develop a plan to manufacture this vaccine at a U.S.-based facility that has the capacity to manufacture 300 million doses of monovalent vaccine over a 1-year period.

We have three additional areas where we believe strategic investments will move us toward achieving the annual and pandemic influenza supply goals. In addition to providing support for cell-based vaccines, we hope to further diversify vaccine technology by supporting recombinant pandemic influenza vaccines. We also are going to invest in production technology that will increase the efficiency of manufacturing and planing to support research and development of strategies that will stretch the number of vaccine doses produced by decreasing the amount of flu virus antigen that is needed in each dose.

While these are only the first steps toward the development of an expanded, diversified, and strengthened influenza vaccine supply, the U.S. is leading the global effort to develop vaccines and vaccine technologies to meet this challenge.

Thank you for your attention to this topic, and I look forward to your questions. Thank you.

[The prepared statement of Bruce G. Gellin follows:]

PREPARED STATEMENT OF BRUCE G. GELLIN, DIRECTOR, NATIONAL VACCINE PROGRAM OFFICE, OFFICE OF PUBLIC HEALTH AND SCIENCE, OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Chairman and members of the Committee, I am Dr. Bruce Gellin and I am the Director of the National Vaccine Program Office of the Department of Health and Human Services. I am pleased to appear before you today to discuss the U.S. influenza vaccination program and the role of the National Vaccine Program Office (NVPO) in strengthening U.S. influenza vaccine supply.

The National Vaccine Program Office was established in 1988 to improve prevention of disease through vaccination and to improve prevention of vaccine associated adverse events. NVPO has responsibility for coordinating and ensuring collaboration among the many federal agencies involved in vaccine and immunization activities. We have addressed this mission by communicating and coordinating with HHS' agencies, the Department of Defense and the US Agency for International Development, and through the National Vaccine Advisory Committee.

NVPO's mission is to:

- Coordinate and integrate activities of all Federal agencies involved in immunization efforts;
- Ensure that these agencies collaborate, so that immunization activities are carried out in an efficient, consistent, and timely manner;
- Develop and implement strategies for achieving the highest possible level of prevention of human diseases through immunization and the highest possible level of prevention of adverse reactions to vaccines; and
- Ensure that minimal gaps occur in Federal planning of vaccine and immunization activities.

The development, production and delivery of influenza vaccine every year underscores the complexities of vaccine production. Because they involve living organisms, developing and producing vaccines poses different challenges than drugs. In the United States, the protection of the population through vaccination depends on vaccines produced by private companies for profit as well as for public good.

U.S. Vaccine manufacturers are faced with substantial challenges including the costs and uncertainties in developing new products, limited returns on investment for vaccines compared with other pharmaceutical products, a regulatory environment that has high standards for safety and effectiveness, concerns about liability issues, and variable demand from one influenza season to the next. Consequently, the number of companies that produce licensed vaccines for the U.S. market is small and each type of vaccine is made by a limited number of suppliers. In many cases vaccines that we rely on in the U.S. are supplied by a single manufacturer.

Producing influenza vaccine has additional challenges. It is a vaccine that has to be redesigned and produced each year and delivered on-time to provide protection to tens of millions of people over a several month period in the fall in advance of the annual influenza season. The fragility of this system was clearly documented during the past influenza season, when one of the two large influenza vaccine manufacturers could not supply vaccine to the U.S. market. Recent years also have seen surges in demand and delays in the delivery of influenza vaccine creating mismatches between vaccine availability and enhanced demand resulting in de facto shortages.

While we are optimistic that an increased number of manufacturers are interested in the U.S. influenza vaccine market by, presently only three companies are licensed to sell influenza vaccine in the U.S.; two produce inactivated influenza vaccine while the third produces a live-attenuated vaccine that is delivered by nasal spray. All U.S. licensed influenza vaccines are developed from viruses that are grown in embryonated eggs in a process unique for influenza vaccine. Because of the tight time lines to produce influenza vaccine, the influenza vaccine manufacturers begin production of the following season's vaccine even before the FDA's Vaccine and Related Biological Products Advisory Committee meets in mid-February to review global influenza surveillance data and officially select the components—the virus strains—that are projected to be the predominant strains circulating in the U.S. during the following season. Both CDC and FDA contribute to influenza vaccine manufacturing by providing vaccine companies with vaccine reference strains—so-called "seed viruses"—as the starting point for large scale manufacturing In a rotating fashion, each of the three vaccine virus strains selected for the following year's

vaccine composition are adapted to grow in eggs and are injected separately into millions of fertilized eggs, which are subsequently incubated to allow the influenza virus to grow. These egg-grown viruses are subsequently inactivated, purified, tested for potency, blended into the trivalent vaccine, and filled into syringes or vials. The number of influenza vaccine doses produced is limited by the capacity of the production facilities, the availability of embryonated eggs, the yield of influenza virus from each egg, and the length of time that manufacturing continues. Companies need to plan the amount of vaccine they will produce well in advance of the influenza season so that they can secure the needed egg supply in which vaccine viruses are grown. Production of annual influenza vaccines, which contain three different influenza viruses, takes about six to nine months. Any disruption of the production schedule may lead to a delay in vaccine availability. Annual variation in the timing and severity of influenza outbreaks has resulted in significant fluctuations in demand for vaccine so that in some years supply is tight while in others, millions of vaccine doses go unused. Although it is possible for production to continue beyond the summer and into the fall, there is a substantial risk that late-season vaccine will go unused since the later vaccine is produced; the later it will be available to the clinics. Traditionally there has been little interest in "late season" vaccination—which in the United States is around Thanksgiving. .

Thus, the current fragility in influenza vaccine supply largely is related to:

- A limited number of U.S.-licensed manufacturers
- Uncertainty regarding annual demand and the ability to sell all vaccine produced
- An inability to stockpile trivalent vaccine for longer than a year due to annual changes in the influenza viruses that circulate and cause disease such that vaccine not used in one season is generally not useful the following year
- A solely egg-based production system that has limited flexibility and surge capacity
- Financial and other barriers, to development and U.S. licensure of new influenza vaccines, and
- Limited interest by most of the public and health care community in providing "late season" vaccination

The limitations and disruptions of influenza vaccine supply also must be put within the context of continued high rates of mortality and morbidity each year from influenza disease and the need to improve our prevention program. In 2004, Acting Assistant Secretary for Health, Dr. Beato, asked the National Vaccine Advisory Committee (NVAC) to assess the influenza prevention program and to make recommendations on how this program could be improved. NVAC recommendations to strengthen influenza disease prevention included:

- Improving our understanding of influenza vaccine demand—and why so many of those for whom annual influenza vaccine is recommended do not get vaccinated (e.g., persons > 65 years of age, pregnant women and even health care workers),
- Reviewing the evidence that would support further expansion of the groups recommended for annual vaccination;
- Implementing systems to better track the burden of influenza illness and the effectiveness of the vaccination program; and,
- Conducting a thorough review of the Department's influenza research program to identify gaps, and strengthening of cross-Department collaboration.

A sufficient and secure influenza vaccine supply is a prerequisite if we are to implement these recommendations and improve influenza disease prevention by increasing vaccination coverage and expanding groups recommended for vaccination.

Influenza vaccine supply issues also are critical for pandemic influenza preparedness since the pandemic vaccine supply is directly related to existing influenza vaccine manufacturing capacity. Many experts believe that the risk of an influenza pandemic—or global epidemic—is higher than it has ever been in the past because of the spread of avian H5N1 influenza in multiple wild and domestic bird species across much of Asia. Since January 2004, 88 people, mostly young and otherwise healthy, have been confirmed by the World Health Organization to have been infected with the H5N1 influenza virus, and nearly two out of three of people who are known to have been infected have died as a result of this infection. Should this virus develop the capacity to be easily transmitted among humans, either through a mutation or by mixing genes with a human influenza virus, a pandemic could result. Because H5 influenza viruses have not previously spread among people, the entire global population would be susceptible

We are all keeping a watchful eye on the current situation in Asia while at the same time recognizing that, in recent years, there also have been outbreaks of avian influenza infections and sporadic human cases caused by other influenza virus subtypes originating in Europe and in Canada as well as in Asia. A pandemic can

unpredictably occur, could be caused by an influenza subtype other than H5, and could originate in any country.

Ensuring the ability to meet current annual demand for influenza vaccine, to improve the prevention of influenza disease, and to prepare for an influenza pandemic all require strengthening the influenza vaccine supply in the U.S. Building on the response to the influenza vaccine shortage in the 2004-05 season, NIH and FDA have worked to facilitate the clinical evaluation of an influenza vaccine produced by GSK and to expeditiously consider a licensure application such that this influenza vaccine may potentially be licensed for the upcoming season.

Several additional HHS influenza vaccine supply initiatives have been put in place to address pandemic preparedness needs and will also help to achieve annual influenza prevention goals. The objectives of these initiatives are to secure and expand U.S. influenza vaccine supply, diversify production methods, and establish emergency surge capacity. To support these activities, HHS received $50 million in FY2004 and $99 million in FY2005. The President's Budget for FY2006 includes an additional $120 million to further strengthen this component of the overall pandemic influenza preparedness efforts.

Because influenza vaccine is produced to meet the seasonal demand in the fall, production also is seasonal and embryonated eggs have not been available to manufacturers year-round. To enhance our Nation's ability to produce influenza vaccine at any time during the year, HHS issued a five-year contract to Sanofi-Pasteur of Swiftwater, Pennsylvania, on September 30, 2004 for $40.1 million. Under this contract, Sanofi-Pasteur has already begun to change its flock management strategy to provide a secure, year-round supply of eggs suitable for influenza vaccine production at full manufacturing capacity. It also will increase the number of egg-laying flocks by 25% to provide contingency flocks in case of an emergency. These eggs may be used to support additional production of annual influenza vaccine in the event of a vaccine shortage with the doses being delivered later in the fall.

Diversification of influenza vaccine production methods also will help strengthen the system. Cell culture technology is a well-established vaccine production method for other vaccines such as the inactivated poliovirus vaccine and two companies have registered their cell-culture based influenza vaccine technology in Europe. This production technology does not require eggs as a substrate for growth of vaccine virus, thereby avoiding the vulnerabilities associated with an egg-based production system. It also may be more amenable to surge capacity production when influenza vaccine supply needs to be expanded rapidly such as at the time of a pandemic. Additionally, cell culture technology uses a closed system that dramatically reduces the possibility for contamination. Finally, the new cell-based influenza vaccines provide an option for people who are allergic to eggs and therefore unable to receive the currently licensed vaccines.

Secretary Leavitt announced last month that the Department of Health and Human Services issued a five-year contract on March 31, 2005 to Sanofi-Pasteur for $97.1 million to develop cell culture influenza vaccine technology and conduct clinical trials, with the goal of obtaining an FDA license for this vaccine. Under this advanced development contract, the company also has committed to develop a plan to manufacture this vaccine at a U.S.-based facility with a capacity to manufacture 300 million doses of monovalent pandemic vaccine over a one year period.

These important steps to strengthen our national influenza vaccine supply through assuring the egg-supply and diversifying and expanding production capacity will be followed this year by additional measures to increase influenza vaccine production capacity and expand the number of influenza vaccine doses made using that capacity. Supported by the pandemic influenza vaccine initiative in the FY 2006 budget request for $120 M, we posted synopses of three additional areas where we believe strategic investments move us toward achieving annual and pandemic influenza vaccine supply goals in the March 17, 2005 edition of FedBizOpps. On April 29, 2005, the first of these requests for proposals was posted, providing support for the development of cell-culture based and recombinant pandemic influenza vaccines. This contract, which we hope will lead to the licensure and U.S. production of a next generation influenza vaccine, will further increase production capacity and diversification of the manufacturing base.

Whereas building new influenza vaccine production facilities is an intermediate approach to expand the influenza vaccine supply, other strategies are more short term and expand the current vaccine capacity by increasing the efficiency with which influenza vaccine doses are produced. Influenza vaccine is manufactured in a series of steps—developing an influenza virus master seed for vaccine production, inoculating the virus into eggs, growing, harvesting, purifying, splitting, formulating, and filling it into vials or syringes. Improving efficiency at any step in this process can increase the eventual yield and number of vaccine doses produced. A

second RFP will be issued this spring and will support improvements of the manufacturing process to increase overall influenza vaccine production at current manufacturing facilities.

The third RFP that will be issued is to provide support for research and development, leading to licensure of strategies that will stretch the number of vaccine doses produced by decreasing the amount of influenza virus antigen that is needed in each dose. The concept underlying these "dose-stretching" strategies is that by changing either the influenza vaccine or the way it's administered, you may be able to improve the immune response to vaccination and provide protection while using less of the vaccine antigen. By using less antigen in each vaccine dose, the number of doses that can be made at any level of production capacity would be significantly increased. The two most promising antigen-sparing approaches are either to add an adjuvant—a substance that stimulates the immune response to a vaccine formulation, or administering the vaccine into the skin (similar to the approach used in a skin test for Tb) where large numbers of immune cells are located. Both strategies have been evaluated in clinical trials and have the potential to expand influenza vaccine supply several-fold.

The increases in the FY 2006 President's Budget request will support ongoing activities to ensure that the Nation will have an adequate influenza vaccine supply to respond better to yearly epidemics and to influenza pandemics. While issuing the requests for proposals and completing the contracts is only the first step toward the development of an expanded, diversified, and strengthened influenza vaccine supply, the U.S. is leading the global effort to develop vaccines and vaccine technologies to meet this challenge.

Thank you for your attention to my remarks this morning—and more importantly to the attention that you have paid to the prevention and control of annual and pandemic influenza.

I would be happy to answer any questions from the Committee.

Mr. WHITFIELD. Thank you.

Dr. Goodman, you are recognized for 5 minutes.

TESTIMONY OF JESSE L. GOODMAN

Mr. GOODMAN. Thank you, Mr. Chairman.

Mr. Chairman and members of the committee, I am Jesse Goodman. I am the Director of the Center for Biologics, Evaluation and Research for the FDA. I am also an infectious disease physician. I appreciate the opportunity to update you on our readiness efforts for the 2005 and 2006 and future flu seasons, and I am actually pleased to report continuing progress. I also want to assure the American public and yourselves that the safety, effectiveness, and availability of vaccines are among FDA's highest priorities.

Talking first about last season, flu vaccine is highly cost-effective and beneficial to the public, as many of you have emphasized. However, also, as we have emphasized in previous testimony, flu vaccine manufacturing is particularly complex and challenging, and the market is also very fragile, in part because of our successes. Increases in demand have been coupled by a decline in the number of manufacturers. As Dr. Burgess happened to mention also, this is something that we see in other sectors of the vaccine industry.

As you know, in October 2004, the British regulatory agency, the MHRA, suspended the license of Chiron, and FDA also concluded that the safety of the vaccine Chiron produced for 2004 could not be assured.

Now, I want to say that as soon as we learned this, really within hours, FDA worked with great urgency and in close collaboration with HHS and CDC and other components and with the private sector. We engaged them very quickly, and we obtained 5 million additional doses of U.S.-licensed vaccine, and this increased the supply last year to 61 million doses.

We were still concerned that needs could outstrip supply, particularly if we had a significant flu season, so we sought additional vaccine licensed in other countries with quality regulatory agencies that might be made available as investigational new drugs urgently. FDA immediately sent teams to the facilities of such potential sponsors. Our staff carefully evaluated their manufacturing processes and reviewed a large volume of manufacturing clinical data, and this was all done within just a few weeks. These efforts resulted in INDs that could have permitted the use of approximately 4 million doses of GlaxoSmithKline's vaccine and 1 million doses from Berna Biotech if they were needed.

The interactions with these and, in fact, other manufacturers have provided valuable information that is helping us now. They have stimulated interest in a number of companies in pursuing U.S. Licensure, and this is at least one constructive outcome of the challenges we all faced last year. I am very proud of the efforts and accomplishments of more than 50 FDA professionals as well as many HHS colleagues in working collaboratively for long hours on these challenges.

Well, what are we doing going forward? We, too, the last thing we want to see is this problem recur, whether it is this year or the future years, and we need to work both for this year and for future years. We are doing everything we can to improve flu vaccine for this coming season and in future years, and we are taking a dual-track approach.

First, because Chiron's correction of its manufacturing processes is a major factor, FDA is doing all we can to facilitate that effort. As Ms. Schakowsky alluded to the problem of information sharing, agreements have been put in place with both Chiron and MHRA that have allowed full sharing of information, and this has been extremely productive. FDA and MHRA collaborative reviewed Chiron's remediation plans, and these are extensive plans, and are providing ongoing feedback as they are implemented and as manufacturing activities startup. So this is a very rich, interactive relationship.

FDA and the MHRA, the British regulators, are working closely together and actively communicating also on inspectional activities. We accompanied MHRA on inspections of Chiron Liverpool in December of 2004 and again in February. We are continuing to coordinate with them on these inspectional efforts and plan a joint effort again right now; one is in the planning stages for the upcoming time period.

As a result of a great deal of progress at the Liverpool facility, as most of you know, the British regulators, MHRA, lifted its license suspension on March 2, 2005, allowing Chiron to proceed with manufacturing. To get an updated overview of some of these ongoing efforts, last week I met with MHRA leadership in London and I also visited Chiron's Liverpool facility to meet with their senior leadership team onsite. Chiron reported to me on their progress and specifically their progress in addressing the issues of concern including changes made at their facility, changes in their manufacturing process, and improvements in their quality systems.

Once Chiron has completed implementation of its key remediation measures and the critical stages of manufacturing are in full

swing and can therefore be adequately evaluated, likely in the late spring or early summer, FDA will conduct its comprehensive inspection to assure that Chiron has adequately addressed its problems.

It is too early to predict the final outcome of Chiron's remediation activities, but, nonetheless, I can say the company has made significant progress in a short time. However, there are great demands in applying the necessary changes that have been made to full-scale manufacturing in a very tight timeframe. So this is the challenge that remains.

Because of this, and because of the long-term issues that we have all discussed, FDA is simultaneously working on a second track. That track aims to facilitate greater capacity and diversification, an issue raised by Ms. DeGette, in the U.S. influenza vaccine supply. It is important to emphasize, though, that the demand for vaccine—the demand for the vaccine and other economic issues are really the primary factors here that determine whether a manufacturer will seek and maintain a license in a country, including the U.S., the strength of the manufacturing infrastructure in the United States, and the amount of vaccine that a manufacturer will decide to produce.

Some of the developments in those areas right now, Sanofi-Pasteur, as you know, has indicated that it can produce the same or more doses of its vaccine for the coming flu season. MedImmune plans to produce a similar amount of vaccine and is also performing studies that, if successful, may allow future further use of its vaccine in future years in additional age groups.

FDA, as Dr. Gellin mentioned, has informed manufacturers that it will consider new approaches to influenza vaccine licensing, such as accelerated approval based on surrogate markers like the antibody response that are likely to predict benefit. GlaxoSmithKline, as a result, has stated that in the near future it expects to submit a license application to FDA seeking accelerated approval of this influenza vaccine and that, if licensed, it should be able to supply 10 million doses for the 2005 to 2006 season.

But also we have challenged ourselves to identify other lessons learned, something identified by Congresswoman Baldwin, from this past year's influenza season to do whatever we can from our end to help prevent similar future problems. One that many of you are aware of is that we are now conducting inspections of flu vaccine manufacturers on an annual basis. This can't solve all problems, we can't manufacture the vaccine for them, but what it may do is allow earlier recognition and intervention, and perhaps in a preventive mode, when problems occur. We have completed additional information-sharing agreements with numerous foreign regulatory agencies focusing on ones where flu and other critical vaccine information sharing is important.

Finally, again mentioned by Dr. Gellin, in terms of the pandemic preparedness, we are extremely actively engaged with sponsors and manufacturers who are interested in developing new technologies, including cell-culture-based and recombinant vaccines. Although a lot of work remains to be done on these technologies, they provide important alternatives to egg-based production, and they may help

reduce the time requirements and certain risks of contamination inherent in egg-based production.

So, to conclude, we are doing everything we can in conjunction with other public health service agencies and industry to enhance the availability of flu vaccine both now and in the future. An adequate vaccine supply supplemented by effective antivirals can greatly decrease our vulnerability and provide protection against influenza. All the steps we have discussed will not only help protect Americans from flu every year but can help strengthen our infrastructure and its capacity and better prepare us for a pandemic, and we welcome the opportunity to work with you in Congress to accomplish these important health goals. So I thank you for having me to discuss this important issue, and I am happy to participate in answering your questions.

Thank you.

[The prepared statement of Jesse L. Goodman follows:]

PREPARED STATEMENT OF JESSE L. GOODMAN, DIRECTOR, CENTER FOR BIOLOGICS, EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION

Mr. Chairman and members of the Committee, I am Dr. Jesse Goodman, Director of the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration (FDA) and also a practicing infectious diseases specialist. I appreciate the opportunity to update you on FDA's recent and ongoing efforts, in collaboration with other Department of Health and Human Services (HHS) agencies and with the private sector, to address issues surrounding the influenza vaccine supply needs for the next flu season and to do what we can to help prevent the problems encountered last season from recurring. These efforts should also better prepare us for the next global influenza pandemic.

FDA is responsible for the regulation and oversight of vaccines in the United States. Vaccines are among our most important and cost-effective medical interventions, preventing disease in those who receive them and reducing the spread and risk of infections through our communities. I want to assure the American public that the safety, effectiveness and availability of vaccines are among FDA's highest priorities and that we work closely with DHHS, the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), as well as with manufacturers, in addressing this important area of public health preparedness.

THE 2004-2005 INFLUENZA SEASON

As you know, influenza vaccine is unique because its active ingredients—the virus strains used to develop the vaccine—change almost every year. Therefore, manufacturers must produce tens of millions of doses of a new vaccine each year. While promising technologies such as cell culture and recombinant protein and DNA-based influenza vaccines are in the research and development stages and we are working with our HHS colleagues to advance their development, the most efficient vaccine production methods currently available involve the use of millions of live, non-sterile eggs to grow three different strains of influenza viruses annually. This is a complex process that spans several months during which manufacturers cultivate the appropriate strains to make the vaccine. These factors present an enormous challenge for manufacturers and create uncertainty for vaccine supply.

Each year, FDA begins working with manufacturers at the earliest stages of vaccine development, and we continue to assist them throughout the production phase. We do this not only through our regulatory evaluations, but also by providing needed influenza strains and standards that can be used for efficient manufacturing. Specifically, we provide reagents to assure that the vaccine is potent and we further evaluate the vaccine through the use and review of laboratory tests that help assure the safety and efficacy of the vaccine. Throughout this process, FDA frequently discusses technical and manufacturing issues with manufacturers.

Influenza vaccine is highly cost-effective and beneficial to the public. Over the last decade, health care providers, CDC and others have been very successful in expanding the number of Americans who receive the vaccine. However, as we have empha-

sized in previous Congressional testimony, the influenza vaccine market is very fragile because the increasing demand has been coupled with a decline in the number of U.S-based and U.S.-licensed manufacturers. Importantly, the market returns for producing this and many other vaccines are usually minimal, while the financial and other risks involved are great. Further, vaccine manufacturing requires careful and comprehensive controls, a complex and sometimes unpredictable manufacturing process and highly specialized facilities that can be expensive to maintain and update. For the 2004-2005 season, only three U.S. licensed manufacturers began production of influenza virus vaccine: Chiron Corporation and aventis pasteur produced inactivated vaccine, the form currently used for most high-risk individuals, while MedImmune, Inc. manufactured FluMist, a recently-approved, live, attenuated (weakened and safe) influenza vaccine.

As you know, on October 5, 2004, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) suspended Chiron's license to manufacture influenza vaccine due to good manufacturing practice deficiencies that led to sterility failures in filled vials of the vaccine. FDA and MHRA's review of Chiron's investigation of the root cause of the company's sterility failures and our own review and inspections of their facility pointed to problems that led FDA to the conclusion that the sterility, and therefore safety, of the vaccine Chiron produced for the 2004-2005 influenza season could not be assured.

Efforts to Obtain Additional Vaccine

The loss of Chiron's planned contribution to the U.S. influenza vaccine supply posed serious challenges. FDA worked with urgency, aggressiveness and in close coordination with CDC and other components of HHS and the private sector to explore all viable options to secure additional doses. FDA worked with sanofi pasteur and MedImmune to secure approximately five million additional doses of U.S. licensed vaccine. Sanofi pasteur increased production to 58 million doses of Fluzone, and MedImmune scaled up to produce three million doses of FluMist. FluMist is currently recommended for healthy individuals 5 to 49 years of age, and therefore provides an option for those who would not receive vaccine under CDC's priority guidelines, such as the U.S. military. Therefore, to expand further the supply of vaccine to those with the greatest need, then-Secretary Thompson, in cooperation with the Department of Defense, announced that the military would maximize its use of FluMist as a substitute for inactivated vaccine, making an additional 200,000 doses of injectable vaccine available to HHS for high-risk civilian populations. Because sanofi pasteur produces pediatric dosage forms of vaccine for the U.S. market, the supply of vaccine available for high-risk children was, fortunately, not reduced. Through these collaborative efforts, manufacturers increased the available supply of licensed influenza vaccine for the U.S. population to 61 million doses for this past influenza season, compared with approximately 83 million doses distributed in 2003-2004 and in 2002-2003, 77 million doses in 2001-2002 and 70 million doses in 2000-2001.

Because there was a concern that the need and demand could still outstrip supply, particularly if we faced a severe influenza season, we sought additional doses of vaccine that could be safely used in an emergency. Thus, in addition to enhancing the supplies of vaccine approved for use in the U.S., we were able to rapidly identify suppliers of approximately five million doses of additional vaccine, licensed in other countries, which could potentially be made available under an FDA investigational new drug (IND) application. With remarkable cooperation from several companies and from other regulatory agencies (including the Paul Ehrlich Institute, Germany; Therapeutic Goods Administration, Australia; Swiss Medic and Health Canada) FDA immediately sent inspectors and scientists to the manufacturing facilities of potential IND sponsors to evaluate their manufacturing processes. Coupled with these efforts, we also reviewed a large volume of manufacturing and clinical data, all within a few weeks. These efforts resulted in INDs that would have permitted the use of approximately four million doses from GlaxoSmithKline (GSK) and one million doses from Berna Biotech, had they been needed. HHS and FDA's coordinated interactions with these and other influenza vaccine manufacturers and regulatory agencies also provided valuable information and strengthened relationships that helped stimulate interest by additional influenza vaccine manufacturers to pursue U.S. licensure. This is one constructive outcome of the challenges we faced this past flu season. I am very proud of the efforts and accomplishments of more than 50 FDA employees, from multiple offices, as well as our HHS and CDC colleagues, working collaboratively for long hours to help meet this public health challenge.

Efforts to Enhance Antiviral and Pneumococcal Vaccine Supplies

Following the loss of the Chiron vaccine, FDA also contacted manufacturers worldwide in an effort to identify additional supplies of antiviral medications that could be used, if needed, for treatment of millions of influenza cases and for prevention in high-risk individuals in epidemic settings.

Serious morbidity and mortality from influenza is often due to the complication of bacterial pneumonia. In particular, pneumococcal pneumonia is one of the most common serious complications of influenza in high-risk individuals. This complication is preventable through use of an inexpensive, yet underutilized, pneumococcal vaccine. The influenza vaccine shortage provided an impetus to increase the availability of vaccine against pneumonia. In cooperation with HHS, Merck & Company tripled its production of its pneumococcal polysaccharide vaccine from 6 million to more than 17 million doses. The beneficial effects of pneumococcal vaccine last for five to ten years, and CDC and other public health agencies strongly encourage its use.

PLANS FOR 2005 AND FUTURE YEARS

At the same time that we have addressed the past year's shortage by facilitating the availability of additional vaccine, antivirals, and pneumococcal vaccine, we are doing everything we can to help improve supply for future years. We are applying a dual-track strategy.

First, the most important single factor that will affect the status of the U.S. influenza vaccine supply for the coming year will be whether Chiron can correct its manufacturing problems at the Liverpool facility and supply vaccine for the U.S. market. To succeed, Chiron must implement extensive improvements needed to satisfy both FDA and the U.K. regulatory authority. We have come a long way since October 5, 2004, when MHRA could not legally communicate with FDA about its pending enforcement action.

After MHRA's suspension of Chiron's license to manufacture influenza virus vaccine at the Liverpool facility, Chiron gave MHRA and FDA permission to discuss information that could not otherwise be shared. This arrangement allowed free exchange of information as the company initiated efforts to address the problems at Liverpool. Then, on February 14, 2005, FDA signed a general information-sharing agreement with MHRA that, among other things, permits advance communication on important issues and not limited to Chiron's influenza vaccines. Chiron developed an extremely comprehensive remediation plan which has been undergoing implementation during recent months. FDA and MHRA reviewed and provided extensive input on this plan and the Agency continues to provide extensive feedback to both Chiron and MHRA.

FDA and MHRA are also working together and actively communicating on inspectional activities. For example, FDA accompanied MHRA on inspections of the Chiron Liverpool facility in December 2004 and February 2005, and has had very frequent interactions with both Chiron and MHRA concerning implementation of the remediation plan and start up of manufacturing activities. As a result of progress in the Liverpool facility, MHRA lifted its license suspension on March 2, 2005, which has allowed Chiron to proceed with manufacturing plans. FDA is continuing to interact intensively with both MHRA and Chiron as the company further institutes its remediation plan and begins to gear up for manufacturing.

FDA will continue to coordinate with and accompany MHRA on future inspections—one of which is currently in the planning stage. FDA will continue to provide MHRA and Chiron with feedback and information. Once Chiron has implemented all key remediation measures and critical stages of manufacturing are in full swing (likely in late Spring or early Summer), FDA will conduct a complete and comprehensive inspection of Chiron's Liverpool facility to verify that Chiron has adequately addressed its problems. Our continuing interactions with Chiron indicate the significant progress that has been made in a short period of time, but it is also clear that full scale manufacturing and all its associated challenges remain and will require continuing intensive efforts that will need to succeed under very tight time frames. Only after passing MHRA and FDA inspections will Chiron be able to provide vaccine for the U.S. market. Chiron's vaccine will have to meet all FDA-required standards, including sterility and other safety testing, prior to distribution to the public. While it is too early to predict the outcome of Chiron's remediation activities, Chiron is making continuing progress toward its goal of being able to supply vaccine for the US market for the upcoming season.

While working hard to facilitate Chiron's efforts to correct its manufacturing problems, FDA is also working on a second track to improve preparedness for this and future influenza seasons and facilitate greater overall capacity and diversification

of the U.S. influenza vaccine supply. It is important to recognize, however, that demand for vaccine and other economic factors are, and will, remain the primary factors that determine 1) whether a manufacturer will seek and maintain licensure, 2) the strength of the manufacturing infrastructure in the U.S., and 3) the amount of vaccine that manufacturers produce for the U.S. market. These factors also apply to other vaccines and the U.S. vaccine supply infrastructure in general. CDC and FDA are working to encourage extending vaccination throughout the flu season, including January and February. If such demand exists, manufacturers can increase total doses available by producing vaccine that becomes available during these months. Because influenza cases usually continue or peak well after the November-December time period when most people seek immunization, continuing vaccination is beneficial to recipients and should be encouraged.

MedImmune is performing studies that, if successful, may support future use of its vaccine in additional age groups. MedImmune has also stated that, if successful, it should be able to produce additional vaccine to support those needs. Sanofi pasteur has indicated that it has the capability to produce the same or more doses of Fluzone for the 2005-2006 influenza season as it did in 2004-2005. Greater influenza vaccine production capacity and an increase in vaccination rates are also critical for improving our preparedness for a global pandemic. In the event of a pandemic, we would need the capacity to rapidly produce a new vaccine and make it available to all who need it.

While greater production by currently-licensed manufacturers will enable us to meet some of these needs, recent events highlight the potential benefits of having more U.S.-licensed manufacturers. In recognition of this, FDA has been doing everything possible to stimulate interested foreign-licensed manufacturers to provide or, where needed, develop the safety and effectiveness data required for U.S. licensure. FDA has interacted constructively with several interested firms in this regard. FDA has informed manufacturers that it is willing to consider new approaches to influenza vaccine licensing, such as accelerated approval based on likely surrogate markers (e.g. the degree of antibody response to the vaccine), followed by post-licensure clinical effectiveness evaluation. The National Institute of Allergy and Infectious Diseases (NIAID) supported clinical studies of GSK's influenza vaccine. Thanks in part to that research, GSK has stated that it expects to submit the needed data to FDA to seek accelerated approval of its influenza vaccine for the U.S. market in the near future. GSK has stated that if its vaccine is licensed, it expects to be able to supply 10 million doses of vaccine in time for the 2005-6 season. ID Biomedical of Canada has also indicated interest in seeking accelerated approval for its influenza vaccine. It has stated that it expects to complete needed studies and submit a license application in 2006 and that, if licensed, vaccine would potentially be available in time for the 2006-7 season.

So, in preparation for the upcoming influenza season, we are continuing to do everything we can to facilitate both Chiron's remediation and GSK's licensure efforts so that these vaccines can potentially be available to help meet the 2005-6 flu season's needs. In either case, potential difficulties should become apparent during the summer. If it becomes necessary to obtain additional vaccine for use under an IND, the experience and relationships built this year through reviewing and obtaining vaccines licensed by other regulatory authorities will be helpful.

OTHER IMPORTANT ACTIVITIES

We have challenged ourselves to identify other lessons learned from this past year's influenza season and to examine how we can use our recent experience to help prevent similar problems in the future. For example, as I previously mentioned, we have identified the need to allow free flow of information between FDA and our international regulatory counterparts, and vice versa. We committed to do so and have now completed confidentiality commitments that allow such information sharing with regulatory agencies in the UK, Australia, Canada, the European Commission, Japan, Mexico, Switzerland, Singapore, and South Africa. We are also in final negotiations on an agreement with New Zealand. We are undertaking discussions with several additional European countries where vaccine manufacturing important to U.S. public health takes place. In addition, we are continuing to inventory foreign manufacturing to identify any additional information-sharing needs. We also plan to seek agreements with other national regulatory authorities where necessary. These commitments will help assure that legal barriers do not inhibit critical communication between these agencies and FDA.

As in past years, FDA will work closely with CDC, WHO and others to develop materials for standardization and evaluation of influenza vaccine for the 2005-2006 flu season. FDA will continue to identify and evaluate influenza virus strains suit-

able for manufacturing purposes and provide to manufacturers the high growth reassortant viruses they need to help to facilitate efficient, timely and adequate production of vaccine.

Recent events highlight the importance of FDA's technical support for the U.S. and global vaccine manufacturing infrastructure and the need for manufacturers to invest in more efficient, reliable and modern methods for producing influenza vaccine. With adequate supply and widespread immunization, we will be more likely to meet the challenge of annual influenza epidemics and future pandemics.

CBER has also initiated a vulnerability analysis of foreign manufacturing of U.S. licensed products that are critical to U.S. public health. This analysis will include other vaccines and help to identify areas where consideration of actions to support supply may be needed, such as stockpiling or seeking additional licensed manufacturers. In addition, in the hope that more vaccines can be licensed and available to multiple regions of the world, FDA has been working with our foreign regulatory counterparts and with manufacturers to enhance international communication with the goal of more efficient product development. We are also encouraging development of scientific and regulatory standards for safety, potency and effectiveness that will help achieve these goals. FDA serves as a designated Collaborating Center of the World Health Organization (WHO), and we work closely with our sister agencies at HHS and WHO on pandemic preparedness and responding to other emerging infectious diseases.

Under FDA's Critical Path initiative, we are working collaboratively with HHS agencies and the private sector to facilitate the rapid development, evaluation and availability of medical products and related manufacturing, safety and effectiveness standards. The rapid development and implementation of a West Nile Virus screening test for the blood supply provides a good example of the effectiveness of this type of a collaborative public-private approach to meet the threat of emerging infections.

To help manufacturers overcome challenges such as the problems Chiron is experiencing, FDA, under its current Good Manufacturing Practice for the 21st Century initiative, is working with industry to encourage the use of advanced technologies, quality systems and risk-based approaches that build quality into the manufacturing process. FDA is also using the same quality systems and risk-based approaches to modernize its manufacturing-related regulatory responsibilities. Recognizing that clarity and quality in vaccine GMPs is of increasing importance, CBER has planned increasing outreach in this area for the coming months, including international workshops and meetings.

The experiences of the past six months have taught us important lessons about manufacturing and inspectional activities with respect to influenza vaccine. The annual changes in the flu vaccine and the increased dependence on a smaller number of manufacturers highlight the risks of unexpected manufacturing difficulties. For these reasons, in 2005 and the future, we plan to inspect influenza vaccine manufacturers annually. Further, while FDA has always interacted extensively with influenza vaccine manufacturers throughout the vaccine production cycle, we plan additional interactions, including foreign regulatory agencies where appropriate, based on findings or events that raise concerns.

PANDEMIC PREPAREDNESS

HHS is working to help transform the influenza marketplace and reinvigorate the influenza vaccine infrastructure by investing in promising new technologies, securing additional licensed vaccines and medicines and preparing stronger response plans and capacity. Furthermore, the lessons we have learned and insights gained from recent experiences with influenza vaccine are critical in preparing for an influenza pandemic. This is something that FDA and others in the public health community are very concerned about, given the eventual likelihood of a pandemic and the recent outbreaks of avian influenza in Asia. More widespread vaccination during periods between pandemics not only has direct health benefits but also will increase vaccine production capacity and help America and the global community better prepare for an influenza pandemic.

As part of HHS' efforts to support pandemic preparedness, NIAID contracted for the production of pilot lots of potential pandemic vaccines from two licensed U.S. manufacturers. HHS contracted for the production of two million doses of vaccine against H5N1 avian flu, the influenza type of current concern in Southeast Asia. NIAID recently initiated critical clinical studies of the first H5N1 vaccine under INDs that FDA oversees, and both agencies will be working together to evaluate the results. While much work remains, these steps to produce and evaluate pandemic influenza vaccines are a critical component of our preparedness efforts. They will inform us about the needed dosing and schedule of pandemic vaccine and help pave

the way for evaluation and potential licensure and broader use of a vaccine against avian flu if needed.

In addition, NIH and FDA support studies to develop vaccine strategies that could lead to longer-lived immunity and the production of an immune response that could potentially allow one year's vaccine to better provide immunity for multiple flu seasons. FDA is actively engaged with sponsors and manufacturers interested in developing new technologies for influenza vaccine manufacture, including cell-culture based and recombinant vaccines. FDA has extensive experience in overseeing the development and licensure of cell-culture based and recombinant vaccines including those for prevention of other infectious diseases, such as chicken pox, polio, rubella, and hepatitis A and B.

FDA's goal is to support a process to produce pandemic influenza vaccine in the shortest amount of time possible and protect the largest number of people, using a vaccine that is safe, effective and easy to deliver. The full details of the draft Pandemic Influenza Preparedness and Response Plan are located on the HHS website at: http://www.dhhs.gov/nvpo/pandemicplan/annex5.pdf. Through all these efforts, and with enhanced global surveillance by CDC and its partners, we have the unique opportunity to effectively intervene and potentially blunt a global pandemic, should one occur.

CONCLUSION

HHS has proposed spending of $439 million Department-wide on influenza related activities in the FY 2006 President's Budget. This amount is an increase of $397 million over the FY 2001 level of $42 million, and represents the Administration's commitment to addressing this important public health concern.

Although we may never completely prevent influenza outbreaks, we can greatly decrease our vulnerability and provide protection against influenza with a robust vaccine supply supplemented by effective antivirals. FDA recognizes the need to continue to work with multiple partners, including manufacturers, to increase supply and to support progress toward more modern, dependable methods of production. All of the steps we have discussed will not only help protect Americans from flu every year but will help prepare us for future influenza seasons or in the event that a pandemic strikes. We welcome the opportunity to work with Congress to accomplish these important public health goals.

Once again, thank you for inviting me to testify on this very important issue.

I am happy to respond to your questions.

Mr. WHITFIELD. Thank you very much for your testimony.

I will start the questioning period here.

First of all, we are dealing with a very complex issue, when you consider the limited capacity, because I guess we only have two or three manufacturers that are licensed to sell in the U.S., the availability of embryonated eggs is limited, the yield of the influenza virus from each egg, and trying to determine the best guess of the three strains that should be intermixed to meet the needs for the following year.

I would like to ask you initially, you each represent three different departments in HHS. So, as you plan—could you explain to me briefly how you interact with each other? And is there a lead agency that, if something goes wrong, that the Secretary of HHS could come to this agency and say, I am holding you responsible because you are the lead agency in this projection? Could any of you—would each of you address the interrelationship between your departments on this issue?

Ms. GERBERDING. I think it would be fair to say that, collectively, HHS is accountable for this problem, but we each have specific responsibilities.

From a CDC perspective, it is our responsibility to identify strains that are emerging in this year's flu season at the end of the season that would best predict the vaccine strains that should be included in the following season. So we have the responsibility for getting those isolates, for characterizing them, for developing the

seed virus that can be used for vaccine, and then getting that to the FDA and to the manufacturers in time for them to work on getting the production started.

Mr. WHITFIELD. So you simply identify the strains and provide the seed virus?

Ms. GERBERDING. Correct.

Mr. WHITFIELD. And then the vaccine policy?

Mr. GELLIN. The National Vaccine Program Office, as I mentioned, was established in 1988 to do exactly as you suggested, was to keep the arms and legs of the Department of Health and Human Services going in the same direction on vaccine and immunization issues. I am in the Secretary's Office, and it is my job to keep everybody connected on this, recognizing that there are different missions of the different agencies of the Department. Missing from this table is NIH, who has another piece of this, and their research and development piece plays into this as well as broader issues about the future of influenza vaccine.

Mr. WHITFIELD. Then FDA, I am assuming it is your responsibility to make sure that the product is safe.

Mr. GOODMAN. Yes. Our primary responsibility is to meet the expectation of you and the American people that it is safe and effective and consistently and properly manufactured.

I will say, on flu vaccine, we go a good bit beyond that, as Bruce mentioned, in terms of providing strains from our laboratories, providing the reagents to the manufacturers to help them in manufacturing. Also, in the recent year, in response to this public health problem, trying to do what we can to facilitate additional people entering the market.

Mr. WHITFIELD. Now, last year when Chiron had their problem and we lost all of their dosages of vaccine, I understand that there was some constraints on obtaining information from the MHRA. Could someone explain to me specifically what the problem was?

Mr. GOODMAN. Well, MHRA viewed that under their laws for their regulatory body they could not inform anyone of their impending regulatory action until they took that action. So in fact they told us subsequently that they did not make the decision to suspend Chiron's license until October 4, the day before; and then all the rest is history. But they said subsequently that they felt like they could not inform us or any other regulatory body, WHO or others, until they had actually taken the action. So the steps we have taken are executing a high-level information-sharing agreement between MHRA and the FDA.

I will say we recognize that, if this problem occurred in vaccines, it could occur in other areas. So this is a rather global agreement between the agencies; and it has already been used, for example, by our drug center for sharing information about drug safety.

Mr. WHITFIELD. So, prior to October 5, FDA had no idea that there was a problem at Chiron?

Mr. GOODMAN. Oh, no, we knew there was a problem at Chiron. But the issue is that we did not know—of course, as I said, MHRA said they didn't make a decision to suspend the license until October 4. But we did not know of that decision or that that was on the map. We were working and receiving information about their contamination problem and their interpretation of that.

Mr. WHITFIELD. Recognizing that there is a multitude of new sources in the U.S., there was quite a bit of confusion among the public last year as a result of this shortage. I would like for each of you to give your views on the way in which the media or your Department handled communications to the public concerning the Chiron situation and whether you see any room for improvement in the way it was handled last year.

Ms. GERBERDING. I certainly think there is room for improvement. The challenge that we faced was starting out the flu season expecting to have the most-ever vaccine. So, in order to use it, we worked real hard to encourage the broadest number of people to seek vaccination, and that is what they were doing until October 5 when suddenly we had to backtrack and start delivering a very different message about only the highest-risked people getting vaccinated first.

Every year, whether we have an ample supply or not, we have a terrible time getting people to get vaccinated after Christmas; and we typically plan for a late season push. This year, flu actually peaked in late February. There was time for people in many communities to get vaccinated in January, and yet we simply could not get that done in many communities.

So what we are doing now is working on the science of communication, working with people trying to understand what do they think, what are they worried about, what would help, how can we be more effective in engaging clinicians, how can we be more responsive to their needs and be able to get them vaccine faster, all of the things that would help us communicate not just to the public but also to the clinicians and the suppliers of vaccines that have to make decisions in conjunction with their health agencies.

Mr. WHITFIELD. Do either of you have any comment on this communication issue?

Mr. GELLIN. I only want to add it is further complicated by the avian flu or pandemic flu, because we want to make sure that people have an understanding of each of them. At the same time, it is hard for people to often sort those out. I think there is special communications, particularly given the reporting on the avian flu and the concern that we all have about it.

Mr. WHITFIELD. Let me ask you, what manufacturers do you expect to produce flu vaccine for this year?

Mr. GELLIN. Well, the same three that are licensed we expect will be able to produce vaccine. Dr. Goodman has provided insight into his recent visit to the MHRA and Chiron facility.

In addition, I think that part of the lesson we learned from last year is that other manufacturers are interested in the influenza market in the United States. GSK particularly is seemingly the farthest along, and there is a hope that the data that has been assembled will allow them to get a license for a vaccine for this coming year.

Mr. WHITFIELD. But we do expect that Chiron will be on line, correct?

Mr. GOODMAN. Well, I should be clear there. You know, as I said in my statement, I think it is too soon to tell. What I did testify to is I think they've put into place and made substantial progress in a very aggressive, comprehensive remediation plan that deals

with their manufacturing and quality control issues. So what we are seeing is a lot of change, a lot of change in the right direction.

But, also, as I mentioned, the rubber has to meet the road. They are going to have to go soon into their full-scale manufacturing, and then we are going to go in there, and our inspectors and scientists will do their job and evaluate whether the remediations they have put into place have been effective. So I think things are in a positive direction, but it is too soon to tell. So we do need to be prepared for all possible contingencies.

Mr. WHITFIELD. One other comment on this communication. I know within a week of the October 5 announcement about Chiron, there are around 12 different agencies within HHS that do have some responsibility for the flu policy, and within a week no fewer than five agencies, including the Secretary, weighed in through the press on the topic of the flu vaccine supply. And with those five different messages coming, there was confusion out there, and we are concerned the public might not know really who to listen to. It would seem it would make some sense if possible to try to coordinate these agencies on press releases in the future. I am assuming you all would not disagree with that.

Mr. GOODMAN. I agree. I think I did see—just having been there when a lot of this was happening, I am not questioning whether some of that happened, but I do know that among those sitting at the table, for example, there was quite a bit of coordination under very tight timelines and challenging circumstances. But I think you have a very important point, and Bruce and Julie are really the lead on this. We should coordinate our communication as well as we can.

Mr. WHITFIELD. My time has expired. I recognize Mr. Stupak.

Mr. STUPAK. Thank you, Mr. Chairman.

In listening to the answers and the one question the chairman asked about how you all do parts of it to get ready for the flu vaccine, it seems like you try to identify the strain you expect, you provide the eggs, or at least the seeds for it, and really the impression I got, and correct me if I am wrong, then when you tell the manufacturers, here is what we need, they just manufacture it, right? There is a lot of preparatory work done by you all beforehand, right?

Mr. GOODMAN. The only thing I would add, sir, is that they then take the seed strains that we provide them, and they have to see how that performs under real-scale manufacturing conditions.

In certain years, even when everything goes well, we might have a strain that just doesn't grow that well. So they sort of take these tools, but then they are the experts at industrializing it and producing the vaccine.

Mr. STUPAK. You give them the seeds, but they are the so-called production experts?

Mr. GOODMAN. Right.

Mr. STUPAK. Okay. What does an average price per dose of the flu vaccine cost? Does anyone know? You tell us it is going up 17 percent next year.

Ms. GERBERDING. The average price of the flu vaccine depends on whether it is purchased by the government for government use or in the private sector. It has continued to evolve over time, and it

varies depending on the product. We can get you the historical price list over time.

Mr. STUPAK. Do you expect the government's pricing to go up 17 percent?

Ms. GERBERDING. I think that those contracts are under negotiation right now, so I am not sure we know exactly what the price is going to be.

Mr. STUPAK. Here is the part that bothers me, and, Dr. Gellin, looking at your testimony on page 8, you talk about that HHS received $50 million in fiscal year 2004, $99 million in 2005, and 2006 includes an additional $120 million. If we are spending all this money to strengthen it and make it more available and accessible to people, why is it going up? That is just my quick math here. That is a couple hundred million dollars in less than 2 years. Why would the price suddenly go up?

Mr. GELLIN. Let me clarify. Those expenditures are specifically directed for pandemic influenza preparedness, to get around the vulnerability.

Mr. STUPAK. You are still going to need a flu vaccine, right, and you prepare for both each year.

Mr. GELLIN. Except what we are really concerned with it is the capacity, the global manufacturing capacity. The global capacity for influenza vaccine is only 300 million doses a year, and therefore, among the things we are trying to do are to make investments and to provide incentives for manufacturers to go down roads that they might not otherwise go down.

Mr. STUPAK. If you make those investments and provide incentives for manufacturers to get into business, it should actually stabilize or lower the price for vaccine, shouldn't it?

Mr. GELLIN. I can't speak to the pricing, but I can speak to the fact that what we are asking them to do is a broad R&D program and investment in facilities, ultimately so that there is production in the United States, because we are concerned about that. That is a long-range strategy.

Mr. STUPAK. With the investment of all this money, we are really in no different position than we were last year.

Mr. GELLIN. The investments are for our future investments in pandemic preparedness for vaccines that are promising, but aren't there yet. We are trying to move them along faster.

Mr. STUPAK. But we are in no better position than we were last year. In fact, we are in worse shape now than last year. Last year at least we had three licensed, until October 5, and then we dropped the two, and the status of it now is we have two licensed, and Chiron hopefully will be relicensed to produce flu vaccine, right? So what has changed since last year, other than our suppliers have gone down by one?

Mr. GELLIN. Again, let me just clarify these expenditures are long-term investments and not responding to last year.

Mr. STUPAK. My final question was we are actually in worse shape than last year, because last year at this time we had three suppliers. Right now we have got two and one suspended. So if you look at it, we actually have less suppliers or manufacturers of flu vaccine than we did at this time last year, correct?

Mr. GELLIN. Dr. Goodman has commented about the remediation program of Chiron. I think the other lesson we learned from last year is that there are additional manufacturers interested in the market. GSK is an example of that.

Mr. STUPAK. Where is that? GSK hasn't even applied for a license yet, right?

Mr. GELLIN. I will let Dr. Goodman address that.

Mr. GOODMAN. I understand your concern, but they are actually engaged in a very active development program, and they have stated publicly that they plan to submit a license application to FDA in the very near future, and in time, that if the data are good in there, and we review it and approve it, that they would be able to bring vaccine for this year. So I do think that is at least on track.

Another point——

Mr. STUPAK. But it is not a manufacturing license. And when is the drop-dead date that Glaxo can get their license and still be ready by the flu season this year?

Mr. GOODMAN. One of the pieces that is relevant to that to share with you that is good news there is they are a global manufacturer. They are engaged in producing vaccine and are licensed. So they are going to go ahead and produce vaccine no matter what. So the issue is——

Mr. STUPAK. Flu vaccine no matter what. But that is for Europe. They have to be licensed to bring that flu vaccine to the United States, and they haven't even applied for a license yet.

What is the last possible date they could apply for a license and be ready for this flu season here in the United States?

Mr. GOODMAN. I think they could be licensed by us at any time before they distributed the vaccine, and if they are licensed, that vaccine could be distributed here. Then, as I said, as far as we know, they are on track for their plan of submitting an application to us very soon.

Mr. STUPAK. So if they manufacture 10 million doses, that doesn't necessarily mean they will be licensed and used here in the United States?

Mr. GOODMAN. No, if they don't meet our safety effectiveness standards or are unable to submit their application.

Mr. STUPAK. So what is the date when they have to meet your manufacturing standards and be licensed so they are ready to go by this flu season? Because, doctors, there is no difference; in fact, we are in worse shape now than we were last year. So what is the drop-dead date?

Mr. GOODMAN. As I said, vaccine is typically delivered in the fall, so my view would be as long as they succeed in their license application before the fall, they could bring vaccine to the U.S. market.

Mr. STUPAK. I heard a couple of ifs there. The part bothering me is going back to the statement found in Dr. Gellin's statement, it says, "Companies need to plan the amount of vaccine they will produce well in advance of the influenza season so they can secure the needed egg supply in which vaccine viruses are grown. Production of annual influenza vaccines, which contain three different influenza viruses, takes about 6 to 9 months."

If the flu season is October 5, since that seems to be the date we all got in trouble last year, that is like 5 months from now. So if you are 6 to 9 months, we are lessening that window period.

Mr. GOODMAN. I understand your concern. Again, to be helpful in addressing it, what I could point out is they are producing that vaccine. So their plan is to produce it irregardless of our license or decision. They are producing it at risk.

Mr. STUPAK. You are right, because they can produce all they want, but if it is not licensed in this country, it couldn't do us any good. GlaxoSmithKline can do 100 million doses, but if it is not licensed for use in this country, it does us, the American people, no good, correct?

Mr. GOODMAN. You are correct.

Mr. STUPAK. Let me ask you this: Exactly what would an expeditious licensure by the FDA be if Glaxo decided to enter the market, 6 weeks, 3 months, 6 months? What is expeditious?

Mr. GOODMAN. You mean the time from when we receive their application to the time they approve it or don't approve it? I think that what I can say about that is, again, we have made a commitment that if we can get a high-quality application with the data in it that supports the safety and effectiveness of the vaccine, that we would be able to review that, and, if the data support approval, approve it before the flu season.

Mr. STUPAK. How long will it take, 3 months to approve it, 2 months to approve it?

Mr. GOODMAN. I think it depends on whether—you know, we are doing a scientific job there. It depends on what the data show, whether there are any concerns raised and we have to ask the company additional questions, et cetera. There is some positive information there in terms of they were one of the firms that we interacted with and inspected back in October-November to try to get IND vaccines. So they are not starting from a zero knowledge base.

Mr. STUPAK. The answer would depend upon the quality of their application, right?

Mr. GOODMAN. The quality of the application.

Mr. STUPAK. Scientific data with it?

Mr. GOODMAN. Absolutely.

Mr. STUPAK. Then do you have to do a full-scale investigation as to their manufacturing safety?

Mr. GOODMAN. We were there last year, but we would again go, and the American people expect us to review their manufacturing. We would do that expeditiously also.

So you are correct, there are ifs there. I wouldn't want to promise something that basically is a scientific process.

Mr. STUPAK. Sure. I am just trying to get some kind of timeframe here.

Dr. Gellin, the committee staff talked to the British counterparts. They mentioned that Britain did not rely on just one or two manufacturers for their influenza vaccine like the U.S. Does. That was a problem we had last year, but the situation again is exactly the same.

Sanofi will be the supplier of at least 75 percent of our flu supply if we get the 80 million doses normally consumed, and Chiron will

supply most of the remainder. It looks like the situation will not change in the near future. So what are you doing at the policy level to sign up new suppliers, or are we still at the mercy of the market?

Mr. GELLIN. Our goal, I think, beginning last year was to try to have a better understanding of the market and particularly what was going to be the incentives for new companies to come into this market.

Mr. STUPAK. So what are those incentives?

Mr. GELLIN. As Dr. Gerberding mentioned, the incentives there is increased demand, there is increased interest in the product, and the price has gone up substantially to make it a more interesting market for them.

Mr. WHITFIELD. The gentleman's time has expired.

At this time I recognize the chairman of the full committee for his question period.

Chairman BARTON. Thank you.

How many flu shots did we end up giving to American citizens this flu season?

Ms. GERBERDING. We gave approximately 57 million.

Chairman BARTON. Fifty-seven million. As it turned out, everybody who really needed one got one; isn't that right? At the time we thought there were going to be a lot of people that wanted them that couldn't have them?

Ms. GERBERDING. Let me distinguish need and want. From our perspective as doctors and public health officials, we believe that about 185 million people need a flu shot, because the science says they would have a serious benefit from it.

In terms of the number of people who want flu shots, that seems to be influenced by concerns about scarcity and concerns about the severity of the season. About this year 57 million people wanted a shot.

Chairman BARTON. What is the most inoculations we have ever given?

Ms. GERBERDING. Eighty-three million in the year that we had a supply of about 87 million doses.

Chairman BARTON. When was the 83 million?

Ms. GERBERDING. That was in 2002-2003 flu season. I should add that in every single flu season, regardless of how much we have, we always end up wasting somewhere between 4 to 12 million doses of vaccine that manufacturers produce but people didn't want.

Chairman BARTON. Given everything that you all have done in the last year to prepare for next year, and you are continuing to do, what is the most probable number of flu shot vaccination doses that are going to be available in the coming flu season?

Ms. GERBERDING. We have to plan for all three scenarios. We have to plan for the scenario where we don't get these licensed products here and available for us, so we will have about the same amount of vaccine that we had last year; we have to plan for the scenario where we might have the most ever, if everybody produces and brings their vaccine to market here; and, of course, as a backup, we have to plan for sort of the worst-case scenario, that something goes awry with our primary suppliers.

Chairman BARTON. Give me three answers then. Worst case. What is the minimum number?

Ms. GERBERDING. Well, the worst-case scenario, I would say, is we would have somewhere around 53 million doses.

Chairman BARTON. So the worst case is a little bit less than last year. What is the best case?

Ms. GERBERDING. Probably around 98 million doses.

Chairman BARTON. Ninety-eight million, which would be more than we ever used.

Ms. GERBERDING. Correct.

Chairman BARTON. What is the most probable case or the mid-term case?

Ms. GERBERDING. I can tell you what the middle-range scenario is. That is 75 to 83 million doses.

Chairman BARTON. Unless we have a worst-case outcome, this committee can be reasonably confident that every American next year that really needs a flu shot is going to be able to obtain one? Is that a fair statement?

Ms. GERBERDING. That is not quite true. Again, it is the difference between needing and Americans who want a shot.

Chairman BARTON. The most we have ever given was 83 million. Last year we gave 53 million. You just said the most probable case is in the 70 to 80 million range. So probably everybody on this panel up here needs a flu shot. I am not going to ask for a show of hands, but I didn't get one last year, because if I had, I probably would have been accused of favoritism. Since I have never had a flu shot, I figured I could go 1 more year without getting one.

Ms. GERBERDING. Maybe you would like to talk to me later.

Chairman BARTON. If you talk about need, I am probably at the top of the list of need.

What we don't want to do is go through another year like last year where at the beginning of the flu season there are all these press stories that there is a shortage, and that you kind of have panic vaccination mode. And then in the middle of the flu season it turns out we have got more doses available, and that is to the credit of you three, that you went out, and the Secretary of HHS went out, and we talked to our friends overseas, did a lot of good work and got more doses. So it turned out to be not as bad as we had thought. As people who get elected, we don't want to go through this feast and famine in the middle of a flu season.

So this subcommittee, the reason of this hearing is to find out what you are doing different from last year, what the prognosis is for next year, and whether we need to really, really, really do aggressive oversight. If your midcase estimate is right, I am going to assume that things are in reasonably good shape, and we need to monitor it and touch base with you, but most Americans are going to be able to get a flu shot next year. If I am wrong in that assessment, this is the time to tell the subcommittee that, and if we need to do something legislatively or in the appropriations process or encourage some sort of negotiations overseas, now is the time to do it.

Ms. GERBERDING. Let me emphasize two things. One is that the highest priority is to get those vulnerable people vaccinated. Right now, even under the worst-case scenario, we would be able to come

close to having the amount of vaccine we did this year, and we will know that at the beginning of the year. So we do feel like our most vulnerable people will have a pretty good chance of getting a vaccine.

Chairman BARTON. Do the other two witnesses share that assessment?

Okay.

My last question: If I need to call one person and get the straight answer on some of these issues, and we got three of you, but my assumption is that one person would be the Secretary of HHS, Governor Levitt. Is that the person I should call, or is there somebody else?

Ms. GERBERDING. I don't want to speak for the Secretary. He obviously is very engaged and very up to speed on this. I am sure if you called him, he would either give you the straight answer immediately or send you to one of us.

Chairman BARTON. Who would you call?

Ms. GERBERDING. I would probably call him, too.

Chairman BARTON. Okay. What about the other two? Is that who you would call?

Mr. GELLIN. Well, he calls me pretty often about these same issues.

Chairman BARTON. He calls me, too.

Mr. GELLIN. That is where it all gets put together.

Chairman BARTON. You agree with that?

Mr. GOODMAN. I think that is appropriate.

Chairman BARTON. Thank you, Mr. Chairman.

Mr. WHITFIELD. We have a vote on the floor. We still have 12 minutes to go. I am going to recognize Ms. DeGette.

Ms. DEGETTE. Thank you so much, Mr. Chairman. I just have a few questions.

I am wondering, we have been talking about GlaxoSmithKline entering the market, and they are not licensed, and are all hoping they will be licensed. What backup plan do you have in place if they are unable to provide the expected 8 to 10 million doses?

Ms. GERBERDING. There are two backup plans. One is the one I mentioned about the scenario planning, so we are planning as if we couldn't get that vaccine, and that is why we are going to start focusing vaccination early in the season on the high-risk people and letting other people know that if everything goes right and we have the vaccine supply we think we are going to have, we will make clinics available for other people later in the season.

The second backup is what we refer to as the insurance plan, and that is we have in the proposed budget $30 million so we can buy monoviral bulk vaccine from any one of the manufacturers that would be available to us, either as a licensed product or as an investigational product, that can be then brought into dosage forms if necessary if everything else fails. It is not the ideal backup, but it is a way for us to expand our market even further beyond Glaxo, beyond Chiron, into anybody in the world who manufactures flu vaccine.

Ms. DEGETTE. Why is that not ideal?

Ms. GERBERDING. Because it is investigational, and it means we would have to get consent from people to be able to use it.

Ms. DEGETTE. It also seems like it could make people really nervous and even more upset than they are about the real liability.

Ms. GERBERDING. It is insurance. It is the backup to the worst-case scenario.

Ms. DEGETTE. Well, let me ask you this: I am still concerned that pharmaceutical companies, as I mentioned in my opening statement, are not motivated to manufacture vaccines, and I am wondering, maybe from you, Dr. Goodman, what we could do to improve this situation?

Mr. GOODMAN. Well, I think it is an important question, and it is something we need to pay a lot of attention to. I think recognizing in pricing and purchasing and in our health care system the public health value of some of these interventions can be very helpful.

Ms. DEGETTE. I don't know what that means. Does that mean we should let them charge higher prices or what?

Mr. GOODMAN. Well, you know, we at FDA don't get into the pricing issue at FDA, but what I will say is in terms of the public health benefit, if we look at the prices charged, if we look at prices that are paid for various things in terms of public health benefit, vaccines are often very cost-effective.

One comment I was going to make, although we have identified serious problems and fragility in the vaccine infrastructure, and you are very concerned about that, there are some positive developments, too. People are making new vaccines against human papilloma virus, which causes human cervical cancer. We have had the first "blockbuster" vaccine, pneumococcal vaccine against pneumonia in children, which has huge sales every year. So a number of companies are actively engaged in developing new vaccines in the vaccine market.

Ms. DEGETTE. But if the FDA's job isn't to get involved in figuring out the public good versus the pricing, then it seems like we are acting at odds against the public interest, because if prices of these vaccines go up, fewer people will have them, and then when we have our pandemic or whatever, it is going to be worse. It seems to me there have to be other ways to incentivize the economical and widespread manufacture of vaccines from a public interest standpoint. This is not about can the pharmaceutical companies make a profit on vaccines, it seems to me.

Mr. GOODMAN. No, I agree that is an important area. For example, in flu vaccine, I know CMS in recent years has, to some degree, done this by its reimbursement policies, and that has affected flu vaccine use.

Ms. DEGETTE. Is that something we should continue to look at, that policy, Dr. Gellin?

Mr. GELLIN. Absolutely. I don't have the numbers in front of me, but that has gone up dramatically as far as reimbursement costs of those. I think we can get into that a little bit here, but maybe we can have a separate opportunity to talk about the vaccine industry at large.

I think, as I mentioned, the flu vaccine is somewhat of a special case, but I think some of the things going on and the awareness that we have of a number of companies that manufacture influenza vaccine and are interested in the U.S. market gives us promise

that some of those pieces will attract additional manufacturers to the marketplace.

Ms. DEGETTE. Mr. Chairman, I think this would be a ripe issue for a future hearing.

Ms. GERBERDING. May I just add that the flu vaccine is actually the lowest priced of any of the vaccines that we routinely recommend.

Ms. DEGETTE. As it probably should be.

Ms. GERBERDING. We have to say why wouldn't a manufacturer be in the market that should be selling 185 million doses? One issue is that they are not confident they can get a fair price. Another issue is it is tremendously risky.

One of the things that I think Dr. Gellin referred to earlier that I don't want to be lost on the committee is the fact that the Department has provided hundreds of millions of dollars to the manufacturers to say, please modernize your vaccine production. Let's get out of eggs into cells. Let's move forward and build some plants. Let's get the show on the road here. So they have been providing these incentives to move this forward.

Ms. DEGETTE. What is happening with that process?

Ms. GERBERDING. Those contracts, the most recent round was just announced, I think, last week.

Ms. DEGETTE. Is it working?

Ms. GERBERDING. Science takes time, so it will be a while before the actual research and development gets to the point where we have a product, and not before flu season this fall, I am absolutely certain of that. But it is an important step. For the government to incentivize this kind of R&D in a very targeted way, I think, is the appropriate step, and I am glad we are able to do that.

Ms. DEGETTE. I just have one more question. Dr. Gerberding, you were talking about this throughout the afternoon. Part of the problem last year, and it is going to be a problem if we have limited supplies again in the fall, is this whole issue of the people who should get the vaccine don't get it. This happened last year where we had a shortage, so a lot of the target population didn't realize they were the target population, they didn't get it, and then as time goes by, they just sort of forget.

I am wondering if you can supplement your answers by providing for the record some kind of plan for how you are going to reverse that thinking. Just saying you want to reverse it, you know, that is not going to solve the problem next year.

Ms. GERBERDING. We will be happy to provide that.

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

Mr. WHITFIELD. We have 5 minutes left to go cast a vote, and then we will have one more vote, which we will vote on immediately. So we are going to recess this hearing. We will be back here in 10 to 15 minutes. We will recess for 10 to 15 minutes.

[Brief recess.]

Mr. WHITFIELD. We will reconvene the hearing. I will recognize the gentleman from Texas for his questions.

Mr. BURGESS. Thank you, Mr. Chairman.

If I might just back up a little bit. I know Mr. Stupak asked the question about the cost per influenza vaccine, and I don't know

that I actually heard the number. Can you tell me that, Dr. Goodman or Dr. Gerberding?

Ms. GERBERDING. What I have is the catalogue price. So for a multidose vial of the Sanofi Pasteur vaccine in 2005, the catalog price is $9.95. For the thimerosal-free syringe, a half millimeter is $13.25. The MedImmune single dose is $24.50.

Mr. BURGESS. Okay. I know you went through, Dr. Gerberding, a scenario of the various numbers of the flu vaccine that were used when the chairman asked the question, but what is the greatest number of doses that the market can handle in a given year? Is it that upper figure, that 83 million doses are the highest that have ever been given?

Ms. GERBERDING. The most doses that have ever been purchased was the 83.1 million.

Mr. BURGESS. Is that the upper limit for the market?

Ms. GERBERDING. No, I don't think so. That number was used in a year when we had not yet made the recommendation about immunizing infants, and the number of infants to be included is approximately 6.5 million more. If we got 50 percent of those, that would increase that.

We are also working harder and harder on some of our hardest-to-reach risk groups, like children with other medical conditions that makes them especially vulnerable to influenza, and all the time more data are being scrutinized by our scientists and our advisers that might expand the market indications even further as we learn.

For example, it is possible in the future we may learn for all children there is an advantage to immunization. It may be less days missed from school or less days missed from work for their parents. But those are the kinds of questions emerging in our research portfolio on an ongoing basis. So it is not a static situation, it will evolve over time.

Mr. BURGESS. Very well. Since you brought it up, I wasn't going to say the word thimerosal, but you brought it up. Will the cost for that thimerosal-free syringe, are we reimbursing the manufacturer at a rate where they can make a profit on that?

Ms. GERBERDING. I really can't speculate. I would assume so, because they wouldn't do it if they didn't find it to be a profitable enterprise. But I would have to defer to their economists to answer that question.

Mr. BURGESS. But there aren't that many of them doing it. Now, with thimerosal-free vaccine, is that pretty much what everyone has gone to?

Ms. GERBERDING. The Department and the CDC have recommended for several years now that all vaccines for children be free of thimerosal as a preservative, and manufacturers have done that with all other vaccines.

The current flu vaccine manufacturers are converting over to be completely thimerosal preservative-free, and I believe the GlaxoSmithKline product that is in the pipeline is being formulated that way to start out with. So in a brief period of time, I believe the manufacturers will be utilizing vaccines that do not contain thimerosal as a preservative.

Mr. BURGESS. For all of us, for adults and children alike?

Ms. GERBERDING. The issue is if you are using a vial of vaccine that has more than one dose in it, it needs to have a preservative.

Mr. BURGESS. Very well. Now, last fall when I wasn't on this committee, but I was on the Government Reform Committee, and you testified in front of that committee, we talked a little bit about the ability to dilute the vaccine that was available. Were there any studies undertaken last fall with diluting the available flu vaccine stocks to try to extend them further?

Mr. GELLIN. I am not certain. I think I need to get back to you. The Defense Department may have participated in a study like that. We will get the facts back to you.

Mr. BURGESS. So at this point no data is available. If we come up against another crisis, Mr. Stupak is concerned that nothing has changed from last year. But one thing that might have changed is we might have some data on what happens if we dilute the vaccine in the more healthy of the population and extend our vaccination range that way.

Mr. GELLIN. Recognizing that we would have to then apply—if it was last year's vaccine, it would have to make the link between next year's vaccine as well. But I think that is the case.

Mr. BURGESS. Dr. Goodman, when we heard the testimony last year on the Government Reform Committee, the contaminating agent, I was told, was a bacteria called Serratia, which is not a very pathogenic organization and one that likes to live in water baths and so forth in labs. Do you know where the Serratia came from that contaminated the vaccine last year?

Mr. GOODMAN. There is not a definitive answer to that question. It was clearly an environmental problem in the facility. I believe that we feel it was introduced in the environment most likely at steps involved in not the initial growth of the vaccine, but the formulation, and it points out the importance of environmental control in this kind of facility.

Mr. BURGESS. Are there any procedural changes that have been undertaken to avoid this happening again, or is that all depending upon getting away from the egg-based system to a cell-based system?

Mr. GOODMAN. No, there are quite a number of steps in terms of the manufacturing process that in this case Chiron has improved to reduce the risk of that kind of problem. These problems—I should state you are correct in asking about egg-based vaccines in general. These kind of problems, the egg-based production is more prone to them. But what is needed then is the testing and quality system in place to, if problems occur, promptly identify, isolate it, and assure it doesn't affect your general production.

Again, quite a number of the steps that were proposed in their remediation address exactly this kind of issue; keeping the clean areas clean, assuring prompt and proper action when problems are detected, and handling the process in a way that is as aseptic as possible.

Mr. BURGESS. When you say when problems are identified, taking prompt action, what type of action? Would that be to sequester that part of the lab or that batch of vaccination?

Mr. GOODMAN. There could be many different kinds of problems detected, and the responses might be different. Let's say, for exam-

ple, vaccine manufacturers do frequently and carefully monitor the environment in which manufacturing is performed and look for excursions that suggest problems with control of the environment. When you find those, it is important to act quickly, investigate the cause and prevent further problems. That would be one example; then certainly if you note this in a product, very promptly investigating and trying to understand, by looking at safe samples, looking at the process that occurred, where did that occur, and do we understand that that is isolated and that the other lots are acceptable.

Mr. BURGESS. Again, I would just point out, that might be one other thing that would fall into the broad category of what has changed since last year when we found we didn't have enough vaccination.

Let me just state for the record that I did not take a flu vaccine last year. The only people that were concerned about it were CNN, but they did seem to be very interested if I did have a vaccination. I didn't. If it will help you, Dr. Gerberding, I will take one this year. But you tell me if it is okay. I will wait for your word.

In the brief time I have left, I will ask Dr. Gerberding, you have described several scenarios for us, best-case, worst-case scenario. Do you have in mind, and I don't mean to get too far into the science fiction aspect, but do you have an idea of what the pandemic scenario would look like? What would we see as Members of Congress, what sort of reports would be coming to us from the field, what would you all be seeing before we were aware of it, what would you be doing and how would you make us aware that there was, in fact, a problem creeping up on us of that magnitude?

Ms. GERBERDING. Thank you. As you know, we are very concerned about the situation with avian flu in Asia. That is a good example to use the what if story from.

The first thing we would expect if this new pandemic unfolded the way the previous ones did, we would begin to see more clusters of flu in people and evidence that those clusters were expanding in time. In other words, one person is infecting their neighbor and the next person. So we would see an expanded timeframe for the clustering.

Often as flu evolves, it doesn't just make a sudden jump to become very transmissible in people; it gradually gets there over a period of weeks or months. So those clusters are very important sentinels of impending transition to a virus that could be more easily transmitted and potentially cause a pandemic.

The main reason we are worried about pandemic with this virus is because no human beings around the world have ever seen it. None of us have preexisting immunity to it. So that is where we are so especially concerned about this avian flu.

What we would do is identify the clustering and also have the viruses themselves so that we would be able to characterize them in our laboratories or in the World Health Organization collaborating laboratories and try to make a connection between what is going on in the people and what is going on in the virus. We would also take those viruses as they emerged and work on making a seed virus very quickly so we could put it into the manufacturing processes that we have for flu virus.

One scenario is that we would convert from making the regular seasonal flu virus, which, incidentally, has three virus strains in every vaccine, into a vaccine that had only the pandemic strain in it. So instead of having a global capacity to make 300 million doses, we would be able to at least get 900 million doses out of it. So we would try to expand our supply by making a single-strain vaccine. But the timing to do that, as you know, is many months, so in the interim, what we would concentrate on is, first of all, containing the outbreak at the source through quarantine, isolation and use of our antiviral drug Oseltamivir.

In addition, if we had a limited supply, we which we do now of this particular pandemic vaccine, we would use that to help support immunization in the people closest to the exposed cases and try to buy some time while we were scaling up our vaccine supply.

But if you think about SARS where we had no drugs and no vaccine, the world was able to contain that outbreak by using old-fashioned methods of isolation and quarantine. The one difference is, of course, that flu is probably transmitted much more efficiently than SARS was, in retrospect.

So it would be a very big challenge, and that is exactly why we are spending so much time every day at the Department preparing all the steps in the process, the detection steps, the stockpiling of the drugs to treat the flu, the development on a fast track of the manufacturing processes for an avian vaccine that would allow us to scale up and reduce the time to produce it by a few months under emergency conditions.

All of that has to include not just the government at the Federal level, but communities across America as well as the globe.

Mr. BURGESS. Mr. Chairman, I should point out that with the SARS situation, NIH identified that virus with gene sequencing techniques, and within 30 days they pretty much knew the virus; is that correct?

Ms. GERBERDING. No, actually it was CDC that did that.

Mr. BURGESS. Oh, was it. I am sorry. Thank you.

Mr. WHITFIELD. I recognize the gentleman from Washington for his questions.

Mr. INSLEE. Thank you, and thanks to the panel for waiting for us. We appreciate that.

Dr. Goodman, I wonder if you could tell us what incentives exist, what you are working on, if anything, both through a commercial aspect and through regulatory aspect to really create incentives for new entrants into the market domestically?

Mr. GOODMAN. Well, we at FDA don't have financial incentives to offer. What we can do is try to provide what I would classify as a very rich, productive, helpful interaction with manufacturers, and also to try to be sure that the expectations that we put forward in terms of safety and effectiveness and how manufacturers meet them are balanced and get us the information we need without creating undue burdens. So we have been very engaged in that with the flu manufacturers.

Every year, even with the existing manufacturers, we have extensive interactions. As you heard, we provide them with seed viruses and reagents that are helpful to them.

In addition, the other thing we challenge ourselves to do is say can we look at the data and say can we help them speed the clinical development program, and that is where we came up with the accelerated approval mechanism based on the likelihood that good antibody levels against the virus will predict protection. This has allowed, for example, in the case of GSK, them to accelerate their plan by 1 to 2 years to come to licensure.

So those are the kinds of things we can do to help make this a faster, more economic way to market. But we can't provide ourselves any economic incentives. The market provides those.

Mr. INSLEE. Any thoughts from the other two agencies in that regard?

Mr. GELLIN. Let me add to that. As Dr. Goodman said, there is the market piece. It is also important to appreciate the demand and use of influenza vaccine over time that Dr. Gerberding has mentioned. The peak of our use has been in the mid-80 millions, but recognizing just as briefly as maybe 10 years ago, the marketplace was far smaller than that with maybe 30 million doses as the annual allotment.

So I think a big part of it has been not only the increased awareness by the population of protective value of the vaccine, but the expansion and recommendations has created a bigger marketplace overall.

Mr. INSLEE. Dr. Gerberding, any thoughts?

Ms. GERBERDING. I would agree that driving the demand for the vaccine is an important and critical step actually. We do this by science. We do the research, we find out who is going to benefit from the vaccine, what is the benefit, what is the cost-effectiveness of the vaccine. And as we identify that in new populations, we make recommendations that we should be vaccinating these people. That influences what the government pays for; that influences what CMS reimburses for. So we can drive forward the market, and we have done that over the past 15 years, by expanding the number of people that we recommend in the immunization pool.

There is consideration now, though there has been no decision on this, that the pool be expanded even further. I mentioned the possibility that we would end up with enough evidence to recommend universal vaccination of children, for example, for flu every year.

I think ultimately the big payoff will be the manufacturer who identifies a better vaccine, and by that I mean a vaccine that we don't have to give every year, a vaccine that could be given once or twice in life like all of our other vaccines and really get us beyond this annual challenge that we face.

That is a matter of basic science, and that is why these investments that the Department is making in motivating the science, not just through the research grants that the NIH is putting out, but also through these contracts with manufacturers to try to develop a better vaccine, are so critical for the mid to far term of this problem.

Mr. INSLEE. Given this pandemic possibility, which is kind of disconcerting, should we be giving thought to accelerated FDA approval of some of these to try to inspire new entrants into the market? I am told it is about 12 months. Is that realistic? If so, is there anything we can do to accelerate that?

Mr. GOODMAN. We are applying similar principles to the pandemic vaccines as we are to trying to bring additional manufacturers in for the routine vaccines. So you are absolutely right, we see that as an issue, and we are doing that.

In fact, with the U.S.-licensed manufacturers, we view a new vaccine for a pandemic not as a new vaccine that would require a new license, but as a change in strain such as we see each year. So the data we require is very different, and we are able to really facilitate that process.

Mr. INSLEE. So what is the time span then from start to finish?

Mr. GOODMAN. It is primarily related to their ability to manufacture and then submit to us data about that strain.

Mr. INSLEE. What does that end up in the real world being?

Mr. GOODMAN. Well, you know, typically, for example, one of the things, as Dr. Gellin mentioned, is the Department has funded the production of an investigational or new vaccine against the current avian influenza strain. Because the immune response to these viruses, one of the issues why it is a pandemic, it is because you or I have no experience against that virus or its relative, so we can't always predict how good our immune response will be.

But in this case, Aventis Pasteur very quickly produced a commercial scale lot. I actually don't want to give you a number, but it just was within a very few months, and that is undergoing testing. Now, in fact, I think most—a bunch of that testing has already been completed, supported by the National Institutes of Allergy and Infectious Disease.

So a manufacturer with a licensed existing technology and manufacturing capacity, provided with the right virus, can very quickly begin to produce it for the initial testing, and then we would look at that data and be able to evaluate it.

I think the real issue here that we are also concerned about is what is the manufacturing capacity out there to produce the millions and millions of doses that would be needed and the time that is needed to do that. As you have heard, it typically takes several months to ramp up and produce enough vaccine for the whole U.S. population.

Mr. INSLEE. So I am trying to get some sense of the time in days, months, weeks, portions of centuries, some timeframe, and if you can break it down from the time they have some manufacturing capacity demonstrated, from there, how long would it take the FDA to do the evaluation to really get the certification?

Mr. GOODMAN. As I said, we would not consider it a new vaccine, so the major factor there is how long it takes them to produce the vaccine.

Mr. INSLEE. Say it takes 3 months to produce a vaccine. How much longer?

Mr. GOODMAN. They would do a clinical study, for example, to show the immunogenicity and safety of that strain. We would probably require limited data, and they would submit that data. They could potentially do that study, I think, as has been done, for example, by GSK, within a matter of a couple of months. Then they would submit that data, and we would look at it very quickly. We do this every year.

So, again, we would not be the limiting factor there, unless a problem with the vaccine were to occur.

Mr. INSLEE. Say it takes 3 months to do the manufacturing capacity, 2 months to do the clinical trials. How long—if you would give me some parameters of how long it takes the FDA to finish that? I am just looking for parameters.

Mr. GOODMAN. Each year we review a new strain submitted. For example, if they change a strain in a vaccine, each year we review that, and we typically do that within a month. This may be more complex if there is more data.

Mr. INSLEE. Okay. Could you give us any thought about the difference between the European system and ours relative to their experience with this? I sense there is—and maybe it is this one difficulty we have run into—is there a different bar, a different screen they are running through to have a different experience, and if so, does that give us any thoughts on ours?

Mr. GOODMAN. Regulatory?

Mr. INSLEE. Yes.

Mr. GOODMAN. Well, there is not one European regulatory system, so for traditional vaccines, there are multiple countries that can review and approve those vaccines. They may do it similarly or differently.

For the routine strains, there are some differences. For example, each year clinical studies and clinical information is required by the Europeans, so in other words, they take the new vaccine that is made each year for annual influenza production and actually require that the manufacturers provide a small clinical trial of that vaccine. At FDA we view them as strain changes for licensed vaccine, and we don't require that. So, that is one difference that each year they require clinical data, and we don't. I would say that is a major issue.

Similar to us, they have inspections, and you can see, for example, with Chiron, there was an independent inspection by the EUK regulatory authority of that manufacturer, which was located in England.

But the main difference is—I can't say there is one systematic difference, that one country is tougher or weaker or anything like that, but there is this one major difference, which is that they are required to provide clinical data there each year. We feel we have had enough experience with the routine strain changes and the licensed manufacturers that we are comfortable just making sure that strain is exactly what it is supposed to be and the potency and safety of it are proper.

Mr. INSLEE. Great. Thank you very much.

Mr. WHITFIELD. Thank you.

I recognize the gentlewoman from Tennessee for her questions.

Mrs. BLACKBURN. Thank you, Mr. Chairman. I want to thank all of you for your patience. I know it is disconcerting sometimes as we are in and out and going for floor votes.

Director Goodman, I think I will come to you first. I had done a little bit of reading in preparation for the hearing today, and I found a great article, What Is Wrong with Our Flu Vaccine Supply, and actually highlighted a few points in here. I found it quite interesting. It seems like basically if you were to say the underlying

problem or the root of the problem goes back to being this, and it is because of liability, because of regulation, because of maybe some changes in public policy through the 1990's that the U.S. has become a less friendly environment for U.S. vaccine manufacturers. Then you begin to look at some of the situations that arise because of that and the liability and the different situations that exist because of that.

With all that said, taking that as a premise, a question that I have got, in reading this, I was looking at the developmental strategy, the multiple developmental strategy of when you are looking at a strain, and why is it impossible to have a multiple strategy, a multiple developmental strategy, for one of the vaccine formulations? And then how could we get to the point that we have multiple developmental strategies for the vaccines, for a specific vaccine, for a certain flu, to be certain that—I think Dr. Gerberding mentioned earlier that sometimes you pull a certain strain, but you don't know if that is going to be what you end up needing or not or if it is going to replicate itself well or not.

So, how do you get to the point that you develop those multiple strategies?

Mr. GOODMAN. I want to be sure I understand your question before I answer it. I can see two questions there. One is would it be possible to develop a vaccine that protects against multiple different strains? The other would be if we have problems such as Dr. Gerberding mentioned occasionally where a strain is circulating and we didn't predict that it would be important, could one have prepared a vaccine against that ahead of time?

Mrs. BLACKBURN. Right. Take both questions.

Mr. GOODMAN. The first one is really a science question. It is something that the Department and NIH and FDA are all supporting research on. It would be ideal to have a vaccine that protects against multiple strains without having to every year go out and find all those strains and grow all those strains. So people are trying to find proteins in the vaccine, in the virus, that might provide protection in multiple years or against multiple strains. That kind of research is going on. There is some evidence that there may be some advantages for live attenuated vaccines in providing that kind of protection.

So there is a lot of work going on in that, and it is a Holy Grail, and it would be very desirable and could even help protect us against pandemics potentially. But the science isn't there yet, and it has been difficult to achieve.

The other question is really again limited by the capacity of the industry. So as manufacturing gears up, the industry, based on CDC and WHO's surveillance data, FDA's expert committees, tries to examine what has gone on out there in the world and pick the strains that are likely to threaten our population and put them in the vaccine. In general, they have done a remarkable job at doing that, but occasionally there is a strain that circulates in one part of the country or another that causes a problem and isn't well covered by the vaccine.

As you said, you could deal with that by potentially, if you saw something possibly emerging, making some vaccine against that strain. The tradeoff there is right now the total capacity is limited,

so you would have to cut back on someone else. So right now we are unfortunately in the situation of people making the best educated decision and then going ahead and producing. I don't know if Dr. Gerberding or Dr. Gellin want to add to that.

Mrs. BLACKBURN. Well, I think that is probably one of the things that is just a continuing source of frustration. And I am sure Director Gerberding has a certain amount of that. It seems there is a flu virus that you all, if I am understanding that correctly—you may identify something in the spring, and then by the fall there is another strand that you have nothing for that is actually causing the flu, the outbreak, the epidemic, whatever. And then is there anything that you can begin to do, either through preparation or through science that the CDC can do, to take some steps to forestall that?

Ms. GERBERDING. The virus is very unpredictable, and it is usually not just one virus circulating during a flu season; there are several, usually at least three and often many more variants than that. And so we use our experience and our predictions based on the past early in the spring to look at what is present at that point in time, because in most years what is present in the spring is what is going to be present in the fall. That doesn't always prove to be correct.

But what usually happens—and this example happened last year where the vaccine predicted strain was a toss-up. We didn't know if it was going to be a Fujian strain or whether it was going to be a different strain, and we wanted to have the best chance of coverage. Unfortunately, the Fujian strain didn't grow very fast when we were trying to create the seed virus. And we had to make the decision we had better go with the one we can get a vaccine to because there is no room to wiggle in the timing of getting these products to market.

So the vaccine that was produced that year wasn't a perfect match for what turned out to be the dominant strain that fall. Fortunately, there was crossover. So the strain that we did use was a close cousin, and there was some protection afforded to people. And that is usually what happens even if it is not a perfect match. If it is a cousin instead of a twin, we get reasonably good protection of the people who need it the most.

But there is right now no way to accurately predict which one of the swarm of viruses is truly going to emerge, and sometimes we don't get it right. What Dr. Goodman is really describing is the fantasy that we all have, that we will find a way to make a vaccine against some part of the flu virus that doesn't change every year, some other molecule in the virus that is consistently there that would be a good enough source of protection that would allow us to just vaccinate using that, and then it didn't matter about all these other changes that go on and on and on. But we have no proof of that principle yet, and, believe me, everyone would like to find such a vaccine. It is a little bit like the AIDS vaccine, where the virus changes so much over time, you can't pin it down and find something that will uniformly protect against all strains.

Mrs. BLACKBURN. And if I am understanding correct, ma'am, it is basically what is happening with this is that you mentioned the wiggle room, and you have very little time to move. You do a lot

of work on faith, basically, and informed science and then a little bit of faith. And then you move forward into production, but you don't have a lot of time for testing.

Ms. GERBERDING. That is exactly right. If we pick the strain, let us say we find it in February or March, we have to make the seed for the vaccine from that in a matter of weeks, get that off to the FDA and the manufacturers who have to put it into production mode. And it is not just about popping it into some eggs. It actually takes time to grow in the eggs. It has to be harvested; it has to be processed so that all of the potential contamination from the eggs is removed. That was the problem that Chiron was experiencing. And then it has to be packaged. It has to be tested to make sure that all of packages have exactly the same amount of antigen in them. There are all kinds of quality control steps that have to go on in there. Everything has to work exactly right for that vaccine to be available in September when we need it.

Mrs. BLACKBURN. Okay. Thank you very much.

Mr. Chairman, I yield back.

Mr. WHITFIELD. Thank you very much.

We will begin a second round. And I would recognize Mr. Stupak for 8 to 10 minutes of questions.

Mr. STUPAK. Thank you, Mr. Chairman.

And, Dr. Gerberding, in response to Mr. Burgess' questions, you had indicated that the cost for the vaccine is—you gave three different costs, 9.95, 13.25, and 24.50. Is that this year's prices or last year's?

Ms. GERBERDING. What I am quoting to you are catalog prices for 2005 for three different manufacturers of vaccine. I would be happy to provide you with the list of the catalog prices for your record.

Mr. STUPAK. Very good.

Mr. STUPAK. Catalog price, is that the price the government would pay for?

Ms. GERBERDING. Generally we are able to negotiate a slight discount off of those prices.

Mr. STUPAK. If we want to put—and I think you used the word overexpanding our pool of more and more people getting the flu vaccine, and ideally we would like everybody to get it, I thought you said. So, in a business model, wouldn't the more we produce lower the cost per vaccine?

Ms. GERBERDING. Ultimately that may be true. I think what we are talking about is a market-driven process here. The more people you vaccinate, obviously you can commoditize the vaccine if you get up to a large enough population. If you were thinking about the global community of people who need to be vaccinated, we would be talking about large-scale and potentially very cheap vaccine.

Mr. STUPAK. How about just here in the United States? Because I think earlier in your testimony you said we have spent hundreds of millions to modernize a facility to develop a new culture, to move from the egg to a cell culture. So that would help drive down the cost of manufacturing; would it not?

Ms. GERBERDING. That is an independent investment. We are talking about apples and oranges here. One is the process, by simply making more of what we already know how to make, and the other is making something completely new. And the investments

we are making is a completely different manufacturing process that would involve new factories and a new science and a new regulatory approval process.

Mr. STUPAK. Here is my problem. Those hundred millions came from the U.S. taxpayer, right?

Ms. GERBERDING. Correct.

Mr. STUPAK. And if you look at the first chart you had up, and the ones who get the immunizations first are the high-risk group, people over 65.

Ms. GERBERDING. Correct.

Mr. STUPAK. And young babies probably under 2 years old, right? And if you look at that, over 65, that means Medicare pays, doesn't it?

Ms. GERBERDING. That is correct.

Mr. STUPAK. Under 2, most of that is Medicaid paid, correct?

Ms. GERBERDING. Not necessarily. It applies to all children.

Mr. STUPAK. Okay. Well, children are either covered—well, private insurance, of course. But I think you would find most of the children are probably covered who are getting these shots through either CHIP program, Children's Health Initiative Program, or through a Medicaid program. In my home State of Michigan, that certainly is the case.

Ms. GERBERDING. The children who do not have private insurance are covered under something called the Vaccine For Children Program. So it is a special program that applies to all of the other childhood immunizations.

Mr. STUPAK. So we have got another program then. Okay. The point being, why can't then the government negotiate deeper discounts then, if we are putting hundred of millions into the manufacture to modernize the facilities, most of the costs or the payments on these immunizations are coming through the government on Medicaid, Medicare, CHIP or the children's immunization program. I would think we could get bigger discounts, because I am really bothered by the 17 percent increase.

And just a thought there. If we—you also mentioned something about 30 million in insurance. Is that 30 million set aside to buy immunizations if we should run out in this country? You mentioned 30 million in insurance. Do I understand that right?

Ms. GERBERDING. In this fiscal year we have $20 million available to purchase bulk vaccine. And what that means is the manufacturer at the end of the season can continue the production, but not necessarily take that big vat of vaccine and convert it into individual vials. So it is a very cheap purchase because we buy it at an earlier production process.

Two things—well, three things could happen. One is we turn out to need it, and we would need that late-season vaccine. Maybe it is a bad season, maybe we've got a failure in somebody else's manufacturing process and we need it. So they can go ahead and complete the production and utilize it the way we would the regular vaccine purchase.

The second thing is that we may not use it this year, but by luck sometimes one of this year's strains is also the strain in the next year's vaccine. So we are a step ahead of the process; we have already purchased some vaccine for the following year. And when it

is in monovalent form like that, we have got three different strains sitting in those formulations, so there is a good chance that one or two of them will be able to be used the following year.

The third thing could happen is that that wouldn't be the case, and that would go to waste. But if we are wasting it, it is a cheaper waste than buying the fully manufactured vaccine and wasting that.

So it is a way for us to partition the risk to the taxpayers, but the opportunity to develop a little more vaccine at the end of the season if it turns out that we need it, and in a year like this we would have liked to have had that.

Mr. STUPAK. So in your strategies development and in your policy development, do you have any monies then set aside in case we do have a bad flu season; we use up everything we have, and we have to get more into this country to help out that high-risk population? Is there any backup plan?

Ms. GERBERDING. We have, in addition to the $20 million I mentioned for the monovalent, we have $20 million at least proposed in the 2006 budget for vaccine purchase. It is not specific to purchasing at any particular place or time, but we will be negotiating contracts for that. We also purchased through the Vaccines for Children Program that you mentioned before a stockpile of influenza vaccine again so that if we end up late in the season and we need that, the government has purchased some to protect those children.

And, as Dr. Goodman has stated, we have a good chance of getting an international manufacturer interested. And we are not stopping there; we are obviously continuing to work with at least two other ones to encourage them to get their licenses and their applications.

Mr. STUPAK. This $20 million for purchase and reserve that you sort of are holding on, did you have this in reserve last year, too? Did you have that amount of money, $20 million, in reserve to purchase immunizations if you needed it last year?

Ms. GERBERDING. We had a stockpile for the first time this past year. So that was one step that had already been taken. We also had a stockpile of drugs for the first time this past year in part of our overall flu preparedness, not anticipating. And then during the flu season, the additional doses were purchased under the investigational new drug category, which is not the optimal way to get vaccine, but if we don't have it any other way, that is the resort we had to use.

Mr. STUPAK. Well, when you purchased the IND, where was that purchased from?

Ms. GERBERDING. That was purchased from two companies, one, the GSK purchase, and then I can't remember the—Berna Biotech.

Mr. STUPAK. Berna Biotech, was that the Canadian company?

Ms. GERBERDING. I think so.

Mr. GOODMAN. Swiss.

Ms. GERBERDING. Right. Sorry. That is right, we didn't buy the Canadian.

Mr. STUPAK. So you have no objections to reimportation of drugs then if it is necessary on this flu vaccine if we need it.

Ms. GERBERDING. This would not be considered reimportation. This is purchasing vaccine from an international manufacturer in a plant that we have certified as having good manufacturing practices and a chain of custody of the product that would assure our Americans that it arrived here safely.

Mr. STUPAK. And we inspect drug manufacturers all over the world, don't we, to make sure that they are safe and there is a chain of custody, Correct?

Ms. GERBERDING. If the drug is going to be sold in the United States and licensed in the United States, I believe that is——

Mr. STUPAK. In fact, we get a lot of our drugs from India; do we not, Dr. Goodman?

Mr. GOODMAN. Certainly it is an increasingly global market with global manufacturing. One important difference here, of course, is those, the GSK and the Berna Biotech that Dr. Gerberding mentioned, were not U.S.-licensed vaccines. And so they were purchased by the government basically for emergency use, and they would have been used under the nonlicensed category of investigational new drugs, so they would have required informed consent by the recipients. So there is some of the same issues, certainly, but these were not licensed products.

Mr. STUPAK. Sure. And my time is running short here. But we have FDA inspectors all over the world inspecting plants all over the world to make sure that they meet standards and qualities, right?

Mr. GOODMAN. That is certainly increasingly the case.

Mr. STUPAK. Sure. So the issue on reimportation is to make sure we have people who can do the inspections and make sure the chain of custody is intact, right?

Mr. GOODMAN. I think—I am not an expert in that field, I am a biologics person. But certainly a critical requirement would be to be sure the product is what you think it is, that it was properly made, and that it has been in custody and proper care. And that is a very resource-intensive——

Mr. STUPAK. Let me ask you one more question. Mrs. Blackburn brought up about the liability issue there and her multistage strategy or whatever it was. In the vaccines that are made for flu, does the Federal Government back up or indemnify the manufacturer if there is a claim?

Mr. GELLIN. There is an vaccine injury compensation program that is defined by a vaccine that is given universally to children. This year for the first year the influenza vaccine was added to that list because of the recommendation for this past year that all children 6 to 23 months of age receive it.

Mr. STUPAK. So medical liability really shouldn't be an issue in this, then, if it is being backed up or indemnified by the Federal Government.

Mr. GELLIN. Again, the flu vaccine is now included in the program.

Mr. STUPAK. So medical liability would not be an issue.

Mr. GELLIN. Again, I am not an expert in that. There is always the potential for people to go outside that program, given the way it is designed, but it is there as really the first stop.

Mr. STUPAK. If we modernize the plants, we are the biggest purchaser, we indemnify them for medical liability, I can't figure out why we can't gain more entrance into the flu vaccine area.

Mr. WHITFIELD. Thank you.

Just to follow up on Mr. Stupak for a minute, is the FDA concerned that, in times of shortage, that State and local agencies might look beyond the established U.S. manufacturers to get a vaccine supply?

Mr. GOODMAN. Well, I think we recognize that with what happened with flu last year, you know, if I were a Governor—I was in a State not too long ago and worked with the State health department as part of what I did. I can see that there was really a desire to get vaccine quickly. I think what we are concerned with is that any vaccine that is administered to the American people meet the high standards they expect for safety and efficacy. So if that were being done in a way that raised concerns about that, we would be concerned.

Mr. WHITFIELD. But the policy right now is that, as I think Dr. Gerberding explained, if you have to go out in these emergency situations now, these plants are licensed, and you have the custody issue; and, if not, then you have to have informed consent. Is that correct, Dr. Gerberding? I mean, under your insurance policy that you were discussing, you can go out and buy additional vaccine and if there is a real need. But you do that only under certain circumstances.

Ms. GERBERDING. We are buying incompletely manufactured vaccine as a backup.

Mr. WHITFIELD. Okay. At this time I would recognize our doctor from Texas for 8 minutes of questions.

Mr. BURGESS. Thank you, Mr. Chairman.

Well, let us continue on that line that Mr. Stupak just brought up now on the vaccine injury compensation fund. Is that only for children? If adults are immunized with the flu vaccine and have an adverse reaction, are they also indemnified by the vaccine fund?

Mr. GELLIN. The program is designed around a vaccine, and if a vaccine is recommended for all children or a group of children, then anybody who receives that vaccine would be covered by the program.

Mr. BURGESS. Now, does that limitation of liability, would that indemnify a company if they had thimerosal in their vaccine?

Mr. GELLIN. It is not an indemnification program; it is an injury compensation program.

Mr. BURGESS. Would that cover an injury that was purported to be covered by thimerosal?

Mr. GELLIN. There is a list of compensable reactions to these vaccines, and that is not currently on the list of adverse reactions to influenza vaccine.

Mr. BURGESS. So if a family wished to bring a charge or a case against a manufacturer for placing thimerosal in their product, that would be outside the compensation range of the injury fund, the vaccine compensation injury fund?

Mr. GELLIN. I am sorry. I guess this gets beyond my expertise and the nuance of the program. So I think we should supply you with the details about that and about the program.

Mr. WHITFIELD. Did you want to respond to that, Dr. Gerberding?

Ms. GERBERDING. I think that anyone can bring a claim to the injury compensation fund. Whether or not it would be settled in favor of the claimant is something that would be based on the merits of the claim. So that is the extent of my knowledge of the program as well.

Mr. BURGESS. Well, Mr. Stupak was making the point that since there was complete release of liability, he didn't understand why the manufacturers would not be in the game. But it is my understanding that the additive in the flu vaccine, if that is the target of the lawsuit, that that may be outside what is covered by the vaccine injury compensation fund.

Ms. GERBERDING. I think right now it is important to think of risk in an even more comprehensive way. There is certainly the risk to the individual who receives the vaccine, a risk that the manufacturer experiences as the manufacturer of vaccine that's caused the risk to an individual. But the risk that is really in play this past year is the risk to the manufacturer of not being able to produce vaccine and get it licensed because the process and the methodology used is so prone to problems. And we have seen this happen over and over again.

You are starting with an egg, which is intrinsically not a sterile product; you are growing something in it, and in the end you have to end up with a vaccine that is free of any kind of contamination. So just getting from the egg to the vaccine is a very risky prospect from the standpoint of the people who are manufacturing it. And I think that is one of the kinds of risks that is very difficult to eliminate. You need an insurance policy for that kind of risk to replace the profit that was lost because your license was pulled due to a manufacturing methodologic issue. And I am not aware that we have that kind of insurance program for vaccine manufacturers.

Mr. BURGESS. I am not either. We do it for farmers, I think.

On the issue of the price increase, I guess what is being referenced is a Wall Street Journal article from May 4, which is today, and it talks about the 17 percent increase. The actual dollar amount of that increase was $1.40 above 2004 prices and the first rise in 3 years, if I am reading this article correctly. Any speculation on what amount of that price increase is there because of liability concerns or other manufacturing risk concerns?

Ms. GERBERDING. I couldn't speculate about that. I think that would have to be addressed to the manufacturer.

Mr. BURGESS. Mr. Chairman, do we have any way of obtaining that information?

Mr. WHITFIELD. We will submit that question for the record and do some follow-up on it and see what we come up with.

Mr. BURGESS. Well, the line of questioning previously seemed to indicate an environment that was free of risk for the manufacturer, a guaranteed purchase by the Federal Government, and a guaranteed pool of purchasers. It looks to me to be a field that is fraught with a great deal of more peril than was previously outlined.

Mr. STUPAK. Would the gentleman yield on that point?

Mr. BURGESS. Well, I was going to say I will yield back my time because I know the other side has some additional questions. Thank you, Mr. Chairman.

Mr. STUPAK. Would you yield on that point? It was Mrs. Blackburn that brought up the liability issue with her questions, multistrategy, as she called it. So I was trying to probe the depth of it. And I knew that the Federal Government does provide some funds there to patient protection. I am not trying to get into a malpractice argument with you. That is for another day.

Mr. WHITFIELD. But we will note the doctor's question, and we will follow up on that and get that into the record.

Mr. BURGESS. Well, it really wouldn't be a malpractice question, it would be a products liability question, defective product from the thimerosal standpoint.

Mr. WHITFIELD. Do you have any other questions?

Mr. BURGESS. No, sir. I will yield back.

Mr. WHITFIELD. At this time I will recognize for 8 minutes Ms. Schakowsky of Illinois.

Ms. SCHAKOWSKY. Thank you.

In 2004, knowing that a severe flu season without an adequate supply of vaccine could result in a disaster, especially among the elderly and the chronically ill and the very young, Illinois Governor Rod Blagojevich began looking for additional vaccine for Illinois. He asked a licensed regulated wholesaler in Europe to see if they could find and secure approved European flu vaccine on our behalf. After an intensive search, the wholesaler found vaccine and began securing doses to meet Illinois' request.

On October 25, Illinois officials sent a letter to the FDA asking it to review and approve vaccine made by Aventis Pasteur in France and GlaxoSmithKline in Germany. And 4 days later the officials, Illinois officials, came and met in person with the FDA to answer their questions. And that started a dialog between Illinois experts and the FDA over the origin, custody, storage of the vaccine, volumes of documentation. And while the FDA didn't respond, Illinois, it gave the CDC approval to import millions of doses from the very same German made GlaxoSmithKline vaccine for use in the United States.

And then early December, after numerous exchanges between Illinois experts and the FDA, Acting Commissioner Lester Crawford stated in a press conference that Illinois had answered their questions and provided all the information they needed, and that the FDA would have a response very soon. As of today, 5 months later, Illinois still has not received a response from the FDA.

I would like an answer, Dr. Goodman. What went wrong, and why can't Illinois, after its best effort in working with you, come to an agreement on how to take care of its own constituents, its own residents?

Mr. GOODMAN. Well, a couple of comments. I don't have all the details on the correspondence between or communications between the Office of Regulatory Affairs, the inspectorate force, basically, who were working most intimately with Illinois to document the nature of the vaccine. But what I can tell you is we met very early on with the Illinois people. I appreciate, and I told them at the time and so did others at the FDA, the demands being made upon

them and their desire to get vaccine for their citizens. So we very much appreciate that.

Ms. SCHAKOWSKY. That is all very nice.

Mr. GOODMAN. Well, we made the point very early on that apparently the vaccine was extensively in distribution, was not clearly—they were not clear about whose hands it had been in. Some had been shipped to other countries. It was not in the manufacturer's distribution. And we said to them that we would work with them, but it was a very difficult task they would have ahead of them to provide adequate documentation that the vaccine was what it was, had been properly stored so that it would be safe and effective. And another important point is this is not U.S.-licensed vaccine, so that it would then have to be used under IND.

My understanding is, to answer your question, that the information—first of all, they told us we would provide that information right away. It took quite some time to provide information. The information was reviewed in the Office of Regulatory Affairs. The message was given that there were numerous gaps in the documentation.

Ms. SCHAKOWSKY. And why did Dr. Crawford state in a press conference that Illinois had answered all their questions and provided all the information that was needed?

Mr. GOODMAN. Well, again, my understanding from the Office of Regulatory Affairs is that their last information given by them to the representatives of the State—and I can't say whether this was a letter or from whom or in what form—was that the documentation provided had deficiencies; and that given concerns about the safety of the vaccine, how it had been handled, what it was, that additional information would be needed. And I also understand that it was suggested and later offered, I believe, through the Centers For Disease Control, that vaccine that had been clearly under control, stored, and in the manufacturer's control, which was why we worked on getting that right away at the Secretary's request, would be made available, in fact, to Illinois or others who wanted it under the CDC's IND. So you had the opportunity for a well-characterized, well-known vaccine that we knew to be safe, where there had been extensive review of the manufacturing and the pedigree of that vaccine. So I think we made a good-faith effort together working with your folks.

I think there were deficiencies in the data. I think then, when that was the case, we also made a good-faith effort to get this other vaccine where there were not deficiencies in the data and to make it potentially available. I would be happy to talk more with you about it or——

Ms. SCHAKOWSKY. I think we need to talk more about it, because I think there was a clear understanding in December that Lester Crawford had clearly stated that we had—and Illinois met all the requirements, and that still there was—and that there would be an FDA response very soon, and that none of that happened. So I hope that we can clarify that.

I had to step out for a little while, and I am just wondering if you did finally answer the question that Mr. Stupak had asked if we—and I am quoting now from the Wall Street Journal: It also

shows that the vaccine production infrastructure remains nearly as fragile and outdated as it was before last year's crisis.

Let me just say that, hearing Dr. Gerberding's numbers, it sounds to me like even the middle case doesn't even begin to meet what is—your statement of what is a public health need. I understand demand and need are different, but what it also says to me is that we need to promote getting the vaccine in a more aggressive way to a large population that isn't even asking for it. And, second, were they to ask for it, even under the very best of scenarios, we cannot provide it. Now, so are we in as good a shape, better shape, worse shape than we were last year? Anybody?

Mr. GOODMAN. Well, I am happy to take the first crack at that. I think we all recognize there is a clear problem with the fragility of the flu vaccine manufacturing infrastructure. I think there is some progress that has been made, but there is still a problem. The progress that has been made is that, as mentioned, GlaxoSmithKline, in part because of the work on the IND, has stated that they are going to apply for U.S. Licensure under the accelerated approval mechanism we provided. So they expressed clear interest to enter the market for this year. That is potentially more diversity. Another bit of progress is the—while the jury is still out, the improvements that Chiron has made in its manufacturing. Then I would go one step further and say there are at least a couple of other manufacturers that we have been working with who have indicated long-term interest in the U.S. market.

But, yes, you are absolutely correct. Challenges remain both in the underlying technology and in the market forces. And it is almost a vicious circle, because if you can't provide a stable vaccine supply, how can you continue to ramp up demand? And if you don't continue to ramp up demand, how do you have a stable supply? We are all living that, and we definitely support things to occur on both ends, stabilizing the supply and increasing uptake and demand.

It is helpful to realize that I think about 10 years ago there were only about 20 million doses of flu vaccine administered in the United States. So while it seems we have a long way to go, and as a public health person I think we do and we share that concern, there has been progress over a 10-year period.

Mr. WHITFIELD. Ms. Schakowsky's time has expired. Do the two of you want to respond to her last question, or do you feel—okay.

One comment that I would just make on this Illinois situation, and you can tell me if I am correct or incorrect, but it was my understanding that the FDA, did they actually receive appropriate drug master files on the vaccines from Illinois?

Mr. GOODMAN. I would have to get back to you on the drug master file. The drug master file would be what the manufacturer possesses that says everything about the product. I think—I would need to get back to you because there were at least a couple different manufacturers involved. But the manufacturers, to my knowledge, signaled a willingness to help in this.

The issue that was definitely where there was a deficiency was in the data that documented every—how that vaccine had been handled after it left the manufacturer. And I think that is where the Office of Regulatory Affairs had a safety concern.

Mr. WHITFIELD. Okay. Well, that concludes today's hearing. I want to thank the witnesses for your patience. And we are going to keep the record open for 30 days, and ask that any questions for the record be submitted within 7 days to be answered.

Obviously this is a particularly important subject, and your testimony today, I think, provided enlightenment not only for the committee members, but also for the general public. And we do commend you for the work that you are doing and look forward to working with you as we move forward to address this important issue.

With that, the hearing is adjourned.

[Whereupon, at 5:12 p.m., the subcommittee was adjourned.]

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