

**FUNDING NEEDS FOR PANDEMIC  
INFLUENZA PREPAREDNESS**

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**HEARING**  
BEFORE A  
SUBCOMMITTEE OF THE  
COMMITTEE ON APPROPRIATIONS  
UNITED STATES SENATE  
ONE HUNDRED NINTH CONGRESS

FIRST SESSION

**SPECIAL HEARING**  
NOVEMBER 2, 2005—WASHINGTON, DC

Printed for the use of the Committee on Appropriations



Available via the World Wide Web: <http://www.gpoaccess.gov/congress/index.html>

U.S. GOVERNMENT PRINTING OFFICE

25-120 PDF

WASHINGTON : 2006

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## FUNDING NEEDS FOR PANDEMIC INFLUENZA PREPAREDNESS

WEDNESDAY, NOVEMBER 2, 2005

U.S. SENATE,  
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN  
SERVICES, EDUCATION, AND RELATED AGENCIES,  
COMMITTEE ON APPROPRIATIONS,  
*Washington, DC.*

The subcommittee met at 9 a.m., in room SD-106, Dirksen Senate Office Building, Hon. Arlen Specter (chairman) presiding.

Present: Senators Specter, Cochran, DeWine, Harkin, and Murray.

### OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Good morning, ladies and gentlemen. It's 9 o'clock, and the Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies will now proceed.

We have a hearing of unusual importance in a subcommittee which characteristically has hearings of very great importance, but this tops the list of any in recent times. We are looking at a very substantial appropriation to meet the imminent threat of a pandemic flu. I had the opportunity to hear the President's speech yesterday at the National Institutes of Health, and the President really laid it on the line with the potential problems, which are enormous.

Last week, when we had full Senate consideration of the appropriations bill, Senator Harkin took the lead, having spotted this problem some substantial time ago, and we worked through a very substantial add-on to our appropriations bill, in the amount of \$7,975,000,000. We carefully fenced the money so that the expenditures would be at the discretion of the President and his very able team, many of whom are assembled here this morning. But we did not want to face a situation where Congress adjourned and then the program came forward. We will be looking, perhaps in late November, at a supplemental with the Congress out of session. Supplemental appropriation bills are extraordinarily difficult. They become what we call Christmas trees for many, many other items, so that if we can appropriate for it in due course, which we are moving ahead on, that's the way to handle it.

The President has come in with a figure of \$6,660,000,000. We have the defense appropriation bill, which has \$3,913,000,000. We have an amendment offered by Senator Frist, the majority leader, to the reconciliation bill for \$3.954 billion, slightly under \$4 billion.

So, we're talking about a great many figures, and we're going to—we're going to work them out.

That's under 3 minutes, and now I want to save time for our witnesses, and I yield to my distinguished ranking member, Senator Harkin.

STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. Thank you very much, Mr. Chairman. I want to join with you in welcoming our Secretary and Dr. Gerberding, Dr. Fauci, Dr. Gellin, Dr. Raub here to this very important hearing this morning.

I, first, want to salute the President for coming forward with a plan to prepare our country for avian flu. It is long overdue. We are behind. I—that's not to say that—to blame anyone, other than all of us. We've—all, I think, shoulder a little bit of the blame for not coming forward a long time ago. So, I'm not pointing at any one person. I'm just saying that we've all, sort of, kind of, put this off and put this off, until finally it's staring us in the face. I might exempt from that people who—like Dr. Gerberding and others at the Centers for Disease Control and Prevention, who have been warning us about this for some time, and her predecessor there, Dr. Copland, Dr. Fauci and others at the National Institute of Health, who have been warning us about the lack of the research we needed for vaccines, and others in the past. But I think we all share a little bit of responsibility for not coming forward with something before now.

I also want to say, I thought the President's tone was correct yesterday. His tone was correct. I listened very carefully as he sounded the alarm but drew the curtain on panic. We need to have the alarm sounded, but we don't need to have people panic. I thought his tone was absolutely correct in the way he outlined it yesterday.

So, now we have a plan from the administration, we have an appropriation here of about \$8 billion. Again, this was a bipartisan effort. Senator Specter said—was giving me a lot of undue compliments for that. Actually, Senator Specter has been the lead in this for a long time. We've worked very jointly together. Actually, nothing really happens around here unless we, kind of, have all worked together on this thing. We worked together on this amendment last week, as we did on the one before, on the defense appropriations bill, to try to come up with, you know, What is it that we need? What are the parameters? What do we need to focus on?

Quite frankly, I was pleased, but maybe not too surprised, that the President's plan very closely tracked the one that we had offered 1 week ago. I got to thinking about it, and I thought, well, of course; we're all talking to the same people. We're talking to the Secretary, we're talking to NIH, we're talking to CDC, and we're talking to the drug companies. So, we all, kind of, have the same inputs on this. So, they are very closely aligned.

There is only one or two elements that I would like to discuss with you this morning. One is just on State and local preparedness, where I think we have focused a little bit more here than the President has. I think we need to talk about that, because with the buildup of vaccines, the stockpiling of anti-virals and stuff, if we don't have the public health infrastructure out there to educate

people, to handle the stockpiles, to deliver the medicines, then it doesn't do much good we have all these stockpiles. So, that's the one area where I think there's a slight difference between our approach and what the administration has asked. But, that said, that's about it. I think we're going to have to, kind of, just focus on that a little bit and get those straightened out.

Last, I would just hope that this remains as an emergency. I was informed this morning by the Secretary that—it's something I missed yesterday—that the President had asked for this as an emergency. That's the way we put it in our appropriations bill. I hope that the House will acquiesce in that and not try to get into some battle over offsets and things like this. This is a true emergency, and it ought to be handled as such.

Last, this is the proper place for this, in the Labor, Health and Human Services, Education Appropriations Subcommittee of the full Appropriations Committee. I, again, thank my chairman, Senator Specter, for taking the lead on this, as he has on so many other events and things that deal with the health of the American people.

With that, Senator Specter, thank you very much.

Senator SPECTER. Thank you very much. Thank you very much, Senator Harkin.

We're pleased to have with us the chairman of the full committee, who's also, in addition, a member of this subcommittee.

Senator Cochran, would you care to make an opening statement?

#### STATEMENT OF SENATOR THAD COCHRAN

Senator COCHRAN. Mr. Chairman, thank you for convening this hearing. We appreciate your leadership and the leadership of the President in this effort to protect the public health of our country.

The President has submitted a comprehensive proposal to defend against, and to prepare the Nation for, pandemic influenza. It will require our best efforts. This includes the Congress, our Nation's research facilities, and the capacity of our public health officials and private industry all working together to help ensure that we protect the public health of our country.

We thank the witnesses. We appreciate the time and effort you have put into this effort to this point, and your willingness to come discuss the details of the proposal and funding needs for successfully defending against pandemic influenza.

I thank you very much.

Senator SPECTER. Thank you very much, Senator Cochran.

Senator Murray, would you care to make an opening statement?

Senator MURRAY. I would.

#### STATEMENT OF SENATOR PATTY MURRAY

Senator MURRAY. Thank you very much, Mr. Chairman, for calling this really critical hearing. I think that we all recognize that a flu pandemic is a major public health threat, and we can't afford to play catch-up after a major outbreak.

Yesterday, we did see the President unveil his new national strategy, and I think it's important to hear now from the administration about how we plan to carry this out.

But it's also really important to find out how we responsibly pay for this \$7.1 billion effort. Yesterday, the President indicated, as Senator Harkin just mentioned, that it would be funded through emergency spending. I agree that a flu pandemic is an emergency, and it meets the requirements of an emergency demonstration. I hope the administration doesn't make the same mistake it made last week in its latest Katrina package, something we all considered an emergency, where the administration proposed \$2.3 billion in cuts to pay for part of that Katrina package. I don't understand, frankly, how something is an emergency one day and then requires corresponding budget cuts the next day. So, I hope there is no attempt to offset this flu pandemic package with cuts to other programs. Some of my colleagues may be inclined to take the money away from other health programs to pay for this plan, but that would create a lot more problems and more funding shortfalls. We can't forget with this that it's the local hospital, the local community clinic, and the local emergency room staff who are going to the—on the front lines of any outbreak. So, if we cut other funding from our public health infrastructure to fund this new strategy, we're going to make it even harder for those on the front lines to respond effectively.

So, I would just encourage my colleagues to remember that cutting our public health infrastructure to fund this new strategy is going to create problems and dangers when local communities are required to respond to any outbreak.

We have a lot of work ahead to do to protect our citizens. We don't have a vaccine that's ready to be administered on a global scale, and that puts an even greater emphasis on giving our local public health officials the tool to diagnosis and contain any outbreak that may occur.

So, Mr. Chairman, I thank you very much for holding this hearing. I appreciate the Secretary, CDC, and NIH for being here, and I look forward to your testimony.

Thank you very much.

Senator SPECTER. Thank you very much, Senator Murray.

Secretary Leavitt is joined by part of his really outstanding team. We're pleased to have Dr. Julie Gerberding here, Director of CDC. When I wanted some spot information recently, she was available, in Bangkok, and—accompanying Secretary Leavitt on a trip there on the scene. Dr. Fauci is here today—does outstanding work as Director of the National Institute on Allergy and Infectious Diseases; and Dr. Bruce Gellin, Director of the National Vaccine Program Office; and Dr. Raub, Science Advisor to the Secretary.

We appreciate all of your being here, because we may ask some questions which go beyond the testimony of Secretary Leavitt.

Secretary Leavitt is the 20th Secretary of the United States Department of Health and Human Services. He's had a very distinguished record in public service—the Administrator of the Environmental Protection Agency, elected Governor of the State of Utah on three occasions, served 11 years in that position, has a bachelor's degree in economics and business from Southern Utah University.

Mr. Secretary, we appreciate the job you're doing. You've got your hands full, and we want to help. We won't have any clock running for Secretary Leavitt, unlike the clocks for the Senators.



The floor is yours, Mr. Secretary.

**STATEMENT OF HON. MICHAEL O. LEAVITT, SECRETARY OF HEALTH AND HUMAN SERVICES, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**ACCOMPANIED BY:**

**DR. ANTHONY FAUCI, DIRECTOR, NATIONAL INSTITUTE ON ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**DR. BRUCE GELLIN, DIRECTOR, NATIONAL VACCINE PROGRAM OFFICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**DR. JULIE GERBERDING, DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**DR. WILLIAM RAUB, SCIENCE ADVISOR TO THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES**

Secretary LEAVITT. Thank you, Mr. Chairman. I'll do my best not to abuse that privilege. I will summarize, briefly, so we can get on to questions.

In my opening statement, I think it would be valuable for me to just frame the subject. Pandemics. The bottom line is, they happen. Ten times in the last 300 years, and three times in the last 100 years, viruses have mounted a massive pandemic assault that has made masses ill and caused millions to die. They happened before, they'll happen again, and we need to be prepared. Whenever there is a human-to-human transmission of a dangerous killer virus, there is risk everywhere in the world.

Leadership, as Senator Harkin pointed out, right now is creating an atmosphere of information without inflaming. It is inspiring preparation and not panic. Our deliberate moving forward on this plan constitutes that action.

The current worry, of course, is the H5N1 virus. It is primarily an animal disease right now. The probability of it making the transition to a human-to-human transmittable virus is unknown, uncertain, but the troubling signs are clearly there. The ramifications would be so significant, so world-changing, that we have no alternative but to prepare. But if it isn't the H5N1 virus, it will be another virus, as it has in past, because, in fact, pandemics do happen.

As indicated yesterday, the President laid out a broad national strategy. He called upon Congress to appropriate the \$7.1 billion that's been mentioned. Later today, or today—simultaneous with this hearing, I will be laying out with more granularity the plan that HHS is putting forward on the medical and public health portion of it. It constitutes roughly \$6.7 billion of the \$7.1 billion.

I'd like to take just a moment and describe, in broad outline, the nature of that plan. I've put a placard up that lists the six primary components. I'll review them briefly.

The first is international surveillance. Many have compared a pandemic to a forest fire. If you're there when the spark happens that sets the fire off, you can mitigate its damage simply by snuffing it out. If it's allowed to burn, it will burn beyond containment very rapidly. In order to identify when the spark happens in a pandemic or a forest fire, you need good surveillance. In pandemics, good surveillance means laboratories, it means epidemic investiga-

tors, it means rapid-response teams, it means American experts on the ground in Southeast Asia and other countries where we can be of assistance to them, it means having a joint containment plan with our friends and neighbors around the world so that when the spark happens, if we can get there fast, we can contain it and save the world from the destruction it could bring.

The second point is domestic surveillance. Just as in the international arena, if a pandemic virus reaches the shores of the United States, we need to know. We need to know fast, and we need to know that—with the most possible certainty, how broadly it has spread so that we can contain it. That, again, means laboratories, it means medical training for local providers, it means a good communication network.

The third point on the plan is the foundation of this plan, which is vaccines. The good news is, we have a vaccine. The scientists at NIH have developed a vaccine that produces sufficient immune response that it can protect a human being when given at the proper dosage. The bad news is, we fundamentally lack the capacity to manufacture it in sufficient volumes in time.

The plan lays out two broad objectives. The first is to develop 20 million courses of the closest vaccine possible, given our information today, and then the capacity to produce, within a 6-month time, up to 300 million courses of the appropriate vaccine once the virus has been detected and isolated.

To do that, we'll undertake three major tasks. The first is to expand our egg-based vaccine production. The second is to develop new cell-based technology. The third is to test adjuvant technologies, which are dose-sparing technologies, allowing us to spread the limited vaccine that we have available further.

In the long run, we would expect to see that 300 million courses that we could produce within a 6-month period break down roughly to 62,500,000 egg-based vaccines and roughly 237,500,000 cell-based vaccines.

As we begin the development, we obviously need to have a great deal of flexibility in the way we approach it. We would see ourselves developing a strategy that would operate within four corners.

The first is that these technologies need to be domestically produced. In a pandemic, it is a broad view that we will undoubtedly only have the vaccine we can produce on our shores. So, what we develop needs to be produced here. Second, we need to achieve the lowest-cost, highest-quality quotient. The third is that we need to have flexibility, the ability to move within the technologies. If one is working better than another, we need to be able to shift our capacity there. Fourth, we need to produce continuous annual flu benefit so that we're developing a public health asset in doing so.

The fourth category that you'll note is anti-virals.

I'd like to make an important point. Anti-virals are an important part of a comprehensive plan, but anti-virals are not the equivalent of preparation. There is no certainty of their effectiveness on any particular virus. There is no capacity to change the anti-viral if the virus adapts. There are distribution dilemmas.

Nevertheless, it's a very important part of a comprehensive plan, and the plan does call for us to build a stockpile of 20 million

courses. The vendors have represented to us that those could be delivered by the fourth quarter of 2006, and we could build our collective stockpiles to 81 million by the summer of 2007. Again, that's a date vendors are able to meet.

We will focus on this as a locally deployable asset. Senator Harkin, you mentioned the fact that we need to work very closely with State and local officials. The timeframes involved in the deployment of anti-virals are crucial.

I would like to point out that, in the anti-viral category, 400 million of it would be focused on the development of new and better anti-virals. We think that's an important part of a comprehensive plan, is the continual upgrading of our anti-viral arsenal.

The fifth category is communication, informing the public with available information so that every community knows what to expect. We need to begin the development of these materials before a pandemic strikes.

The last piece I would point out is State and local preparedness—again, something that Senator Harkin and Senator Specter both commented on. This is a unique kind of disaster. It is not like Katrina or Rita or any other hurricane, where we have a confined area of disaster. It is a disaster of unlimited distribution, with an unconfined time, and has to be managed locally. The President indicated, in his speech yesterday, the need for us to immediately begin working with State and local officials to develop readiness plans in every community.

Last, I would just say, the budget that's been presented is in two major accounts: vaccine and anti-virals. The vaccine and anti-viral portion totals \$4.7 billion, and the other public health efforts, roughly \$500 million.

In conclusion, I would like to just make this point. We don't know whether the H5N1 virus will be the spark that will set off a global pandemic. We do know that, at some point in time, a pandemic is likely to happen. History makes that very clear. There may be those, if H5N1 does not become the spark, that look back and say we overreacted, or there may be some who would say, "Well, they cried wolf." But I would like to suggest that this is about long-term pandemic readiness, and that at the conclusion of this plan, there will be five things that will be true of this country that are not totally true today.

The first is that we will have cell-based technology that will be the key to surging up the production of pandemic flu vaccines quickly and establish an enormous asset scientifically and in public health.

The second is, we can make a giant step forward on our annual flu capacity to be able to protect the citizens of this country on a year-to-year basis.

Third, our State and local governments will be better prepared, not just for pandemic, but for every kind of medical emergency.

Fourth, we'll have an international network of surveillance that will protect not just citizens of the United States, but people around the world.

#### PREPARED STATEMENT

Last, we'll have the peace of mind of knowing that we are ready.

Thank you, Mr. Chairman.  
[The statement follows:]

PREPARED STATEMENT OF HON. MICHAEL O. LEAVITT

Good morning Senator Specter, Senator Harkin, and members of the Subcommittee. I am honored to be here today to present the President's request for funds for the HHS Pandemic Influenza Plan, which is an integral component of the National Strategy for Pandemic Influenza, which the President announced yesterday. In the event that an outbreak of pandemic flu hits our shores, it will surely have profound impacts on almost every sector of our society. Such an outbreak will require a coordinated response at all levels of government—Federal, State, and local—and it will require the participation of the private sector and each of us as individuals. HHS has been a leader in this effort, and today, with this budget request and the release of the HHS Pandemic Influenza Plan, we are taking another major step forward to improve our preparedness and response capabilities.

The threat of an outbreak of pandemic influenza is real. An influenza virus strain with potential to cause a pandemic of human disease could emerge with little or no warning and in almost any part of the world, as occurred 3 times during the 20th century. Influenza viruses infect birds, pigs, and other animals, as well as humans. The ability of these viruses to cross the species barrier from time to time creates the possibility for the appearance of new viral strains that have the potential to be highly infectious, readily transmissible, and highly lethal. If a pandemic virus strain emerges, it is estimated that upwards of 30 percent of people exposed could become infected and the death rate will likely be considerably higher than that seen with seasonal influenza. Faced with such a threat, the United States and its international partners will need to respond quickly and efficiently to reduce the scope and magnitude of this serious health threat.

Today's threat is the H5N1 avian influenza strain, which is spreading widely and rapidly in domestic and migratory fowl in Asia and now in Eastern Europe. While the virus has not demonstrated the ability to spread efficiently from person to person, it has infected more than one hundred people in Asia and approximately 50 percent of these known cases have died. The virus is now endemic in many bird species and in several countries, so elimination is not feasible. The feared pandemic could become a reality if this virus mutates further, remains highly virulent, and acquires the capability to spread as efficiently from person to person as do the commonly circulating virus strains that produce seasonal influenza epidemics. But even if H5N1 does not lead to a pandemic, the likelihood of an influenza pandemic at some point remains high. This is why we need to prepare now in order to swiftly and efficiently respond to an outbreak. I have come here today to ask for your support for funding for the HHS Pandemic Influenza Plan, which is our portion of the National Strategy for Pandemic Influenza.

This week, we are taking important steps forward. Today, I am releasing the HHS Pandemic Influenza Plan, which is a blueprint for pandemic influenza preparation and response. The HHS Plan provides guidance to national, State, and local policy makers and health departments. The goal is for all involved to achieve a state of readiness and quick response.

The HHS Plan includes an overview of the threat of pandemic influenza, a description of the relationship of this document to other Federal plans and an outline of key roles and responsibilities during a pandemic. In addition, the HHS Plan specifies needs and opportunities to build robust preparedness for and response to pandemic influenza. The preparations made for a pandemic today will have lasting benefits for the future.

A pandemic outbreak will allow very little time to develop new capabilities or build surge capacity for response if these efforts are not already in place. Unfortunately, current capacity for domestic manufacture of influenza vaccine and antiviral drugs can meet only a small fraction of the need projected for a pandemic response. If we are to have the capabilities and capacities needed when a pandemic emerges, the investments to bring them about must be made now. That is why the President is requesting additional fiscal year 2006 appropriations for HHS totaling \$6.7 billion for the HHS Pandemic Influenza Plan. Our goals in seeking this funding are to be able to produce a course of pandemic influenza vaccine for every American within six months of an outbreak; provide enough antiviral drugs and other medical supplies to treat over 25 percent of the U.S. population; and ensure a domestic and international public health capacity to respond to a pandemic influenza outbreak.

First, we must establish the domestic vaccine production capacity our Nation will need to protect all Americans within six months of detection of a virus that begins to spread efficiently from human to human. In anticipation of an influenza pan-

dem, we must stockpile in advance sufficient quantities of pre-pandemic vaccine that is protective against circulating influenza virus strains with pandemic potential in order to be in a position to initiate vaccination of health care workers and front-line workers critical to the pandemic response. These pre-pandemic vaccine stockpiles must be regularly reevaluated and potentially replenished as the pandemic virus threat mutates and changes, and as vaccine potency degrades over time. In addition, as the virus strains evolve and potentially escape protection by the existing vaccines, newer vaccines that better match the current pandemic strain will need to be produced and stockpiled. The Nation must also expand its stocks of antivirals, personal protective equipment (masks, gloves, etc.) and other supplies to help provide a potentially over-burdened healthcare system with the means to treat and care for those who become seriously ill in an influenza pandemic.

Second, we must enhance the disease surveillance systems both internationally and domestically and train the personnel needed to reliably detect an outbreak quickly and to accurately determine its lethality and transmissibility. This includes obtaining samples of the virus from infected humans and animals and having laboratory capacity, personnel, and supplies necessary to conduct rapid analysis. Surveillance is our early warning system, and faster detection will enable public health officials to make recommendations about containment protocols, such as limits on travel and the assembly of large groups of people. Faster detection and identification of emerging influenza virus strains facilitate the conversion by industry to mass production of pandemic influenza vaccines. Better State, Federal, and international diagnostic laboratory systems will also allow for increased surge capacity needed to support front-line medical personnel, and effectively guide the use of scarce drugs, vaccines, and other resources.

Improved surveillance systems, including near real-time collection of data from hospital emergency departments in major metropolitan areas through BioSense, will allow us to continuously track the spread of the virus and the morbidity/mortality it produces and to evaluate the effectiveness of our intervention strategies. This information will be critical to determining the best uses of limited supplies of pandemic influenza countermeasures. We will also track vaccines and immunizations to ensure that we maximize its equitable use as well as its effectiveness and safety.

Third, we must develop in advance domestic and international plans for broad public education efforts that are culturally appropriate and provide critical information in ways that acknowledge different levels of health literacy. These efforts before and during a pandemic will help guide individual actions to prevent and reduce infection and clarify the need for prioritization of scarce vaccines and antivirals and other materials. Our request also includes funding for States and local municipalities to develop and/or update their pandemic influenza response plans and to integrate them with Federal plans.

#### INFLUENZA VACCINE

The Administration has been aggressively working to be able to acquire, over a two-year period, enough H5N1 vaccine and antivirals to protect 20 million people should they become infected with the pandemic virus. On July 15, 2005, the Administration submitted an fiscal year 2006 Budget Amendment totaling \$150 million to implement our "20/20" plan. This strategy was designed to give us considerable experience with commercial-scale manufacturing of this new vaccine, and provide some pre-pandemic vaccine to our stockpile. However, as we are only able to obtain pre-pandemic vaccine during the few months of the year when influenza vaccine manufacturers are not running at full capacity making the seasonal trivalent vaccine, we are severely limited in the quantity of vaccine that we can stockpile. In addition to this limitation, since the submission of this Budget Amendment, we received results of H5N1 vaccine clinical trials funded by NIH. As part of this strategy, the NIH has funded clinical trials of H5N1 influenza vaccine—which provided good news and, at the same time, sobering news. The good news was that the vaccine we developed works—it provides a good immune response that augurs well for protecting people against the H5N1 virus. The sobering news was that to achieve the desired immune response, the vaccine needed to be six times as potent as the seasonal vaccine—90 micrograms of the hemagglutinin component instead of 15 micrograms—and that two doses are needed for the protective immune response. This has further driven home a point of which we were all aware—that the nation's capacity to produce enough 90 microgram doses of pandemic vaccine was woefully inadequate. We need an aggressive strategy to achieve the needed domestic vaccine manufacturing capacity as quickly as possible, and to initiate similarly aggressive action to implement other immediate preparedness strategies beyond these critical vaccine needs. This budget request is just such a strategy, building on the July

Budget Amendment and responding aggressively to the results of the NIH clinical trials and our growing concern that a pandemic could involve hundreds of communities across the United States and around the world.

Of today's \$6.7 billion funding request, approximately \$4.7 billion would go toward investments in creating pandemic influenza vaccine production capacity and stockpiles that will ensure that enough vaccine will be available to every American in the event of a flu pandemic. To accomplish this, HHS will pursue a multi-faceted strategy to create, as soon as possible, domestic influenza vaccine manufacturing capacity aimed at producing 300 million courses (two doses of vaccine per person) within six months of the onset of an influenza pandemic. With this immediate investment, the increased production capacity and related stockpile expansion will be achieved in phases between 2008 and 2013.

The initial component of this strategy is to expand the number of licensed domestic egg-based influenza vaccine manufacturers from the single one that currently exists. This would give the United States the ability to develop a 20 million course (40 million doses) pre-pandemic vaccine stockpile by 2009—without disrupting the production of annual seasonal influenza vaccine. In the event of a pandemic outbreak, or perhaps before, the vaccine stockpile would be used to immunize healthcare workers, front-line responders, vaccine manufacturing personnel, and others critical to the pandemic response. Once this capacity is developed, current egg-based production techniques could then provide about 60 million courses of vaccine within six months of an outbreak, or about 20 percent of our goal of 300 million courses within six months.

The ultimate surge capacity goal of 300 million courses of vaccine cannot be achieved from egg-based production alone. Our best hope for creating capacity in the United States for rapidly ramping up vaccine production at any point in time is expansion and acceleration of our investment in cell-based influenza vaccines—and much of our planned investment goes toward this initiative. While promising, success of cell-based influenza vaccine production and licensure is still years off, and not a guarantee. Therefore, our vaccine capacity expansion strategy invests in both cell-based vaccines and the traditional, tried and true egg-based vaccines. Therefore, HHS, in collaboration with the vaccine industry and its academic partners, will invest in the advanced development of cell-based techniques for manufacturing pandemic influenza vaccines. By financing the establishment of new cell-based vaccine manufacturing facilities that could open in 2010, our plan will develop the surge capacity needed to provide for the remaining 80 percent (approximately 240 million courses) of the population within six months of a pandemic outbreak.

The HHS Pandemic Influenza Plan also acknowledges that existing manufacturing facilities can be directed to this effort and finances the retrofitting of existing domestic manufacturing facilities that would enable them to convert to production of pandemic influenza vaccine production, in an emergency. HHS will establish contingency arrangements with vaccine manufacturers in conjunction with the Food and Drug Administration so that, at the onset of an influenza pandemic, they will be able to readily adapt their facilities either to produce influenza vaccines or to provide a critical function, such as fill and finish bulk vaccine produced by other manufacturers.

We will also work with industry and academia to support advanced development of dose-stretching technologies, such as the use of adjuvants and new vaccine delivery systems. These investments, if successful, will extend the pandemic influenza vaccine supply and allow more Americans to receive pandemic vaccines sooner. We will also invest in research that may have potential to lead to broad-spectrum vaccines to protect against multiple and emerging strains of influenza viruses. This would allow for stockpiling of vaccines that could be useful even as the virus strains evolve and change.

However, as we seek to build domestic manufacturing capacity, we also know that the threat of liability exposure is too often a barrier to willingness to participate in the vaccine business. As we recognize the desperate need to create and expand vaccine manufacturing capacity, we have to remove such deterrents to participation by those with the knowledge and experience to accomplish this. It is crucial that those engaged in this work be shielded from unwarranted tort suits. Accordingly, the Administration is proposing limited liability protections for vaccine manufacturers and providers, with an exception to allow suits to proceed against companies who act with willful misconduct. We believe this proposal strikes an appropriate balance of removing the liability risks that dissuade companies from producing pandemic countermeasures, while still retaining appropriate access to court remedies.

## ANTIVIRALS

We also recognize the importance of having available a sufficient supply of stockpiled antiviral drugs to treat and care for infected individuals. For this, we request an investment of \$1.4 billion. These funds would help us achieve the national goal of having available 81 million courses of antivirals, which would be sufficient to treat 25 percent of the U.S. population (75 million courses) and a reserve supply (6 million courses) that could be used to contain an initial U.S. outbreak. Funding would also be used to accelerate development of promising new antiviral drug candidates in collaboration with academia and industry, since none of the antivirals today are likely to work perfectly against pandemic influenza.

Of the 81 million courses, six million courses will be designated to contain the first isolated domestic outbreaks. Of the 75 million courses that will be used to treat those who are infected with the pandemic virus, HHS would fully fund the procurement of 44 million treatment courses to provide protection to the highest priority groups in the event of an influenza pandemic. We will also work with our State partners to encourage them to acquire antivirals for rapid use for their populations. To help support these States efforts, we would establish contractual arrangements with manufacturers of approved antivirals whereby States may purchase up to 31 million treatment courses and HHS would pay for approximately 25 percent of the costs of these drugs. This arrangement will also ensure a more coordinated inter-governmental approach in the acquisition of antiviral drugs and pre-deployment stockpiles of antivirals around the nation. A guaranteed acquisition of up to 81 million courses of antiviral drugs will enable manufacturers to make significant expansion in its U.S.-based manufacturing capacity—thereby positioning itself to meet future demands much more readily than currently is possible.

I have personally been meeting with leaders of relevant vaccine manufacturers to determine how they might participate in preparedness for and response to a pandemic. To facilitate the development of new antivirals, HHS will collaborate with industrial organizations to develop, obtain approval, and establish commercial production of new antivirals that would help protect the citizens of our Nation.

## DISEASE SURVEILLANCE, PUBLIC HEALTH INFRASTRUCTURE, AND RISK COMMUNICATION

In addition to the production and stockpiling of vaccines and antivirals, enhancing domestic and international resources to expand surveillance, strengthening public health infrastructure, and effectively communicating with the public about risks of an influenza pandemic are important components of the HHS Pandemic Influenza Plan, for which we are requesting \$555 million. A critical step in enhancing public health infrastructure and international collaboration will be to implement and refine surveillance and epidemiological response. These investments will help us detect, investigate, and respond to the onset of a potential influenza pandemic anywhere in the world without delay. Because influenza characteristically spreads beyond country boundaries, we have included in our request funding to be used internationally. These funds will follow the evolution of the virus in Asia, detect human cases, and help contain outbreaks, where feasible.

With an enhanced domestic and international early warning system, we will be better positioned to mount an immediate emergency response to characterize the outbreak; obtain viral samples for analysis and possible vaccine production; and we will have a greater chance to prevent, contain, and/or retard the spread of infection. The ability to continually analyze data to help predict the further course of the pandemic will help guide the choice and timing of interventions (drugs, vaccine, and public health measures) and will help assess the efficacy of these interventions.

Enhancing our public health infrastructure also includes expanding the science base at the Food and Drug Administration, thus allowing for expedited regulatory review of pharmaceutical industry initiatives to develop the necessary new vaccine technologies, as well as speeding the licensure of the facilities and vaccines produced within them.

Risk communication is another integral part of an effective public health response plan. We must have in place the capability to employ effective risk communication practices that will guide us in providing the American people with the accurate, timely and credible information they will need to protect themselves and help others during an influenza pandemic. To ensure that our communications efforts resonate with target audiences, we will solicit the public's active participation and involvement in our efforts to develop relevant, easy-to-understand information and materials regarding influenza in general, and pandemic influenza in particular. To help in this effort, we have established a website devoted exclusively to this topic, [pandemicflu.gov](http://pandemicflu.gov).

Public participation and involvement may include engaging the public in discussions on State and local community preparedness; assisting communities in developing procedures for disseminating information and guidance for all segments of our diverse population; and developing targeted informational tool-kits for distribution to particular stakeholders such as educators, physicians, and employers.

#### STATE AND LOCAL PARTNERS

Pandemic planning needs to incorporate every department of the Federal government but must also go deeper than that. Every State and local government must have a pandemic plan. Unlike most disasters, a pandemic outbreak can happen in hundreds or thousands of places simultaneously. The Federal government will play an important role, but engaged state and local partners are necessary for our success. Over the coming days, I will be asking the governors, mayors and State and local health and preparedness officials to join me in a concern we all must share—preparing for a pandemic should one happen. Everyone in society has a role.

For example, the Federal Government can deliver stockpiles of medication and supplies to a city in the United States in a matter of hours—but it is distribution at the State and local level that defines victory. In a moment of crisis, if we are not able to deliver pills to people over wide areas in short time frames, lives will be lost. We need to create a seamless preparedness network where we are all working together for the benefit of the American people. Of the \$555 million for surveillance and public health infrastructure, our Budget request includes \$100 million specifically for State and local pandemic preparedness efforts. And, as mentioned previously, we will provide incentives to States to purchase their own stocks of antivirals by allowing them to buy off of HHS-negotiated contracts and subsidizing about 25 percent of the cost.

The plan and budget request outlined above will greatly improve our short and long term preparedness posture. We are well-positioned to implement the plan and invest these new resources wisely and effectively only because of the substantial pandemic influenza activities already underway at HHS. Scientists at the National Institutes of Health and the Food and Drug Administration, working with industry, have developed a vaccine that produces an immune response sufficient to provide protection from the H5N1 virus. This bodes well for our ability to develop a vaccine against a pandemic virus that may evolve from the current H5N1 strain. In September, HHS awarded a \$100 million contract to manufacture 3.3 million doses of H5N1 vaccine, which at two doses per person would be enough for 1.67 million people. In addition, just last week we announced the award of a \$62.5 million contract to produce even more vaccine. We have also initiated contracts to secure an adequate supply of specialized eggs to initiate surge production at any time of year.

This is not a new undertaking. I have worked with many of you, and appreciate the Subcommittee's commitment to helping our nation prepare to meet this threat. We are making progress, and with your help will continue to do so. We realize we are asking for significant funding at a time when the Administration and Congress are trying to control spending and reduce the deficit. But we have controls in place at the Department, and within the structure of the funding request to ensure that these funds are used wisely and responsibly. When American lives are at stake, we must take action to protect them. We acknowledge that investing in this plan without perfect knowledge of the future is expensive, and not without risk. However, waiting until a pandemic begins before preparedness is undertaken would be so much more expensive in terms of American lives and economic impact. In our view, waiting is not an option.

I look forward to answering your questions, and more importantly, to working closely with you and all members of Congress as we move forward together to protect our citizens.

#### PANDEMIC FLU PREPAREDNESS

Senator SPECTER. Thank you very much, Secretary Leavitt.

We'll now proceed with 5 minute rounds of questioning by the Senators.

Secretary Leavitt, without seeking to ascribe blame, but looking to preventative measures for the future, we find ourselves caught up in an emergency situation. The President was emphatic that nobody has pandemic flu in the United States yet, and there are good reasons, as Senator Harkin points out, to be alert, but not be pan-



icked. But looking backward—20-20 hindsight is great—when did we first have any indication that this kind of a problem might confront us? The subordinate question—I don't like to ask two questions at the same time, but the subordinate question is, Could we have acted sooner to avoid a situation where we're now, in effect, running for cover?

Secretary LEAVITT. As I indicated in my opening statement, Mr. Chairman, pandemics have been with us for as long as recorded history, 10 in the last 300 years, 3 in the last 100. Periodically, they happen. The current virus is our concern.

Senator SPECTER. They killed millions of people, so we know how devastating they are. What is the answer to the narrow question: When did we first have some inkling, however slight, that we might be facing this kind of a problem in November 2005?

Secretary LEAVITT. In 1997, the H5N1 virus first made its appearance. It was in Hong Kong. The Hong Kong Government acted in a bold way. They destroyed 1.4 million chickens and began using basic public health techniques to contain the virus. They did so successfully. It did not begin to manifest itself again until 2001, where there were some limited number of cases, and then in 2002–2003. We began to buy anti-viral medications, in December 2003. We bought them again in 2004. The NIH began working on a vaccine. I'll ask Dr. Fauci to give you a brief answer on this, as well, because, in 2004, they were able to isolate the virus by using a sample from a victim in Vietnam.

Senator SPECTER. What did the U.S. Government do in 1997, when this issue first reared its ugly head?

Secretary LEAVITT. I'm going to ask Dr. Fauci to respond to that.

Senator SPECTER. That was long before your watch, but what was done? Dr. Fauci—

Dr. FAUCI. Mr. Chairman, in anticipation of the situation where we are now with regard to the need for a vaccine, the 1997 isolate from the Hong Kong cases that the Secretary mentions was actually used in collaboration with industry to create a seed virus vaccine and test that vaccine in 1999. In fact, the data that we're looking at now is looking at how that vaccine has now covered the virus as it has evolved into the 2003, 2004, and 2005 version.

We updated the vaccine in 2004, when it became clear that there was a considerable amount of accelerated activity among birds with infections in Southeast Asia. We took a virus from a Vietnamese patient 1½ years ago, made a vaccine, contracted for a certain number of doses for the clinical trial, and the data that we made public this past summer was related to that vaccine trial that we actually started over 1 year ago in isolating the virus and getting it. So, we started in 1997 and continued it along, and accelerated it as we got into 2004.

Senator SPECTER. The information provided to the subcommittee is that the only United States-based influenza vaccine manufacturing facility is an egg-based facility owned by Aventis Pasteur and located in Swiftwater, Pennsylvania. This came to my attention last year. They had an emergency for \$10 million, which is not a huge sum of money. But we had to do handstands to find a way to fund them for \$10 million, or they were about to lose their ability to provide what limited facilities we had.

I'm interested to know—and I'm going to observe the time limits, because I want everybody else to, and I've only got 16 seconds left, but I would like to have, in writing, the chronology of what was known when and what you told Congress and what we could have done to have avoided being precisely where we are now.

[The information follows:]

#### HHS PANDEMIC INFLUENZA PREPAREDNESS INITIATIVES

*1989.*—CDC establishes collaborative agreements between the Institute of Virology, Beijing, and CDC's Influenza Branch were implemented in 1989 to establish six surveillance sites in China, considered a geographic focal point for newly emerging epidemic and pandemic variants of influenza. In 1994, a five year contract was awarded to the Institute to ensure the continuation of the program.

*1993.*—National Vaccine Program Office, in collaboration with CDC, begins review of pandemic preparedness and drafting of national plan.

*February 1995.*—National Vaccine Program Office hosts national stakeholders meeting on pandemic planning.

*1995.*—CDC initiates a cooperative agreement with the Council of State and Territorial Epidemiologists to facilitate and local pandemic preparedness planning.

*May–December 1997.*—CDC assists the Hong Kong Department of Health in the investigation of 18 cases of influenza A (H5N1) in humans, including the initial identification and molecular characterization of avian H5N1 in the index case and 7 subsequent patient isolates.

*On-going since 1997.*—CDC generates sequence information on avian influenza viruses to trace the origin of the H5N1 isolates, design updated primer sets for PCR-based diagnostics and clone genes for vaccine production.

*August 1997.*—CDC conducts outbreak investigations on Avian Influenza (H5N1) infections which occur in both poultry and humans in Hong Kong. This is the first time an avian influenza virus has ever been found to transmit directly from birds to humans. The virus kills six out of 18 people infected. All poultry in Hong Kong are culled (World Health Organization).

*August 1997.*—CDC and FDA publish an update on pandemic preparedness in the *Journal of Infectious Diseases*.

*1997.*—CDC develops a rapid and highly specific serologic testing procedure to detect the presence of H5 antibody in humans which was used to analyze over 2,000 serum samples collected from the Hong Kong investigation. This assay was used to determine if person-to-person had occurred and was a key tool in epidemiological studies to evaluate risk factors for H5N1 infection. Results from these studies (1998) determine that exposure to poultry in the retail markets was the primary risk factor for influenza (H5N1) but that human-to-human transmission, although rare, had occurred.

*September 1997.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to Baylor College of Medicine (Principal Investigator (PI)—Pedro Piedra) to examine whether vaccinating a large percentage of children can protect a community from a possible influenza pandemic.

*November–December 1997.*—CDC develops and distributes over 350 supplemental kits for the identification of influenza A (H5N1) are distributed to domestic and World Health Organization Collaborating Laboratories in response to reported human H5N1 cases in Hong Kong.

*December 1997.*—CDC provides HA genes of 1997 virus to Protein Sciences for production of recombinant HA.

*1997.*—CDC's Influenza Branch initiates development of H5N1 reassortant viruses as candidate vaccines. Two groups, A and B, of influenza A(H5N1) are differentiated using antigenic properties; this observation proves important for selecting potential vaccine candidate viruses (1998).

*1997.*—CDC develops and local planning guide, and funds four States and one local health department to critique it. Over the next 4 years 14 s were funded to develop their own plans: CA, CT, FL, IN, KS, MD, MN, NE, NH, NY, NM, NJ, SC, WA.

*1998.*—CDC begins an active collaboration and provides funding to the Los Alamos National Laboratories (LANL) to develop and improve an international influenza database. The Influenza Sequence Database features a web interface and can be accessed at <http://www.flu.lanl.gov>.

*January 1998.*—In order to detect the possible importation of influenza A (H5N1) strains into the United States, CDC issues recommendations to s public health officials to establish hospital based surveillance for influenza A (H5N1). Specimens col-

lected as part of this effort are sent to NIH's Vaccine Test and Evaluation Unit for viral isolation. No influenza A (H5N1) infections were identified.

*1998.*—CDC develops serology testing to screen for antiviral resistance.

*1998.*—National Institute of Allergy and Infectious Disease (NIAID) awards a contract to Protein Sciences Corporation (PI, John Treanor) for the production of a recombinant H5 hemagglutinin vaccine. Within three weeks, the company produces an investigational vaccine which is tested in NIAID-supported clinical trials.

*January 1998.*—National Institute of Allergy and Infectious Disease (NIAID) awards the “Influenza Pandemic Preparedness in Asia” contract to St. Jude Children’s Research Hospital (PI, Dr. Robert Webster) to:

- Establish an animal influenza surveillance center in Hong Kong.
- Determine the molecular basis of transmission of avian flu viruses.
- Provide characterized viruses suitable for vaccine development.
- Support training of new laboratory personnel in the areas of avian influenza epidemiology and virus diagnostics.
- Produce reagents.

*July 1998.*—CDC broadcasts a satellite videoconference on State and local pandemic preparedness.

*August 1998.*—National Institute of Allergy and Infectious Disease (NIAID) supported scientists discover that human influenza A viruses employ the enzyme plasmin to help chop hemagglutinin in two. The discovery may explain what amplifies the disease-causing power of influenza A virus and makes the virus uncommonly deadly.

*August 1998.*—CDC seeks to strengthen international laboratory diagnostic capabilities, improve surveillance for influenza, and increase networking among participating countries by offering an international course on the diagnosis of influenza viruses in Panama City, Panama.

*1998.*—CDC engages in collaborative efforts toward vaccine development by working with scientists at Aviron to produce an attenuated virus that is immunogenic and protects chickens and ferrets from wild-type H5N1 virus challenge. CDC also provides influenza A (H5N1) cDNA to Protein Sciences for the production of recombinant H5 hemagglutinin vaccine, and to Dr. Harriet Robinson at Yerkes Regional Primate Center for the generation of candidate DNA vaccines.

*December 1998.*—National Institute of Allergy and Infectious Disease (NIAID) awards a contract to Protein Sciences Corporation (PI, John Treanor) for the production of a recombinant H5 hemagglutinin vaccine. The company produces an investigational vaccine which is tested in NIAID-supported clinical trials.

*1998.*—CDC develops a mouse model (mammalian model) to investigate the pathogenesis and immunity to influenza A (H5N1) viruses. This model is also found applicable for H9N2 viruses in 1999.

*January 1999.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to the University of Wisconsin (PI, Dr. Yoshihiro Kawaoka) to investigate the molecular mechanisms of influenza pandemics. NIAID-supported researchers for the first time succeed in engineering an influenza A virus entirely from cloned genes, a breakthrough that could lead to improved influenza vaccines and new influenza-based gene delivery systems.

*March 1999.*—National Institutes of Allergy and Infectious Disease (NIAID)-supported researchers at St. Jude Children’s Research Hospital and the University of Wisconsin demonstrate that a new DNA-based vaccine protects mice from experimental challenge with the H5N1 virus.

*April 1999.*—CDC provides technical assistance to the Hong Kong Department of Health and participates in a notable investigation of influenza A (H9N2) in two humans in Hong Kong. Although the threat from this outbreak was determined to be low, it illustrates the need to rapidly assess and monitor novel influenza viruses in both poultry and humans.

*October 1999.*—CDC delivers 2 courses on the diagnosis of influenza viruses in Beijing, China. Fifty-seven participants from 50 Provincial and Municipal Anti-Epidemic Stations throughout China, as well as the Institute of Virology, participated in these courses.

*1999.*—CDC provides funding to more than 15 Epidemiology and Laboratory Capacity (ELC) sites to improve their ability to culture and subtype influenza viruses and facilitate their participation in the sentinel physician surveillance system.

*1999.*—CDC develops primer sets for Polymerase Chain Reaction and genetic sequencing for all NA and HA genes of all influenza subtypes. These primers enable characterization of “untypable” influenza viruses that are sent to the World Health Organization (WHO) Collaborating Center for Reference and Research on Influenza.

*1999.*—CDC uses molecular techniques to evaluate human influenza A H5N1 virus isolates from China and their relationship to circulating virus in China’s bird

populations. Analysis indicates that the highly pathogenic influenza A (H5N1) from the 1998 outbreak was a reassortant of avian influenza viruses, and although quite pathogenic in humans, no reassortment between avian and human genes had taken place.

*1999.*—CDC evaluates the immunogenicity in humans of the recombinant Influenza A H5 HA vaccine produced by Protein Sciences (John Treanor). The highest rate of response was 52 percent.

*December 1999.*—CDC participates in the global Neuraminidase Inhibitors Susceptibility Network (NISN) which is established to address public health and regulatory concerns regarding the potential emergence, and consequences of drug resistance in influenza viruses after licensure of NIs in several countries. The Network includes representative from the World Health Organization (WHO), the four WHO Collaborating Centers for Influenza, and scientists from academic and public health institutions in regions of the world where increasing use of these drugs is anticipated.

*December 1999.*—CDC produces supplemental reagents kits for the detection of H9 avian influenza viruses for global distribution and shares with international collaborators on an as needed basis.

*2000.*—CDC trains staff from the National Institute of Hygiene and Epidemiology, Hanoi, Vietnam at CDC for 3 months in virology laboratory techniques.

*May 2000.*—National Institute of Allergy and Infectious Disease (NIAID)-supported researchers at St. Jude Children's Research Hospital streamline the use of reverse genetics down to eight plasmids—one for each gene in the virus genomes—making the process simpler and less expensive.

*June 2000.*—National Institute of Allergy and Infectious Disease (NIAID) establishes an interagency agreement with CDC and the Johns Hopkins University School of Public Health to evaluate the safety, infectivity, and immunogenicity of live attenuated influenza A virus vaccine candidates for the prevention and control of pandemic influenza A.

*June 2000.*—A course on the diagnosis and antigenic characterization of influenza viruses is conducted in Buenos Aires, Argentina with support from Pan American Health Organization (PAHO) and in cooperation with the CDC. Seventeen participants from six South American countries participate in the course.

*July, 2000.*—CDC broadcasts a second satellite videoconference on State and local pandemic planning.

*August 2000.*—National Institute of Allergy and Infectious Disease (NIAID)'s Vaccine and Treatment Evaluation Units (VTEUs) conduct a clinical trial to compare the immune responses of healthy adults World Health Organization receive either a full dose or a half dose of flu vaccine.

*September 2000.*—National Institute of Allergy and Infectious Disease (NIAID) awards three challenge grants to industry partners for vaccine development:

- NIAID awards a grant to Aviron for the production of a live attenuated vaccine for pandemic preparedness and to develop a cell culture-based flu vaccine (PI, Dr. Shengqiant Li).

- NIAID awards a grant to Aventis Pasteur for the DNA-based generation of avian influenza virus vaccines (PI, Fred Vogel). The project goal is to use a DNA-based system to rapidly produce influenza vaccine candidates, including those against H5 and/or H7 pandemic influenza, which will be tested in clinical trials by NIAID.

- NIAID awards a grant to Novavax (PI, Dr. Louis Potash) to produce several non-egggrown influenza vaccines, with the goal being that the most promising will be prepared for use in clinical trials by NIAID.

*September 2000.*—CDC organizes in collaboration with the Council of State and Territorial Epidemiologists (CSTE) a 2 day workshop for States on pandemic preparedness planning which includes a tabletop exercise and expert led discussions on key issues.

*2000.*—CDC awards funding to 22 State and local health departments through the Epidemiology and Laboratory Capacity (ELC) and Emerging Infections Programs (EIP). The funds were provided to (1) culture and subtype influenza viruses, and (2) recruit and retain influenza sentinel physicians.

*2000.*—CDC works closely with WORLD HEALTH ORGANIZATION, NVPO, NIH, FDA, Council of State and Territorial Epidemiologists (CSTE) and other groups to develop international, national, and State plans that are necessary to prepare for the next influenza pandemic. Through CSTE, CDC's Influenza Branch provides funding for a pandemic planning meeting in Atlanta for the States. The meeting includes a tabletop exercise as well as discussions on pandemic surveillance, priority groups for vaccination, and the potential role for anti-virals.

*2000.*—CDC works with WORLD HEALTH ORGANIZATION and the Chinese Ministry of Health (MOH) on a 5-year (2000–2004) plan of cooperation between the World Health Organization Coordinating Center for Reference and Research on Influenza (WHOCRRRI) at CDC, the WHOCRRRI at the National Institute of Infectious Diseases in Tokyo, Japan, and the Chinese MOH to strengthen influenza surveillance in China. Eight provinces begin participating in the program in 2000, and 11 more provinces join the program in 2001. The establishment of active surveillance sites in China provides an opportunity to document the early appearance of influenza shift and drift variants, and immediate isolation of these strains in China's laboratories may provide virus candidates suitable for vaccine production.

*2000.*—CDC's Influenza Laboratory develops a supplemental kit for the identification of avian influenza A (H5N1). It is known that viruses of this type circulate widely in China and the possibility of their transmission into the human population cannot be excluded.

*2001.*—CDC establishes a research collaboration on avian influenza with the National Institute of Hygiene and Epidemiology, Hanoi, Vietnam to better understand the human animal interface.

*Ongoing since 2001.*—CDC pathotypes a wide range of avian H5N1 viruses, to better understand potential to cause disease in humans.

*March 2001.*—CDC and NVPO organize a 2-day pandemic preparedness planning meeting of national experts to identify possibly ways to use antiviral agents during a pandemic.

*May 2001.*—CDC produces a reverse genetics PR8 based reassortant H5N1 vaccine against A/HK/491/97 (HA) and A/HK/486/97 (NA).

*May 2001.*—St. Jude scientists and University of Hong Kong (HKU) collaborators detect the reemergence of H5N1 in live bird markets in Hong Kong. More than one million birds are culled and "market rest day" is instituted. Researchers also identify quail as the mixing vessel for the spread of avian influenza viruses from aquatic birds to land-based poultry. Live quail is banned from live-bird markets the following year.

*May 2001.*—CDC provides financial and technical support to World Health Organization (WHO) to conduct an assessment of 111 National Influenza Centers that form the backbone of the WHO influenza surveillance system. Analysis from this assessment helps WHO identify critical gaps and helps the WHO coordinating Centers in Australia, Japan, the UK and U.S. target scarce resources to provide future support for training and technical assistance to countries with specific needs.

*June 2001.*—Funding is made available through the Association of Public Health Laboratories to CDC to train personnel from State veterinary labs in recognition of the need to increase the interface between the veterinary and human sides of influenza research.

*July 2001.*—National Institute of Allergy and Infectious Disease (NIAID) sponsors the Reverse Genetics Workshop, bringing together an international group of researchers in influenza viruses as well as scientists outside of the influenza field with research experience in other human viruses, biosafety, and public policy. The Workshop discussions are centered on using local biosafety committees to examine the research work that will be done at federally funded universities and to make risk assessments and safety recommendations.

*September 2001.*—National Institute of Allergy and Infectious Disease (NIAID)-funded investigators at the University of Wisconsin use reverse genetics to discover that the PB2 gene is key to the virulence of the H5N1 influenza strain. This discovery provides important information that may be useful in understanding the emergence of future viruses that may have pandemic potential.

*October 2001.*—CDC produces H9N2 inactivated whole virus pandemic vaccine candidate to A/ck/HK/G9/99 using conventional reassortant techniques.

*October–December 2001.*—CDC describes an ISCOMs-based parenteral vaccine strategy and a mucosal (intranasal) vaccine strategy that induces strong cross-subtype immunity and protects animals from sublethal H9N2 viruses and/or lethal avian H5N1 viruses.

*October 2001–2003.*—CDC supports a pandemic communications fellow to assist States with assessing and updating their State pandemic plans.

*2001.*—CDC's Influenza Branch joins the World Health Organization Animal Influenza Network (AIN) in recognition of the importance of a strong interface between human and animal surveillance systems to improve pandemic preparedness. CDC provides course material and technical expertise for a laboratory training course in Harbin, China for Chinese laboratorians involved in animal influenza surveillance.

*2001.*—CDC's Influenza Branch works with National Vaccine Program Office and several agencies to draft successive versions of the national pandemic preparedness

plan. The “Pandemic Influenza Action Plan” was approved by the Assistant Secretary for Health in 2001.

*2001–2002.*—CDC conducts a study in collaboration with Dr. Doan Nguyen of the National Institute for Hygiene and Epidemiology in Vietnam on the prevalence of avian influenza viruses circulating among domestic poultry in Asia and the risk of avian influenza infection among poultry workers.

*January 2002.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to the American Registry of Pathology for the complete characterization of the 1918 influenza virus (PI, Dr. Jeffrey Taubenberger).

*February 2002.*—CDC produces an Ann Arbor, cold-adapted, live, pandemic vaccine candidate to H9N2 using A/ck/HK/G9/99.

*March 2002.*—CDC reports findings of cohort studies in Hong Kong poultry workers that suggested an increased risk for avian influenza infection from occupational exposure.

*May 2002.*—CDC organizes another national pandemic planning workshop in Atlanta to help States move further along with their pandemic preparedness plans. Over 200 people from the States attend.

*May 2002.*—CDC published first report on the ferret as a model for avian H5N1 virus pathogenesis studies in mammals. The ferret is now recognized by many in the field to be the model of choice for pathogenesis studies and safety testing of candidate vaccine strains derived from highly pathogenic avian viruses.

*June 2002.*—St. Jude scientists and Hong Kong University collaborators detect the second reemergence of highly pathogenic H5N1. More than 20 farms are found to be infected and more than seven different H5N1 genotypes are identified in wild aquatic birds.

*June 2002.*—CDC produces a whole virus H5N2 vaccine candidate with A/Pheasant/NJ/96 using conventional reassortant techniques.

*August 2002.*—St. Jude scientists determine that the H5N1 avian virus that killed six people in 1997 can bypass natural host defenses, which may explain the high lethality of avian strains.

*August 2002.*—CDC scientists, in collaboration with FDA, reported further studies on generation of cross-subtype immunity based on DNA vaccination using conserved influenza A virus genes.

*September 2002.*—CDC and National Vaccine Program Office publish an update on pandemic planning in Clinical Infectious Diseases.

*October 2002.*—CDC participates on a World Health Organization mission to conduct site assessments for six sites in China to assess gaps and needs in influenza surveillance and make recommendations.

*November 2002.*—CDC provides funding to the World Health Organization in Manila (Western Pacific Regional Office) supported a National Meeting and Expert Consultation for development of influenza vaccine policy and a mid-term assessment of the comprehensive 5-year plan for influenza. Two CDC staff participated.

*November 2002.*—CDC’s Influenza Branch increases knowledge and implementation of influenza disease surveillance to keep pace with recent expansions in viral surveillance by hosting a 5-day CDC/World Health Organization (WHO) influenza epidemiology and surveillance training course in Atlanta. Twenty public health epidemiologists from Asia, the Former Soviet Union, and Latin America were trained by instructors from The Netherlands, the United Kingdom, Japan, and WHO.

*2002.*—CDC Influenza Branch works with national and international colleagues to develop guidelines for the appropriate safety testing of candidate vaccine strains against H5N1 influenza, particularly those derived by reverse genetics, in a ferret animal model developed at CDC.

*December 2002.*—National Institute of Allergy and Infectious Disease (NIAID) expands its intramural program to develop live attenuated vaccines for pandemic influenza.

*January 2003.*—A medical epidemiologist from CDC goes to Hong Kong to help investigate two human cases of avian H5 influenza. The outbreak occurred in a setting of widespread reports of respiratory disease with deaths in various parts of mainland China. It becomes clear that the etiology and respiratory disease was not influenza and SARS CoV was subsequently identified.

*February 2003.*—Using CDC laboratory testing procedures, a new highly pathogenic H5N1 avian influenza virus isolate from a human is compared to previous human and avian isolates and is determined to be antigenically distinguishable from currently and previously circulating H5N1 viruses in Asia, including the viruses previously isolated from humans, which has important implications for H5N1 vaccine development.

*2003.*—A CDC publishes a modeling study in the Journal of the American Medical Association that more accurately predicts influenza morbidity and mortality using

national virus surveillance data in its estimates. An influenza modeling group, with personnel from within and outside of CDC is established to formally proceed with further mathematical modeling of influenza's impact.

*2003.*—CDC generates multiple vaccine strains against avian H5N1, H9N2, H7N7, and evaluates preclinical immunogenicity and protective efficacy.

*2003.*—A CDC performs and publishes a study assessing State pandemic preparedness in the *Emerging Infectious Disease Journal*. (EID 2003;12:1645–8)

*February 2003.*—HHS requests \$100 million in fiscal year 2004 for advanced development of pandemic influenza vaccines.

*February 2003.*—CDC deploys staff to Beijing, China to investigate severe respiratory illnesses in Guangdong province following confirmed H5 cases in Hong Kong.

*2003.*—In response to the SARS epidemic and two human cases of avian influenza A (H5N1) in Hong Kong, CDC designs and tests primers and probes for the rapid detection of influenza viruses in original clinical materials isolated from patients with severe clinical symptoms. This diagnostic format is compatible with real-time PCR methods used for detection of SARS and other acute respiratory infections and facilitates testing respiratory samples for multiple agents.

*2003.*—CDC's Influenza Branch develops and conducts training for a joint World Health Organization/CDC sponsored laboratory training course in Atlanta for scientists from the former Soviet Union.

*2003.*—CDC collaborates with staff from Emory University to model the best use of antiviral agents in a pandemic situation.

*March 2003.*—The World Health Organization and Chinese Ministry of Health request CDC's help to train Chinese virologists in laboratory methods for the rapid detection of avian influenza infections in humans. Two CDC scientists travel to Beijing, China to train students from the Chinese National Influenza Center and virologists from several provinces in South China on microneutralization assays for the diagnosis of H5 in human sera.

*March 2003.*—CDC produces and distributes supplemental H5N1 reagents kits for the identification of the new H5 viruses that have surfaced in Asia.

*May 2003.*—CDC conducts an influenza laboratory course organized by World Health Organization/CDC for Eastern European countries. Sixteen participant from 12 European countries participated in the course in Atlanta.

*May 2003.*—CDC produces supplemental reagents kits for influenza H7 viruses that can be distributed nationally and internationally as needed.

*June 2003.*—St. Jude scientists and Hong Kong University collaborators discover that H9N2 viruses are endemic in land-based birds in China. It is also discovered that gene segments of H9N2 flu viruses found in ducks had undergone many changes, with some new combinations coding for antigens that could infect humans.

*June 2003.*—CDC establishes a ferret model to evaluate the biologic and molecular basis of influenza virus transmission. CDC initiates studies to compare avian-human reassortant viruses for their ability to undergo airborne transmission.

*June 2003.*—FDA licenses FluMist, the scientific basis of which is rooted in the work of National Institute of Allergy and Infectious Disease (NIAID) intramural scientists from 1975–1995. Production of FluMist leads to the establishment of infrastructure for the commercial manufacture of live attenuated vaccines, including vaccines against pandemic influenza.

*August 2003.*—National Institute of Allergy and Infectious Disease (NIAID) expands its Pandemic Preparedness in Asia contract. This expansion supports enhanced animal influenza surveillance sites in Asia, the generation of high-yielding pandemic vaccine candidates, and studies of a newly emerging influenza strain infecting swine in the United States.

*August/October 2003.*—FDA prepares H5N1 antiserum (BEVS-derived A/HONG KONG/213/2003) to be used for surveillance and vaccine potency measurements.

*August/September 2003.*—CDC deploys laboratorians and epidemiologists to Vietnam to assist the National Institute of Veterinary Research, the National Center for Veterinary Diagnosis and the National Institute of Hygiene and Epidemiology in Hanoi with one-on-one laboratory and epidemiological training for H5N1.

*September 2003.*—CDC provides funding to the Western Pacific Regional Office of World Health Organization (WHO) to directly support the National Influenza Center in Beijing, China and 23 provincial surveillance sites for reagents, personnel, and supplies. China sends 160 isolates to the Collaborating Center at CDC in fiscal year 2003.

*September 2003.*—National Institute of Allergy and Infectious Disease convenes an international workshop on the Development of a Clinical Trial Plan for Pandemic Influenza Vaccines to:

—Review data from earlier trials of pandemic influenza vaccines.

- Identify manufacturing and regulatory hurdles.
  - Prioritize pandemic influenza virus subtypes.
  - Develop an agenda for the conduct of clinical trials.
  - Initiate development of a U.S. Pandemic Influenza Vaccine Protocol.
- September 2003.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to Stanford University (PI, Dr. Ann Arvin) to study vaccine-induced and naturally acquired influenza A immunity as a model for in-depth analysis of the innate and adaptive immune response in children and adults.
- September 2003.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to the University of Maryland to understand the transmissibility of influenza A viruses (PI, Dr. Daniel Perez). The project's objective is to study the interspecies transmission of avian influenza viruses.
- August/September 2003.*—National Institute of Allergy and Infectious Disease (NIAID) awards three grants to industry partners for influenza product development:
- NIAID awards a grant to the Massachusetts Institute of Technology to investigate RNA interference of influenza virus infection (PI, Jianzhu Chen) as a new way of preventing and treating influenza infection.
  - NIAID awards a grant to Dynavax Technologies Corp. (PI, Gary Van Nest), to find a relatively stable component for use in a new kind of more broadly protective influenza vaccine. The vaccine candidate combines an internal flu protein that is less likely to be altered through mutation, NP, with a bioengineered molecule called an immunostimulatory DNA sequence.
  - NIAID awards a grant to the University of Colorado at Boulder for the development of a diagnostic microarray for influenza A (PI, Kathy Rowlen), which may serve as a rapid diagnostic. The project's goal is to develop the "Flu Chip," that will provide information as to whether or not an individual is infected with influenza as well as provide both type and antigenic sub-type characterization of the virus.
- October 2003.*—National Institute of Allergy and Infectious Disease (NIAID)-supported researchers at the Vaccine and Treatment Evaluation Units at the University of Rochester and Baylor College of Medicine test an experimental vaccine to protect people against an H9N2 bird influenza. Clinical trials are completed and results are expected in early 2005.
- October 2003.*—National Institute of Allergy and Infectious Disease (NIAID) conducts a Phase II study to evaluate the first trivalent baculovirus-based recombinant influenza virus vaccine. The vaccine, produced by Protein Sciences, was evaluated in healthy elderly subjects and was shown to be safe and well tolerated. The vaccine may also provide a suitable cell culture system for the large-scale production of influenza virus vaccines as a viable alternative to the production of the vaccines in eggs.
- October 2003.*—National Institute of Allergy and Infectious Disease (NIAID) and CDC intramural scientists demonstrate that a live attenuated vaccine against H9N2 is effective in mice.
- October 2003.*—CDC provides funding to Los Alamos National Laboratories to establish an H5N1 sequence compartment for international collaborators working on the sequencing of influenza AH5N1 viruses.
- December 2003/January 2004.*—HHS/OS awards contract to AmeriSource/McKesson for \$10.6 million to acquire 238,000 treatment courses of Tamiflu antiviral drug (tablet & suspension) using SNS funds.
- 2004.*—National Institute of Allergy and Infectious Disease (NIAID) supports animal influenza training courses in Hong Kong and Japan (ongoing).
- January 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to the Wadsworth Center entitled "Discovery of a Novel Promoter in Pathogenic Influenza" (PI, David Wentworth) to further understand the molecular mechanisms of pathogenesis in avian influenza viruses.
- January 2004.*—Fiscal year 2004 appropriations of \$50 million are approved for HHS advanced development of pandemic influenza vaccines.
- January/April/August 2004.*—HHS contract awarded to Roche for \$74 million to acquire 2.1 million treatment courses of Tamiflu antiviral drug (tablet & suspension) using Strategic National Stockpile funds.
- February 2004.*—HHS requests \$100 million in fiscal year 2005 for advanced development of pandemic influenza vaccines.
- January/February 2004.*—CDC sends multiple staff including epidemiologists and laboratorians to participate on the World Health Organization outbreak investigation team for H5N1.
- Ongoing since January 2004.*—CDC performs serological studies to determine extent of human infection with avian H5N1 viruses in Asia. This has involved the



testing of over 1,000 sera from cases, household contacts of cases, health care workers and poultry and veterinary workers from Vietnam, Thailand, South Korea, Indonesia, Cambodia and Taiwan. In addition, individuals from Vietnam, Thailand, South Korea, Singapore, Pakistan, have received extensive training in serological methods so that they can establish serologic procedures to detect avian influenza virus infection of humans in countries of origin.

*February 2004.*—CDC participates at Food and Agriculture Organization meetings regarding avian influenza prevention and control in Bangkok and Rome.

*February 2004.*—CDC plans a regional diagnostic Lab training in collaboration with World Health Organization and the International Emerging Infections Program for approximately 10 countries in Asia for identification of H5 by laboratory diagnosis was held in Bangkok, Thailand.

*February 2004.*—HHS issues Request for Proposals (RFPs) for a secure, year-round egg supply to the domestic influenza vaccine manufacturers and cell based influenza vaccines.

*February 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to St. Jude Children's Research Hospital to study combination chemotherapy for pandemic influenza (PI, Robert Webster) and test the hypothesis that combination therapy with two classes of anti-influenza drugs offers clinical and strategic advantages in the event of an influenza pandemic.

*March 2004.*—CDC plans and leads a laboratory and epidemiology training for 31 provinces in China to train them on laboratory identification of H5N1 in Beijing, China.

*March 2004.*—CDC provides several experts to participate in a consultation on Influenza Pandemic Preparedness to look at interventions before, during and after a pandemic, and to develop surveillance and other guidelines.

*March/April 2004:* FDA prepares H9N2 antiserum (BEVS-derived A/CHICK/HONG KONG/G9/2004) to be used for surveillance and vaccine potency measurements.

*April 2004.*—CDC produces pandemic vaccine candidate for H5N1 using A/VN/1203/04 using reverse genetics and PR8 backbone. This candidate is produced under Good Laboratory Practice (GLP) conditions and is suitable for human use.

*April 2004–June 2005.*—CDC supports another pandemic communications fellow to assist States with assessing and updating their State pandemic plans.

*April 2004.*—CDC conducts vaccine safety testing on SJCRH H5N1 vaccine candidate currently undergoing clinical evaluation.

*April 2004.*—CDC plans and sets up an emergency training for laboratorians from North and South Vietnam. This week long training, conducted in Hanoi, was to train in the laboratory diagnosis of H5N1.

*April 2004.*—CDC organizes and conducts a laboratory training “Modern Methods for Influenza Detection and Typing” for 16 students from 16 States at the Georgia State Public Health Lab. This is the first of three scheduled courses to cover all States on how to do the Reverse Transcription-Polymerase Chain Reaction method for influenza viruses including H5. This was planned and conducted in conjunction with the Association of Public Health Laboratories (APHL).

*April 2004.*—CDC produces additional supplemental diagnostic kits to update the H5N1 reagents so that they can identify the viruses as they have changed and distributes nationally and internationally as needed.

*April 2004/May 2004.*—FDA prepares H5N1 antiserum BEVS-derived A/VIETNAM/1203/2004 H5N1 to be used for surveillance and vaccine potency measurements.

*May 2004.*—CDC participates in planning and conducting a one week training in Tokyo, Japan for approximately 12 countries in the Region on epidemiological surveillance for H5N1 viruses.

*May 2004.*—FDA prepares and calibrates the H9N2 virus reference antigen for pilot investigational lots of vaccine to A/CHICK/HONG KONG/G9/2004 H9N2 for vaccine potency measurements.

*May 2004.*—FDA distributes of bulk antiserum to A/CHICK/HONG KONG/G9/2004 H9N2 vaccine manufactured by Chiron for vaccine potency measurements.

*May 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards contracts to Aventis Pasteur and Chiron Corporation to support the production of an investigational vaccine based on a strain of H5N1 avian influenza. The vaccines will be tested for safety and immunogenicity in Phase I and Phase II clinical trials conducted by NIAID's Vaccine and Treatment Evaluation Units (VTEUs). Studies will test the vaccine in healthy adults first with subsequent studies planned in children and the elderly.

*May 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to Innoject, Inc. (PI, Richard Gillespie) for the development of an auto-injec-

tor vaccine delivery system. Not only could the device be easy to use, but it could be broadly distributed in the event of an influenza pandemic. The clinical trial of the new delivery system, led by Dr. William Barr of Virginia Commonwealth University, will be conducted during the 2005–2006 flu season.

*May 2004.*—CDC provides additional support to the International Emerging Infections Program in Bangkok to enable comprehensive influenza pneumonia surveillance in 2 provinces covering more than 1.1 million people and to enhance technical assistance in the region with support to conduct training in collaboration with CDC and World Health Organization.

*June 2004.*—CDC reports on isolation of highly pathogenic avian H5N1 viruses from healthy birds in Vietnam live bird markets in late 2001. This was the first documentation of spread of H5N1 outside of PRC and Hong Kong SAR prior to Asia-wide outbreaks in late 2003–2004.

*June 2004.*—CDC issues a Cooperative Agreement with World Health Organization (WHO) Headquarters to support the revision of WHO National Pandemic Planning Guidelines, revision of the WHO Laboratory Manual for National Influenza Centers and establishment of a contract for shipping funds with 57 eligible countries to prevent barriers to specimen sharing for influenza.

*July 2004.*—CDC, in collaboration with Western Pacific Regional Office of the World Health Organization and China, conducts site assessments for approximately 6 provinces in China to assess current status of influenza surveillance.

*July 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to the Mount Sinai School of Medicine of NYU (PI, Adolfo Garcia-Sastre) for the molecular and biological characterization of the “Spanish Flu” to examine the reason behind the high lethality of the 1918 influenza pandemic.

*July 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to Washington University for the M2 Peptide Based Vaccines Against Influenza project (PI, Andrew Pekosz). The project’s goal is to generate an influenza vaccine with activity against a variety of virus strains using the M2 protein.

*July 2004.*—HHS issues Request for Proposals for the manufacturing of H5N1 vaccine at commercial scale using licensed process.

*July/August 2004.*—FDA distributes bulk antiserum to A/VIETNAM/1203/2004 H5N1 vaccine manufactured by sanofi pasteur for surveillance at CDC and NIBSC and vaccine potency measurements at sanofi pasteur.

*July/August 2004.*—CDC receives sera and performs major serological analysis of immunogenicity of H9N2 vaccine (National Institute of Allergy and Infectious Disease supported) in clinical trial.

*August 2004.*—CDC delivers complete safety profile of PR-8H5N1 reassortant seed virus to USDA for exclusion from Select Agent Program to enable sharing of seed virus with vaccine manufacturers.

*August 2004.*—HHS/OS awards contract to sanofi pasteur for \$12 million to manufacture 0.33 million doses of H5N1 bulk vaccine (90 g HA/dose) with Strategic National Stockpile funds and \$0.96 million for storage with stability study.

*August 2004.*—National Institute of Allergy and Infectious Disease (NIAID) issues a task order to Chiron Corporation for the production of an investigational H9N2 vaccine. Chiron will produce up to 40,000 doses of vaccine with and without the MF59 adjuvant for clinical trials that will be conducted by NIAID, slated for 2005.

*September 2004.*—HHS/OS awards contract to sanofi pasteur for \$10.1 million to provide secure year round egg supply for influenza vaccine production and clinical lot manufacturing of prepandemic influenza vaccines for clinical evaluation in the base year.

*September 2004.*—CDC establishes an international study involving >16 laboratories to evaluate and standardize the neutralization assay for the serological detection of antibody to influenza viruses, especially those with pandemic potential.

*September 2004.*—FDA prepares and calibrates the virus reference antigen from pilot investigational lots of A/VIETNAM/1203/2004 H5N1 vaccine manufactured by sanofi pasteur for potency measurements of H5N1 vaccine .

*September 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards challenge grants to six industry partners to develop new diagnostics, therapeutics, and vaccines against influenza virus:

- Shire Biologics, Inc., for the development of a tissue culture-derived influenza vaccine (PI, Jonathan Seals).
- Delsite Biotechnologies, Inc., for the development of an inactivated intranasal influenza vaccine (PI, Yawei Ni).
- Biota Scientific Management, for the development of a novel long-acting influenza antiviral drug (neuraminidase inhibitor) (PI, Jane Ryan).

- Columbia University/Griffin Analytical Technologies for the development of new diagnostics (PI, Walter Lipkin) to discriminate between several pathogens including influenza and SARS.
- University of Texas at Austin/Radix BioSolutions for the development of new diagnostics (PI, Steven Kornguth) to discriminate between several pathogens including influenza and SARS.
- BD Diagnostics (PI, Tobin Hellyer), for the development of new diagnostics to discriminate between several pathogens, including influenza and SARS.
- September 2004.*—National Institute of Allergy and Infectious Disease (NIAID) awards a grant to Nexbio, Inc., to develop novel therapeutics for pandemic and epidemic flu (PI, Fang Fang). This novel class of fusion proteins may be capable of blocking infections by all strains of influenza viruses.
- September 2004.*—CDC supports Cooperative Agreement with the Western Pacific Regional Office (WPRO) Manila to conduct laboratory assessments in Mongolia, Laos, Cambodia, Kazakhstan, Myanmar, and Vietnam.
- September 2004.*—CDC details staff to World Health Organization (WHO) in Geneva to work on enhancing collaboration between the animal and human health authorities, particularly Food and Agricultural Organization, World Organization for Animal Health (OIE), and WHO.
- September 2004.*—CDC awards bilateral agreements to 9 countries (China, India, Indonesia, Malaysia, Mongolia, Pakistan, Philippines, South Korea and Thailand) to address influenza surveillance infrastructure and enhance influenza surveillance networks. These grants enable training, technical assistance and funding for infrastructure to fill surveillance gaps.
- September 2004.*—CDC provides funding to Western Pacific Regional Office/World Health Organization in order to provide direct support to the National Influenza Center in Beijing, China and 31 provincial surveillance sites (expanded from 23 sites last year) for reagents, personnel and supplies.
- September 2004–September 2005.*—CDC develops 11 supplements to assist State and local governments in pandemic planning, such as clinical care guidelines, surveillance guidelines, laboratory diagnosis etc. These 11 supplements became part II of the overall DHHS pandemic influenza plan.
- October 2004.*—CDC organizes and conducts a laboratory training “Modern Methods for Influenza Detection and Typing” for an additional 16 students from 16 States at the Georgia State Public Health Lab. This is the second of three scheduled courses to cover all States on to do the Reverse Transcription-Polymerase Chain Reaction (RT-PCR) method for influenza viruses including H5. This was planned and conducted in conjunction with the Association of Public Health Laboratories (APHL).
- November 2004.*—CDC plans and conducts a regional State pandemic planning workshop in Atlanta for States in the Southeast. Immunization coordinators, epidemiologists, laboratorians, and emergency management coordinators participate.
- November 2004.*—CDC and the International Emerging Infection Program (IEIP) organizes, in collaboration with the Western Pacific Regional Office (WPRO), emergency training on neutralization assays for serologic diagnosis of H5. Seven people attended from Thailand, Vietnam, and Malaysia.
- November 2004.*—CDC, in collaboration with Western Pacific Regional Office (WPRO), World Health Organization HQ, and other international experts, organizes and conducts a pandemic tabletop exercise with the Chinese Ministry of Health and CDC and provided feedback on the draft pandemic plan presented.
- November 2004.*—CDC participates on a consultation on renewal of China’s next 5 year plan for influenza surveillance, prevention, and control.
- November 2004.*—National Institute of Allergy and Infectious Disease (NIAID) launches the Influenza Genome Sequencing Project that will put influenza sequence data rapidly in hands of scientists, enabling them to further study how influenza flu viruses evolve, spread, and cause disease and may ultimately lead to improved methods of detection, treatment, and prevention. This project is a collaborative effort among NIAID, National Center for Biotechnology Information/National Library of Medicine, CDC, St. Jude Children’s Research Hospital and others.
- November 2004.*—National Institute of Allergy and Infectious Disease rapidly initiates a Phase III trial to evaluate the safety and immunogenicity of GlaxoSmithKline’s Fluarix vaccine in healthy adults aged 18–64 years. The objective of the study is to generate data to support possible licensure of Fluarix vaccine in United States for the 2005–2006 influenza season. FDA approved the vaccine for adults aged 18 years and older in August 2005.
- December 2004.*—Fiscal year 2005 appropriations of \$99 million are approved for HHS advanced development of pandemic influenza vaccines.

*December 2004.*—National Institute of Allergy and Infectious Disease (NIAID) issues a notice to the NIH Guide highlighting its interest in receiving grant applications focused on influenza research.

*December 2004:* National Institute of Allergy and Infectious Disease (NIAID)'s Vaccine Research Center (VRC) begin conducting proof-of-concept studies for the development of genebased vaccines. If these are successful, VRC will expand and accelerate development of genebased and recombinant vaccines. Synthetic DNAs for multiple constructs are currently in preparation. Current Good Manufacturing Practices (cGMP) manufacture of an H5N1 pandemic flu vaccine construct for human clinical testing is expected to begin in fall of 2005. cGMP manufacture of vaccine constructs for human clinical testing for endemic circulating influenza strains is expected to begin in 2006.

*January 2005.*—CDC posts State pandemic planning tabletop exercises on the website that was developed over the previous several months so that States can test their plans using several different scenarios. Helpful education materials about tabletop planning exercises are also developed.

*January 2005.*—National Institute of Allergy and Infectious Disease (NIAID) expands its Pandemic Preparedness in Asia contract to include surveillance activities in Vietnam, Thailand, and Indonesia.

*February 2005.*—CDC plans and conducts in collaboration with Council of State and Territorial Epidemiologists (CSTE) a regional State pandemic planning workshop for States in the midWest in Denver, CO. Immunization coordinators, epidemiologists, laboratorians, and emergency management coordinators participate.

*February 2005.*—HHS requests \$120 M in fiscal year 2006 for advanced development of pandemic influenza vaccines.

*February/March 2005.*—CDC conducts an in-depth one-on-one training at the National Institute of Hygiene and Epidemiology in Vietnam for Polymerase Chain Reaction techniques and databases.

*March 2005.*—National Institute of Allergy and Infectious Disease (NIAID) conducts a Phase I trial of investigational inactivated H9N2 vaccine formulated with and without MF59 adjuvant. Results are expected in early 2006.

*March 2005–July 2005.*—National Institute of Allergy and Infectious Disease (NIAID) begins recruitment for a clinical trial to investigate the safety of an H5N1 avian influenza vaccine produced by sanofi pasteur (formerly Aventis Pasteur). Clinical sites, part of the NIAID VTEU network, will test the vaccine's safety and ability to generate an immune response in 450 healthy adults. A preliminary review of data from a subset of the study subjects shows that the vaccine is safe and that stronger doses of the vaccine result in higher immune responses. Full data analysis for this clinical trial should be available by the end of 2005.

*April 2005.*—CDC supports and participates in an emergency international World Health Organization consultation in Hanoi to go over latest epidemiological data and assess pandemic risk level.

*April 2005.*—CDC plans and conducts in collaboration with Council of State and Territorial Epidemiologists a regional State pandemic planning workshop in Chicago, IL for States in the North. Immunization coordinators, epidemiologists, laboratorians, and emergency management coordinators participate.

*April 2005.*—CDC awards bilateral funding support to Vietnam for the enhancement and development of in-country influenza surveillance networks.

*April 2005.*—CDC organizes and conducts Laboratory Training: Modern Methods for Influenza Detection and Typing for remaining States at the Georgia State Public Health Lab. This is the third of three courses conducted and will complete the training for the 48 States wishing to be trained on Reverse Transcription-Polymerase Chain Reaction (RT-PCR) methods for influenza viruses including H5. This was planned in conjunction with the Association of Public Health Laboratories (APHL).

*April 2005.*—CDC conducts a session in Kuala Lumpur entitled Human Influenza Surveillance and Control, which included a special half day session for recipients of CDC bilateral agreement funding. This is planned in conjunction with WPRO and SEARO and included 2–3 participants each from Malaysia, Philippines, New Caledonia, Laos, Vietnam, Indonesia, Thailand, Pakistan, South Korea, China, Brunei, Mongolia, as well as additional participants from WORLD HEALTH ORGANIZATION and Malaysia.

*April 2005.*—HHS awards contract to sanofi pasteur for \$97.1 million to facilitate the advanced development of cell-based influenza vaccine towards U.S. licensure in domestic manufacturing facilities.

*April 2005.*—HHS issues Requests for Proposals for funding more contracts to facilitate the advanced development of cell-based influenza vaccine towards U.S. licensure in domestic manufacturing facilities to expand and diversify the domestic pandemic vaccine surge capacity.

*April 2005.*—HHS establishes the first secure year round egg supply for influenza vaccine manufacturing in a contract with sanofi pasteur; these eggs can be made available for off-season production of H5N1 vaccine.

*April 2005.*—National Institute of Allergy and Infectious Disease (NIAID) makes multiple awards examining new influenza vaccine technologies. For example, NIAID awarded the following challenge grants in 2005: Rapid Acting Vaccine for Pandemic Influenza (Corixa Corporations), Alphavirus Replicon Vaccines against Influenza (Alphavax Human Vaccines, Inc.), Replication Defective Adenovirus-Vectored Pandemic Influenza (Vaxin, Inc.), and Biodefense Vaccine for Pandemic Influenza (Vical, Inc.).

*April 2005.*—National Institute of Allergy and Infectious Disease (NIAID) begins supporting animal studies to evaluate the efficacy of Peramivir against seasonal influenza. Additional studies are planned.

*April 2005.*—CDC provides consultation and site visits with Malaysian Ministry of Health and Philippines Ministry of Health to review their national surveillance system and provide on-site technical assistance.

*April/May 2005.*—CDC conducts on site training/consultation in Atlanta for the Director of the National Influenza Center from China.

*May 2005.*—CDC plans and conducts in collaboration with Council State and Territorial Epidemiologists a regional State pandemic planning workshop in Boston for States in the Northeast. Immunization coordinators, epidemiologists, laboratorians and emergency management coordinators participate.

*May 2005.*—CDC conducts vaccine safety testing on the CDC H5N1 vaccine candidate.

*May 2005.*—CDC establishes an interagency agreement with the Navy Medical Research Unit (NAMRU2) in Jakarta to strengthen influenza surveillance in Indonesia and provide regional technical assistance for seasonal and avian influenza.

*May 2005.*—CDC organizes a training course entitled “Epidemiology and Surveillance of Influenza and Respiratory Diseases” and held in Atlanta, Georgia. 20 participants from 10 countries of the Andean and Central America Regions participated in this training which was planned in conjunction with Pan American Health Organization.

*May 2005.*—CDC participates as faculty on World Health Organization (WHO)-sponsored Training Course on Laboratory Diagnosis and Surveillance of Influenza at the Health Protection Agency, Colindale and the National Institute for Medical Research, Mill Hill in London. Fifteen trainees from Middle Eastern and North African countries, selected by WHO and the Eastern Mediterranean Office, are trained in laboratory diagnostics for influenza.

*May 2005.*—CDC conducts laboratory training course for influenza and other respiratory viruses including SARS and Metapneumovirus. One participant from each of Mexico, Panama, Colombia, Brasil, Chile, CAREC and Argentina participated in this training planned in collaboration with PAHO. Diagnosis of avian influenza viruses, including H5N1, was part of the instruction.

*May 2005.*—CDC supports an interagency agreement with Department of Defense NAMRU-3 in Cairo to support technical assistance and training in Oman, Syria, Kingdom of Saudi Arabia, Kyrgyzstan, Ukraine, Georgia, Kazakhstan, Egypt, Kenya, and Pakistan to support human/animal interface studies.

*May 2005.*—CDC provides support for Western Pacific Regional Office (WPRO)/World Health Organization (WHO) to conduct in depth country assessments in Cambodia, Laos and Mongolia. Developed equipment needs list and supported procurement of equipment for these countries through WPRO.

*May 2005.*—CDC supports and participates in an emergency international consultation in Manila and produced the Manila report for the current status of pandemic risk assessment. Consultation included experts from all countries with human H5 infections.

*May 2005.*—National Institute of Allergy and Infectious Disease (NIAID) sub-contracts with Baxter for the production of whole virus, Vero cell-derived H5N1 vaccine formulated both with and without alum as an adjuvant.

*May 2005.*—FDA prepares and calibrates the virus reference antigen from commercial scale lots of A/VIETNAM/1203/2004 H5N1 vaccine manufactured by sanofi pasteur for potency measurements of H5N1 vaccine.

*May 2005.*—CDC details staff to Western Pacific Regional Office of World Health Organization in Manila to provide regional technical assistance for avian influenza, pandemic preparedness, and vaccine policy.

*June 2005.*—CDC supports and participates in an emergency consultation to assess lab results produced by another country suggesting possible alarming increase in positive cases. The outcome of this report was to avert panic in Hanoi by being able to provide expert laboratory analysis which suggested other data was incorrect.

*June 2005.*—CDC produces a conventional PR8 H7N7 vaccine candidate with A/mal/NL/12/00 (H7N3) and A/mal/NL02/00 (H10N7) and conducts vaccine safety testing on this vaccine candidate.

*June 2005.*—CDC supports World Health Organization (WHO) Cooperative Agreements with WHO Headquarters to continue enhancing communications at the animal-human interface, enhance international surveillance, and conduct pandemic risk assessment activities.

*June 2005.*—National Institute of Allergy and Infectious Disease (NIAID) intramural scientists and CDC colleagues developed live, attenuated H9N2 vaccine enters Phase I testing at Johns Hopkins.

*June 2005.*—HHS awards contract to Roche for \$58 million to acquire 2 million treatment courses of Tamiflu antiviral drug using Strategic National Stockpile funds.

*June 2005.*—CDC details staff to Geneva to work on pandemic risk assessment and pandemic planning.

*July 2005.*—Staff from CDC participates in the National Virology Training Course to cover pandemic preparedness and surveillance for avian influenza viruses.

*July 2005.*—CDC performs major serological analysis of immunogenicity of H9N2 vaccine (with or without adjuvant) in clinical trials.

*July 2005.*—CDC conducts serological analysis of subset of samples from National Institute of Allergy and Infectious Disease (NIAID) H5N1 vaccine clinical trials to validate results from NIH contractor.

*July 2005.*—HHS issues Request for Proposals for the manufacturing of H5N1 vaccine at commercial scale using licensed process.

*July 2005.*—National Institute of Allergy and Infectious Disease (NIAID) conducts a trial of intradermal vs. intramuscular delivery of H5N1 vaccine; results are expected by early 2006.

*July 2005.*—FDA distributes of antiserum to A/VIETNAM/1203/2005 virus to MedImmune for development of live, attenuated, H5N1 vaccine candidates.

*July/August 2005.*—CDC trains two Vietnamese laboratorians at CDC in laboratory methods used for detection of human infections of H5N1 viruses.

*August 2005.*—CDC participates in a World Bank consultation on coordination of global avian influenza activities.

*September 2005.*—CDC produces an H7N2 vaccine candidate using A/tky/VA/02 and conventional reassortant techniques.

*September 2005.*—CDC awards 2 new bilateral cooperative agreements to address avian influenza Kazakhstan and New Caledonia which includes a consortium of seven Pacific Public Health Surveillance Network Countries and Territories including Cook Islands, Fiji, Guam, Wallis and Futuna, Palau, and Tonga.

*September 2005.*—CDC and National Institute of Allergy and Infectious Disease (NIAID)-funded collaborators reports on generation and characterization of fully reconstructed 1918 pandemic influenza virus; vaccine studies and evaluation of 1918 virus sensitivity to influenza antivirals are ongoing.

*September 2005.*—In collaboration with World Health Organization (WHO), CDC plans a National Influenza Center satellite meeting in Malta for the purpose of working on WHO actions for NICs interpandemic, pandemic alert and pandemic.

*September 2005.*—National Institute of Allergy and Infectious Disease (NIAID) established a Cooperative Research and Development Agreement with MedImmune, the manufacturer of FluMist, to develop live attenuated vaccines against pandemic influenza.

*September 2005.*—A collaborative effort between National Institute of Allergy and Infectious Disease (NIAID)'s Office of Clinical Research (OCR), Oxford University, Wellcome Trust, and World Health Organization is in the early stages of working to establish a small network of clinical sites in SE Asia to research emerging infectious diseases with an initial emphasis on avian influenza. An oseltamivir treatment protocol is being considered for early 2006.

*September 2005.*—National Institute of Allergy and Infectious Disease (NIAID) signs an Interagency Agreement (IAA) with Uniformed Services University of the Health Sciences (USUHS) to establish a NIAID/Department of Defense Emerging Infectious Disease Clinical Research Program which can include Avian Influenza (AI) research in Indonesia with NAMRU 2.

*September 2005.*—HHS makes a modification of the H5N1 vaccine manufacturing contract with sanofi pasteur for \$1.5 million to manufacture H5N1 vaccines formulated with alum adjuvant for clinical evaluation by NIH in Jan. 2006.

*September 2005.*—HHS exercises options on the contract with sanofi pasteur of \$32.4 million to continue for four more years of securing a year round egg supply for influenza vaccine production and clinical lot manufacturing of pre-pandemic influenza vaccines for clinical evaluation.

*September 2005.*—HHS awards contract to GlaxoSmithKline for \$2.8 million for 87,000 treatment courses of Relenza antiviral drug using Strategic National Stockpile funds.

*September/October 2005.*—CDC staff provides on-site assistance to the Director General of the Indonesian equivalent of CDC and participates in outbreak investigations of H5N1 cases.

*September/October 2005.*—HHS awards contract to sanofi pasteur for \$180 million to manufacture 6 million doses of H5N1 bulk vaccine (90 g HA/dose) with Strategic National Stockpile and Department of Defense funds.

*September/October 2005.*—FDA distributes virus reference antigen and companion antiserum to A/VIETNAM/1203/2004 vaccine to Chiron and Baxter for potency measurements of H5N1 vaccine.

*October 2005.*—CDC provides 2 weeks of on-site technical assistance for the National Institute of Hygiene and Epidemiology in Hanoi for developing and conducting training for the start of the new National Influenza Surveillance system, supported through the bi-lateral cooperative agreement with CDC.

*October 2005.*—CDC produces a new reagents kit for H5N1 for international distribution to keep up with changes in the H5 viruses so that global labs can perform diagnostics.

*October 2005.*—FDA begins preparation of antiserum to H7N7 vaccine manufactured at sanofi pasteur for surveillance and potency measurements.

*October 2005.*—HHS awards contract to Chiron for \$61.8 million to manufacture 2 million doses of H5N1 bulk vaccine (90 g HA/dose) with Strategic National Stockpile funds.

*October 2005.*—HHS/OS awards contract to Roche for \$29 million to acquire 1.2 million treatment courses of Tamiflu antiviral drug using Strategic National Stockpile funds.

*October 2005.*—National Institute of Allergy and Infectious Disease (NIAID) expands its intramural pandemic influenza research with a new initiative focused on the molecular pathogenesis and epidemiology of influenza.

*October 2005.*—National Institute of Allergy and Infectious Disease (NIAID) initiates a trial of investigational H5N1 vaccine in the elderly at 4 Vaccine Treatment Evaluation Units sites.

*October 2005.*—National Institute of Allergy and Infectious Disease (NIAID) initiates an H5N1 vaccine Re-Vaccination Clinical Trial (original study conducted in 1998 by John Treanor—see 24 above on timeline) to determine whether having received an H5 vaccine in the past primes the immune system to respond rapidly to another dose of H5 vaccine.

*October 2005.*—Through National Institute of Allergy and Infectious Disease (NIAID)'s antiviral screening program, scientists screen more than 1,300 compounds for in vitro activity against influenza during the past two years.

*October/November 2005.*—Manufacturing begins of pilot investigational lots of H7N7 vaccine by sanofi pasteur under HHS contract for clinical evaluation by National Institute of Allergy and Infectious Disease (NIAID) in 2006.

*October/November 2005.*—CDC provides in-depth technical support and conducts site visits to the national sentinel hospitals in Vietnam.

*November 2005.*—CDC updates the global diagnostic reagents kits for the identification of H5N1 viruses so that they can now identify the newly circulating viruses from Indonesia.

*November 2005.*—National Institute of Allergy and Infectious Disease (NIAID) plans to begin a chart review in selected pediatric practices that used Tamiflu in infants last year to gather safety data to help inform prospective use.

*November 2005.*—National Institute of Allergy and Infectious Disease (NIAID)/Office of Clinical Research is pursuing a clinical trials agreement with Biocryst Pharmaceuticals, Inc. and jointly developing a protocol for Phase I clinical trials testing peramivir intramuscular and intravenous administration. Investigational New Drug Application (IND) submission is expected by late 2005, with study initiation expected in winter 2006.

*November 2005.*—HHS plans to issue Request for Proposals # ODC V&B 05-08 entitled "Antigen-Sparing Pandemic Influenza Vaccine Advanced Development and Licensure."

*November 2005.*—Manufacturing begins of H5N1 vaccine formulated with alum adjuvant at sanofi pasteur under HHS/OS contract for clinical evaluation by National Institute of Allergy and Infectious Disease (NIAID) in early 2006.

Senator SPECTER. My red light just went on, Senator Harkin. You're up.

Senator HARKIN. No response to that last one?

Senator SPECTER. No, I want it in writing.

Senator HARKIN. Okay.

Senator SPECTER. Others may come back to it, but I want to stop on time.

#### STATE AND LOCAL PANDEMIC FLU PREPAREDNESS

Senator HARKIN. Well, thank you very much, Mr. Chairman.

I just wanted to follow up a little bit, Mr. Secretary, on this situation with State and local governments. This morning's newspaper, Washington Post, said that you're planning for \$644 million: "to help local governments make your own preparations for a flu pandemic." In your testimony, which I just looked at, it carves out \$100 million, directed to State and local public health agencies. What is the correct figure? Is it \$100 million or is it more than that?

Secretary LEAVITT. The \$100 million, Senator, goes to help them with the development of plans and to exercise the plans—specifically, the larger number, the \$555 million, depending on what you add into that category—would go, in general to help enhance public health infrastructure and international collaboration.

Senator HARKIN. Well, if that's the case, Mr. Secretary, I think that that needs to be re-examined. That \$100 million, as I figure it, is about 1 percent—less than 1 percent of the entire package. State and local governments—we're already hearing from them, by the way.

Also, I want to clear up one other thing. It is my understanding that the President's proposal has a provision that States will be required to pay for their own stockpile of anti-virals, up to 75 percent—or 75 percent will have to come from the States—and that HHS will subsidize up to 25 percent. Is that correct?

Secretary LEAVITT. Senator, we feel, as I believe you do, that the State and local governments have to be deeply involved in this process. What makes a pandemic a unique disaster is, as I indicated earlier, it is not confined by geography. It is quite likely that if a pandemic were to blossom, that we would be dealing with pandemic conditions in virtually every State in the country simultaneously. The capacity of any central government to manage every one of those areas simultaneously is nonexistent. So, we want to develop very strong commitments and involvement. This is going to require all of us. It does involve some cost sharing on the anti-virals, for a number of reasons. One is that we want to make certain that they are buying into pandemic preparation and not just looking for a check from the Federal Government to put into a Federal stockpile. The second is that we believe it is going to take the mutual efforts of all of us to get this done. I am persuaded that, in order for us to actually distribute these anti-virals, that the stockpiles are going to have to be kept in the States, for the most part, and distributed according to protocols. at are developed on a State-by-State basis that would be based on their own priorities and protocols. We would make recommendations, but, nevertheless, customize to the State.

Senator HARKIN. Mr. Secretary, I don't think I tracked that too much. It seems to me, then, we're going to allocate scarce resources. We're only talking about 20 million, going up to 81 million



by the summer of 2007. It almost seems, then, that they will be allocated based upon a State's ability to pay. How are you going to ask Louisiana, right now, to come up with money for that? Take Mississippi, I mean, they've been hit hard. I just don't mean to single those two States out. Other States are having problems, too. Right now, the Federal Government stockpiles smallpox vaccine, but we don't ask the States to contribute to that.

Secretary LEAVITT. We, very clearly, believe the States should contribute to this. The actual percentage that they contribute, we're open to discussions on how we do that.

Senator HARKIN. Well—

Secretary LEAVITT. We think, just like in a co-pay for a prescription, that there's a need for co-pay with the States on this.

Senator HARKIN. Then why don't we asking them to pay for smallpox vaccine?

Secretary LEAVITT. Well, I—that opens up a discussion of the broad stockpile issues that I'm anxious to have.

Senator HARKIN. It just seems to me this is a national emergency. It seems to me that the States are going to be involved, obviously, through their State public health agencies and things like that, which we need to help them beef up. But, in terms of the stockpiling of the anti-virals and stuff, I don't think it's right to ask the States to come up with approximately \$500 million to stockpile them. I just—right now, I'm informed that State public health agencies have obligated 89 percent, already, of their fiscal year 2005 funds. So, the money that we have sent out there already has already been basically used up. I really do think we're going to have to re-examine this. There may be ways for the States to buy in and be active in this program. Obviously, we want them to buy into this. You do that through the collaboration between the Centers for Disease Control and Prevention and public health—and their State public health agencies, and you get those meshed. But it just—in terms of paying for the anti-virals, to stockpile them, seems to me you ought to have the same basis there as we would for smallpox or anything else; that this is a national emergency, it should not be allocated on a State's ability to pay. That means some States, poorer States, they don't get it? More wealthy States get it? I don't think that's the correct message to be sending out. I think we have to examine that.

I have more questions, but my time has run out.

Senator SPECTER. Senator Cochran.

#### PANDEMIC PREPARATION

Senator COCHRAN. Mr. Chairman, the request before us is described as an emergency. Can it also be described as urgent, in terms of the need for Congress to act quickly to make these funds available, as requested by the administration?

Secretary LEAVITT. Senator, we find ourselves in a vulnerable position were this virus to become a person-to-person transmittable virus. We are not alone in the world on that measure, but we are clearly in a place—with the virus moving across continents. The troubling signs are that we have people who are getting the disease from birds, and we are also seeing wild birds travel across the planet in the natural flyways, carrying the virus. We have now

seen it go from Southeast Asia, into Europe. There's no reason to believe that those birds will discontinue. There's no reason to believe that the virus won't continue to follow the pattern that others have. We don't know whether it will achieve person-to-person sustainable status, but, if it does, it would be a serious matter, and one that we should have responded to.

Senator COCHRAN. In our use of vaccines for influenza, generally, there is almost a rationing kind of system that we have. We prefer that older members of the population get the vaccine, and then if there is enough available, then other members of the population are eligible or encouraged to take the vaccine. Is this true in this kind of potential challenge? I noticed that children are considered vulnerable. Is this flu different in that respect? Is it no respecter of age or location?

Secretary LEAVITT. I'll ask Dr. Gerberding to respond to that.

Dr. GERBERDING. First of all, the big picture here is that we can finally think about a future where we can take flu off the table, because we will modernize our vaccine, and we shouldn't ever have to face these shortages or this rationing of the seasonal flu again. In the context of the potential H5N1 influenza, right now it's disproportionately affecting children and young people. That may be because those are the people who are having contacts with the affected chickens, and they are coming into direct exposure to the virus. It is really too soon to say how a pandemic would affect the population. We can look back to 1918 and recognize that in that devastating pandemic it was the young people who were disproportionately affected and killed.

Senator COCHRAN. In our State, we've had good success in making sure that vaccinations against other illnesses and diseases are available to children. We had 100 percent. I think we're the first State in the Union to achieve that goal of childhood immunizations. I wonder what kind of program, if any, we will have. Will it be patterned on the experiences that States like ours have had in achieving success in getting the vaccine to the people who need it?

Dr. GERBERDING. The seasonal influenza program obviously affects a broader population than just children. Right now, we don't have those kinds of programs for the adolescent vaccines or for the adult vaccines. We have to give a lot of consideration to what is the most sensible way for delivering vaccines to adults. With children, it's somewhat easy, because they see their pediatrician, and they need to see their pediatrician anyway, and they all start school at a certain age. But, you know, adults are all over the map. So, in addition to using the healthcare system in its traditional format, we are increasingly aware of how important the private sector has been in this—the Wal-Marts, the Targets, the grocery stores that are immunizing increasing proportions of our populations. With the health information technology system that allowed us to track those people using computers and electronic health records, we really could create a very modern system for delivering this product to people. That's not what we're asking for in our emergency budget, but, separate from that, that kind of planning is going on at HHS and CDC.

Senator COCHRAN. Okay. Thank you very much.

Senator SPECTER. Thank you, Senator Cochran.

Senator Murray.

FDA APPROVAL PROCESS

Senator MURRAY. Thank you very much, Mr. Secretary, for testifying before us today. I think we all know that the American people are putting a lot of faith and hope in you, and the agencies that you oversee, in implementing a plan that will protect them. I just have to say that that really makes me pretty uneasy. I'll tell you why. As you well know, for 2 years, FDA dragged its feet and took some really unusual steps in handling the application for the Plan B emergency contraceptives being available over the counter. And, in fact, the FDA overruled its own scientific advisory panel and appears to be putting politics and ideology ahead of drug safety and effectiveness, which is their mission.

As you well know, Senator Clinton and I put a hold on the confirmation of Lester Crawford over this issue. As you also know, in July you write to Chairman Enzi and Senator Kennedy and said, and I quote, "The FDA will act on this application by September 1, 2005." Well, Senator Clinton and I relied on your word and your letter, and we accepted what you told us, and we lifted that hold. In fact, in a subsequent Budget Committee hearing I thanked you for your getting involved in this and moving it forward and bringing us a decision by that date. But what you told us didn't happen. The FDA didn't make a decision. Instead, they issued another delay and, I believe, put science on the back burner and really gave the Agency a black eye.

I have to tell you that that is why I am concerned about the Department's handling this new challenge. As I shared with you, as I talked with you after that happened, this is far bigger than Plan B. It's about the American public's confidence in the agencies that oversee our public health, and particularly FDA, and why it's especially important for this conversation is that this national strategy calls for knocking down regulatory barriers in the approval process so that critical vaccines can reach the public sooner.

We know there have been problems with the FDA. We've seen drugs being recalled, because they threaten public health, and we've seen other drugs, as I just talked about, Plan B, being held up even though the FDA's own scientific panel said it was safe and effective.

So, I want to know how we can be confident now in the FDA, when you plan to speed up approval of vaccines, while still protecting the public health, while treatments that are known to be safe and effective are still being held up at the FDA.

Secretary LEAVITT. Senator, I know how important this issue is to you. You've made—

Senator MURRAY. It's not just important to me. It's important to the American public and their confidence in this critical agency when they go to the store to purchase a drug.

Secretary LEAVITT. The FDA did act, on September 15. They put forward a notice of rulemaking to examine some very important public policy issues that are new. Yesterday, the period closed—we have had nearly 10,000 comments.

Senator MURRAY. Highly unusual to ask for public input to the FDA, adding to the erosion of confidence.

Secretary LEAVITT. Well, it must have been important to the public if they put forward 10,000 comments, which they have. We will now analyze them and move it forward in the way that we said we would.

Senator MURRAY. Well, Mr. Secretary, the point is, we are now being asked, in a very serious public health question, to have confidence in an FDA that we have seen confidence be—erode dramatically, including by pharmaceutical companies who have talked to me, and the American public. I think that it calls into question—as I told you, we’ve got to have confidence. This decision needs to be made. We expect an answer soon.

You know, especially now, when we are urging FDA to approve new vaccines quickly. I would just ask you, are you urging the approval of these new vaccines that—and anti-viral treatments that do not meet current FDA safety standards for approval? What are we going to see happen?

Secretary LEAVITT. We’re going to use the FDA to do what it does well, and that is to protect the American people. Every vaccine that we put forward has to go through FDA clinical trials in a way that I’m sure Dr. Fauci would be very pleased to describe.

#### ROLE OF STATE AND LOCAL GOVERNMENTS

Senator MURRAY. Well, let me just re-emphasize that if we can’t have confidence in FDA following its own scientific panels in the mission that it has to approve drugs, not on politics, but on safety and effectiveness, and it erodes our confidence, it is going to make it very hard for the public, in a public health crisis like this, to have confidence in the agencies that you oversee.

But, having said that, I know I have got 20 seconds, and I know we’re going to have this conversation again. I will keep working on it. It is critical. But I want to add to what Senator Harkin said. This morning, in my hometown newspaper, Seattle Post-Intelligencer, the headline is, “Bush’s Plan to Fight Flu Doesn’t Thrill States.” As Senator Harkin said, the States are extremely nervous about what is going to be required of them. I would say that the public health officials—and you’re all sitting at the table—know that a flu pandemic doesn’t sit within a State boundary, and if one State doesn’t have the financial resources to be able to deal with this on the ground, it will create severe danger and hazards.

So, I am very concerned, as Senator Harkin pointed out, Mr. Chairman, about a plan that relies on public health agencies to come up with the majority of the money, particularly when many of our States are struggling today, and particularly because the administration budget has already reduced funding for State and local health departments by \$130 million. They are already struggling. So, if we add this on top of them and say, “If you want to participate, come up with 75 percent of the funding,” we are going to have a public health crisis. That concerns me greatly.

Secretary LEAVITT. Senator, I would like to clarify that. The plan does call for the Federal Government to pay for the majority of the anti-virals. It also should be made clear that we do not see anti-viral strategies being synonymous with preparation. We do believe that the States have a responsibility in the development of their plans and in the decision on how they should deploy anti-virals.

We're looking forward to working with the States in developing a level of preparedness. This cannot be managed by the National Government. It is too wide. There is no person skilled enough at logistics that they could manage a pandemic in 500 locations or 1,000 locations at a time. If we have a full pandemic, that's likely what we'll see.

Senator MURRAY. Well, I'm positive we'll be pursuing both of those conversations again.

#### FUNDING PRIORITIES

Senator SPECTER. Thank you, Senator.

I was informed this morning, during the course of the hearing, that our other witness, Mr. John Barry, has some travel restrictions and has to leave by about 10:10, but I don't want to keep this panel waiting, so, let's proceed now with 4 minute rounds on the second round to give Mr. Barry an opportunity to testify before he has to go.

Secretary Leavitt, we have a disconnect on what information comes to the Congress from the administration. That occurs because matters are transmitted through OMB, and they not only superintend the requests for money where various secretaries have to fight it out there, but also in what you say. I've found that to be a very serious limiting factor on having Congress discharge its constitutional duty to establish priorities and decide what funding there ought to be.

One illustration which was very emphatically brought to bear was the construction at the Centers for Disease Control and Prevention. This goes back before your watch. This goes back to 1999. And I had heard tales about the terrible facilities in CDC, but not from the Secretary of HHS, not from anybody in the administration. I went to a wedding in the proximity of Atlanta, in April 2000, and went on down to Atlanta and took a look, and was just astounded at what I saw. Senator Harkin joined the visit. Immediately, on the budget then in process, we put up \$175 million, and then \$250, \$266, \$260, and \$269 million. The administration's request came in this year for \$30 million, which is preposterous. We had world-class scientists in hallways and had toxic materials not subject to proper supervision. We have, by reassessing priorities, come up with \$239 million. We've got to finish that.

CDC, the request is down by \$475 million this year. Instead of going down by \$475 million, we've tried to increase funding. We do that, because of the magic of "Senator Taylor" and "Senator Ellen" to find the money. But we need to find some better way to know what the hell's going on, because the executive branch won't tell us. We need some whistleblowers, starting with the Secretary.

I know it's pretty tough to do, but I want to take a look at what you're going to provide us, Dr. Fauci, on the chronology of events. I've been involved in enough investigations and enough oversight to have an instinct that the scientists knew a lot more about the problem than the subcommittee did. We've proved our willingness to buck the system on NIH, where Senator Harkin, Senator Cochran, this subcommittee, have taken the lead at increasing funding from \$12 to \$28 billion, up to \$29 billion this year, if they can hold

it. We have very high regard for what you people do. But you've got to help us help you.

Finally, the alarms have been sounded, and we're prepared to go forward. I'm going to yield back my final 6 seconds.

Senator Cochran, round two?

Senator COCHRAN. Senator Harkin should go first.

#### VACCINE LIABILITY

Senator HARKIN. Thank you, Mr. Chairman.

I just want to join with you on that, and I was just thinking that perhaps, Mr. Chairman, what we need is, because of the importance of us getting the proper information from the basic science community, whether that's NIH, all of NIH, or CDC, perhaps we need to expand the concept of the pass-through budget from the NCI—that is the only one we have now—if we get that pass-through the budget from the National Cancer Institute. Perhaps we need a pass-through budget from other Institutes, or maybe even CDC. That may be one thing we might explore.

Mr. Secretary, I wonder if I could maybe shift on a couple of things. One, we're hearing a lot of talk about liability and how we're going to handle the liability of drug manufacturers and things like that. Congress is going to have to wrestle with that. I hope that—and I just make this statement for the public record, that I hope we also start thinking about the liability aspect that pertains to public health workers that are out on the front lines that are administering the drugs, the vaccines, anti-virals, that type thing. How about their liability protection? We've got to be thinking about them, too. So, I just throw that out there so that we don't forget as we think about that.

I wonder if I might just perhaps ask Dr. Gellin this question, if I might, Mr. Secretary.

Dr. Gellin, we've talked about cell-based vaccines. The Secretary mentioned that we are moving ahead in that area. I've spent a great deal of time talking to drug manufacturers about this new technology. But there's something else that came up on the scope as we began looking at this, this summer, and that's something called "synthetic vaccines," which may even hold more promise. Now, I don't know about the timeframes of this. We have got cell based, we have got synthetic vaccines. Could you just briefly explain the two and whether or not this is something also that we're going to be investing resources in—synthetic vaccines?

#### SYNTHETIC AND CELL-BASED VACCINES

Dr. GELLIN. Yeah, thank you very much. I'll start, and maybe Dr. Fauci will fill in, as well.

The concept here is that we have a tried-and-true methodology to make vaccines, in that we know, at the end of the line, that it is the component of the vaccine that stimulates an immune response. Currently, we grow viruses in eggs that can grow up that amount of—

Senator HARKIN. Yes, right.

Dr. GELLIN [continuing]. Antigen. The conversion to a cell-based system is essentially to do the same thing in a more modern way, using cells to grow virus.

Senator HARKIN. Right.

Dr. GELLIN. At the end of the line, you still have that same antigen. There are a whole range of other vaccine technologies that Dr. Fauci's groups are already looking into that are new ways to stimulate the immune system. You would have to look at the immune system in a different way. Currently, we will use a vaccine and measure the antibody response to those proteins. With newer vaccines, we have to have new ways to evaluate how well the immune system is responding, because it will not just be the equivalent. But there are a range of these technologies. I think the dream is that someday there will be a vaccine—a flu vaccine that would protect all—against all of the flu viruses. It is clearly the Holy Grail. If it was easy, it would be done. But someday, if we are there, then these discussions will be much simpler.

Senator HARKIN. Dr. Fauci, you tell us about synthetic vaccines.

Dr. FAUCI. It is less synthetic, Senator Harkin, that it is getting away from the technology which we have now with flu, which is either a killed vaccine, which is what we have used with the Sanofi and Chiron group, or a live, attenuated, which is the MedImmune version.

When you're talking about being more specific, it is more of the recombinant DNA technology. There are components of the influenza virus that are very constant from flu strain to flu strain. We've not been able to utilize that to get our, quote, "universal vaccine," because many of those proteins are not highly immunogenic, which means they do not stimulate the immune system very well.

Several companies, with and without collaboration from us in the Department—and many times it is in collaboration—are developing vaccine approaches toward influenza, which are trying to look at some of those constant regions. One of them is the M2 protein of influenza, where you make it in a way that when you present it to the immune system, it's highly immunogenic and would hopefully induce an immune response that would really be very beneficial to all of our projects, because what it will do is cover a broad range of different strains of influenza. So, if you really look at the future, that is where we want to be several years from now, where you can actually make a vaccine that covers all the bases of a potential flu. So, I think that's what you're referring to.

Senator HARKIN. Tony, that may have been over my head. I have to think about that.

But this—the briefing I had on synthetic vaccines, is some of this money going to be used for that? I know we're going into cell-based. Is some of this money going into that area?

Secretary LEAVITT. Our purpose is to identify a large range of new, promising technologies. We'll begin to invest in those technologies in the first round. When—then we'll go back and say which of them continue to show promise after our first investments, and we'll begin to narrow the—our investments. We are programming to have multiple providers and to utilize the best technologies that come from a wide range of starts.

Senator HARKIN. Would you send me some stuff on synthetics, so I can read it?

Dr. FAUCI. Will do.

Senator HARKIN. It might take me a little while.

Dr. FAUCI. Okay.  
[The information follows:]

NATIONAL INSTITUTES OF HEALTH RESEARCH ON SYNTHETIC VACCINES

*Question.* "Synthetic Vaccines:" What research is NIAID supporting on cell culture technology, and recombinant and DNA vaccine development, and what promise/advantage do they hold?"

*Answer.* The term "synthetic vaccines" technically refers to vaccines such as peptide vaccines that are artificially synthesized through chemical reactions. NIAID is not currently pursuing the development of a synthetic vaccine against influenza.

However, the development of other types of influenza vaccines has been a major focus of the National Institute of Allergy and Infectious Diseases (NIAID) Influenza Program. NIAID supports strategies to foster the development of new influenza vaccine candidates and manufacturing methods that are simpler and more reliable, yield more broadly cross-protective products, and provide alternatives to the egg-based technology currently used to grow vaccine viruses.

Influenza vaccine production technology using recombinant DNA or cell culture could potentially enable vaccine manufacturers to respond more quickly to public health needs by allowing the rapid scale-up of vaccine production and manufacture to meet demand. For example, the technique of reverse genetics, developed by NIAID-supported scientists, allows scientists to manipulate the genomes of influenza viruses and to transfer genes between viral strains. The technique allows the rapid generation of seed viruses for vaccine candidates that exactly match the anticipated epidemic strain. By removing or modifying certain virulence genes, reverse genetics also can be used to convert highly pathogenic influenza viruses into vaccine candidates that are safer for vaccine manufacturers to handle.

In another approach, NIAID and MedImmune, Inc. are working under a cooperative agreement to produce and test multiple vaccines against potential pandemic flu strains, including the H5N1 avian influenza virus. The agreement specifies that the scientists will select genes from avian flu viruses with pandemic potential and add them into a weakened human flu virus to create multiple live, attenuated virus vaccine candidates. An attenuated vaccine can potentially stimulate a broader and more potent immune response than a killed vaccine formulation. For example, live attenuated virus vaccines for measles, mumps, and rubella stimulate life-long immunity and have a long history of safety and effectiveness. A live attenuated virus vaccine may also stimulate effective immunity to a circulating pandemic virus that differs significantly from the vaccine strain, which would be a major advantage given both the biology of influenza viruses and the lengthy flu vaccine production process. In addition, an intranasal live attenuated virus-based pandemic flu vaccine could be easily administered by non-medical personnel, self-administered, or given as a booster to a killed vaccine.

Although still in the proof-of-concept stage, the ability to manipulate DNA vaccine antigens by recombinant means is a powerful tool against viruses such as influenza and HIV, which have a tendency to mutate rapidly. Recombinant DNA technology allows for the relatively easy addition or deletion of antigens in new combinations. An example of a gene-based method of production is the genetic engineering of baculovirus, an insect virus not related to influenza, to express a gene that encodes an influenza coat protein such as hemagglutinin or neuraminidase. The engineered baculovirus is then grown in insect cell cultures, and the influenza protein that the virus produces is purified for use as a "recombinant subunit" influenza vaccine.

The NIAID Vaccine Research Center (VRC) is developing a candidate "prime-boost" vaccine against influenza, an approach that has also been used to develop a candidate HIV vaccine. The VRC "prime-boost" vaccine is composed of two vaccine components, both of which contain influenza genes, given at different times. The two vaccine components differ in how the genes are packaged. One contains only the naked gene fragments, which cannot reconstitute into an infectious virus. The other uses a weakened type of respiratory virus known as adenovirus as a vector to shuttle the non-infectious influenza gene fragments into the body. This approach may result in enhanced cellular and humoral immunity. The NIAID Vaccine Research Center is also constructing and has pre-clinically tested a number of DNA plasmids which contain proteins from the influenza virus (hemagglutinin, neuraminidase, ion channel M2, and the nucleocapsid protein). VRC studies of vaccines expressing these proteins will serve as the proof of concept basis for a gene-based influenza vaccine.

Senator HARKIN. Thank you.  
Senator SPECTER. Thank you, Senator Harkin.



Senator Cochran.

#### PANDEMIC FLU BUDGET

Senator COCHRAN. Mr. Secretary, I am assuming that this request, as it recommends basic research, infrastructure improvements, and expansion, includes the traditional role that's been played in this area by the Departments of Health and Human Services, as well as Homeland Security and the Department of Agriculture, animal research—where animal research is involved. Do you suggest that funding for basic research in these traditional areas should be increased across these departments as part of this request?

Secretary LEAVITT. The request that you have seen focuses on vaccines in the Department of Health and Human Services. There is a part of this budget—the difference between the \$6.7 billion and \$7.1 billion—that would be contained in budgets of the other departments outside of HHS, for other tasks.

#### USE OF ANTI-VIRALS

Senator COCHRAN. I understand that anti-virals play an important role during annual flu outbreaks. They are used in nursing homes to prevent the spread of flu, and also given to people who, for health reasons, should not take the flu vaccine. How can we ensure that anti-viral supplies are used correctly and in accordance with normal flu needs?

Secretary LEAVITT. I'm going to ask Dr. Gerberding, from the Centers for Disease Control and Prevention to respond to that. We've recently been issuing guidance on that subject.

Dr. GERBERDING. Thank you.

On October 21, CDC issued some updated guidance on management of seasonal influenza. That guidance emphasizes the importance of using anti-virals. First of all, for treatment for people who identify flu-like symptoms and see a clinician within 48 hours, these drugs can reduce the severity and the duration of their symptoms. For people who have risk factors that put them at high risk for complicated flu, they should see their doctor anytime they suspect influenza, because those drugs may be indicated for them, as well.

We do also use anti-viral drugs in cases that you mentioned—nursing homes, for example—where either the people are not vaccinated or we don't have confidence that the vaccine will be 100 percent protective. So, by treating the people in the nursing home for many days, we can often reduce the impact and the death rate among those senior citizens. So, there are specific indications where we use it for preventing flu, but it is important that people recognize that, unlike the situation, you know, 10 years ago, we really do have drugs now that are widely useful for reducing flu complications. Those are the same drugs that we are putting into our stockpile.

#### VACCINE PRODUCTION

Senator COCHRAN. Thank you.

Much of the request deals with the need to increase manufacturing capacity of vaccines and anti-virals. Can you describe how the President's initiative will address this deficiency?

Secretary LEAVITT. Yes, Senator. We intend to do three basic avenues of research. The first is expanding our existing egg-based production. It is tried, it is true. We know it is there. We think particularly with new adjuvant technology, that we can expand the yield of our egg-based production and that it should continue.

Second, we are going to pursue cell-based technologies. There will be a number of different technologies that we will pursue. We have put an RFP out asking for providers to give us ideas where we could pursue the development of a new technology. We intend to pursue those. Then, last, there will be some retrofitting of existing facilities that will be necessary in order to get additional capacity needed to produce 300 million courses of vaccine in a 6-month period.

Senator COCHRAN. Thank you.

Senator SPECTER. Thank you very much, Senator Cochran.

We do want to move ahead and give Mr. Barry his round of—opportunity to testify.

We applaud what the President did yesterday. We applaud what you're doing. We thought it important to have this hearing so that the American people would know that the President is moving, the Secretary is moving, his key people are moving, and so is the Congress.

We did have some problems, Mr. Secretary, in getting information to prepare for this hearing. I'd like to correct—see if those channels of communications are corrected. We understood the New York Times had information 2 weeks ago that we couldn't have access to. They have a louder bullhorn than we do. But they don't have as much money for you as we do.

We need to have a better line of communication so that we find out what's going on, because we can't help you unless we know.

Do you care to make any closing comments, Mr. Secretary?

Secretary LEAVITT. Well, it might not surprise you to know that those aren't always intended, for them to have information before you do. We'll do our best to remedy that situation.

Senator SPECTER. Okay, we'd appreciate it.

Dr. Fauci, any last word?

Dr. FAUCI. No, thanks. I will get you the information you have asked for.

Senator SPECTER. Okay.

Dr. Gerberding, any final words?

Dr. GERBERDING. Just thank you.

Senator SPECTER. We have all this talent here. It's a waste of talent not to have them speak.

Anything further, Dr. Gellin, you'd like to say?

Dr. GELLIN. We look forward to ongoing discussions with you.

Senator SPECTER. Dr. Raub, anything?

Dr. RAUB. No, sir, other than we are available to assist, as we can.

Senator HARKIN. Can I just make one statement?

Senator SPECTER. Senator Harkin, you're called upon for one statement.

## HOSPITAL SURGE CAPACITY

Senator HARKIN. Now, would you please get back to me, Dr. Leavitt. We're just out—or, Secretary Leavitt—we're just out of time here. But, in looking through the plan and asking my staff, there's nothing in there about hospital surge capacity. We never—we don't have time, I guess, to get into that now, but that needs to be addressed. Could you somehow correspond with us on this and let us know what you're doing on that end of it?

Secretary LEAVITT. Yes, sir.

Senator HARKIN. Thank you.

[The information follows:]

## HOSPITAL SURGE CAPACITY

Increasing hospital and health care system surge capacity has been the cornerstone of the National Bioterrorism Hospital Preparedness Program (BHPP) since the program's inception in 2002. State departments of public health, the recipients of BHPP awards, have been directed to work closely with hospitals and supporting health care system to address the various aspects of surge capacity that would allow the system to increase its ability to triage and treat an influx of patients during a bioterrorism event or other public health emergency. Specifically, States have been directed to establish systems to increase bed availability beyond current daily staffed capacity in BHPP-supported hospitals and community-based clinics; upgrade and expand airborne infectious disease isolation capacity within individual hospital facilities and across intrastate health care regions; develop systems to recruit, identify, and deploy volunteer health professional to supplement hospital and health care system personnel, including behavioral health providers; establish hospital and intrastate regional pharmaceutical caches; obtain and maintain sufficient amounts of personal protective equipment to protect daily and surge personnel and train personnel in the proper use of the equipment; and develop and enhance redundant communications systems that ensures connectivity between the health care system, public health, and other first responders.

States departments of public health have supported hospitals and the health care system in greatly enhancing surge capacity in each of these areas, which will certainly improve local, regional, and statewide response to pandemic influenza. In addition, departments of public health and health care communities nationwide have taken additional steps to prepare for a pandemic influenza outbreak. Namely, public health and medical communities nationwide have developed statewide pandemic influenza plans. These plans were initiated in fiscal year 2004, and final plans were submitted to the Centers for Disease Control and Prevention for review in fiscal year 2005. In addition, State departments of public health and health care systems have begun to explore other means of further increasing surge capability to achieve the levels of care necessary to support a pandemic influenza response, including the identification of alternate care facilities and the provision of home health care, delivery of prescription drugs, and delivery of meals. The pandemic influenza supplemental will allow public health, hospitals, and supporting health care systems to build upon the plans that have been developed and ensure sufficient hospital and community surge capacity to respond to an influenza pandemic in many communities across the Nation.

Senator SPECTER. We were joined by the distinguished Senator from Ohio, Senator DeWine. We have one more witness, Senator DeWine, I have said earlier, who has a plane to catch at 10:10, but—

Senator DEWINE. You can proceed, Mr. Chairman.

Senator SPECTER [continuing]. But Senators take preference over—over anything.

Senator DEWINE. I'm fine, Mr. Chairman.

Senator SPECTER. Okay. Thank you all very much.

I'll now call on Mr. John Barry, the author of "The Great Influenza: The Epic Story of the Deadliest Plague in History," author of other award-winning books, Brown University graduate.

We welcome you here, Mr. Barry. It is our custom to limit witnesses to 5 minutes. You have a full allocation before you have to leave, and we might hold your plane just a little bit for you to respond to a question or two, if you have any flexibility.

Thank you for joining us, and the floor is yours.

**STATEMENT OF JOHN M. BARRY, AUTHOR**

Mr. BARRY. Thank you very much. I am not quite—I've got a—probably 10:20, maybe even squeeze to 10:25. So, I appreciate your comments and courtesy.

Senator SPECTER. Well, I wanted to bring you on after—I don't want to keep those scientists here a minute longer than necessary—to interrupt their testimony, because they have a lot of important work to do. But now we want to hear from you.

Mr. BARRY. I thank you very much for the opportunity to testify and give you some background on a disease that, according to the CDC, kills 36,000 Americans in a normal year. By definition, a pandemic would not be a normal year. As you heard, another pandemic is virtually inevitable, because of the nature of the virus. We have no idea when it will occur. It could have started 2 weeks ago, and we don't know it. It might not come for another 20 years. But for the last 500 years, they have occurred, at least the 500 years. The greatest duration between pandemics in the past was 42 years. We're now at 37 years, and counting.

They don't need air travel to spread. In the 1690s, influenza made it from Europe to the American Colonies, when it took 8 weeks to cross the ocean. We have substantial information only about the last four pandemics: in 1989, 1918, 1957, and 1968. 1918, of course, is the one that gets all the press, because the most people died. No one knows exactly how many died, but a Nobel Prize winner, MacFarlane Burnett, who spent most of his life studying the disease, put the estimate at a minimum of 50 million dead, possibly 100 million dead. And that, of course, was in a world only 28 percent the population of today's. In other words, even without adjusting for population, influenza in 1918 killed more people in 24 weeks than AIDS has killed in 24 years.

Even then, though, in the developed world, the overwhelming majority of victims had what we would regard as a normal influenza attack. The mortality rate in the United States was no higher than 2 percent, but so many people are attacked that, in the United States alone, 675,000 people died in a population roughly one-third of today's.

Symptoms could be horrific. People turned so dark blue from lack of oxygen that physicians reported they had difficulty distinguishing between black patients and white patients. People could bleed from their eyes, ears, as well as nose and mouth. The impact on the society was immense.

Part of the problem came from false reassurances from the Federal Government, which were repeated by local governments. The Surgeon General actually said, "There is no cause for alarm." Of course, there was cause for alarm. People would die in less than 24 hours.

This enormous disconnect between horrific symptoms, terrible death tolls, and constant false reassurances from officials, national

and local, and reinforced by the media, which, then, was totally passive, led, ultimately, to a breakdown in trust in all authority, and people became alienated. The Red Cross reported that people were starving to death, quote, “not from lack of food, but because the well are afraid to help the sick,” unquote.

One very sober scientist not given to overstatement said that if the epidemic continued, quote, “for a few more weeks, civilization could easily disappear from the face of the Earth.” That is how serious this impacted the society.

But a 1918-like scenario is not necessary to justify the full attention of the Government to influenza. A best-case scenario will do that. This is because recently, despite antibiotics that would cut deaths from secondary bacterial infections, we have actually become more vulnerable to influenza, not less vulnerable. This is largely because medical science has improved in so many other areas, but lagged in influenza. As a result, the demographics of the population have changed. We now have a much larger segment of the population with impaired immune systems. Most obviously, the elderly, but also, anyone who survived cancer and had radiation therapy or chemotherapy has an impaired immune system, not to mention people with HIV or transplant recipients and some others. As a result, a mild virus would kill far more Americans than in the past, not less.

The 1968 pandemic killed 34,000 Americans. If you adjust for population, that’s about 55,000 today. Yet, CDC currently estimates that if a virus similar to the 1968 pandemic struck, between 89,000 and 207,000 Americans today would die.

Deaths are, however, only one measure of the impact of the pandemic. We are also more vulnerable economically, because of—everything’s more efficient—just-in-time inventories, people’s habits have changed about eating out, going to the supermarket. There are actually far fewer canned goods sold today than used to be the case. Businesses are more vulnerable to supply disruptions.

There is just the one bright spot, and that is, in all the four pandemics that we know about, there was a lag time between 6 months and 1 year when it seems that the virus first surfaced in human populations and became serious. All of those prior four pandemics that we know about had a mild first wave that was barely distinguishable, and sometimes not distinguishable, from a normal course of influenza. So, there does seem to be some time to do something, and a window of opportunity to get things produced, particularly, obviously, vaccine.

I’d like to make one comment that’s not in my prepared remarks. The first responders are the public. I think that public information is extremely important. I also think it’s important to exercise the plans. I’m from New Orleans. People don’t realize that one thing that worked in Katrina very well was the pre-storm evacuation, when, when 80 percent of the city was evacuated. The reason that worked, particularly compared to Rita and the Texas gulf coast was because of Hurricane Ivan, which the city evacuated the year before, and it was a disaster. The—of course, that hurricane missed New Orleans, but the planners looked at what happened, made adjustments, and, in Katrina, those adjustments worked very well on the pre-storm.

## PREPARED STATEMENT

One other point, I gave a talk to the Pennsylvania Public Health Association last week and was informed that the State of Pennsylvania considers its pandemic preparedness plan so sensitive that it is not releasing it to the public, which I find rather ironic and a little bit strange.

On that, I thank you.

[The statement follows:]

## PREPARED STATEMENT OF JOHN M. BARRY

I thank you for the opportunity to testify, and to provide you with some background on a disease that, according to the Center for Disease Control and Prevention, kills 36,000 Americans in a normal year. By definition, an influenza pandemic would not be a normal year and kill far more Americans than that. And although I will tell you about what happened during the pandemic of 1918 and 1919, which killed more people than any other disease outbreak in history, a worst case scenario is not necessary to justify far more expenditures on influenza. The best case scenario is bad enough to get the attention of any American.

Another pandemic is virtually inevitable because of the nature of the influenza virus. It is one of a group of viruses that mutate so rapidly that virologists refer to them as "mutant swarms" or "quasi-species." All influenza viruses originate as bird viruses, but their mutation rate allows them to jump species, from birds to humans. It can jump directly, as happened in 1918, by mutation. It can also jump indirectly when an avian influenza virus infects the same cell as an influenza virus that earlier adapted to humans; the two viruses can swap genes and create a new hybrid virus capable of infecting people. This gene-swapping can occur not only in humans, but in other mammals.

Whenever a new avian influenza virus does transform itself into one that can pass easily from one person to another, human immune systems will not recognize it. This allows it to spread explosively through the world causing a worldwide epidemic—a pandemic.

We have no idea when the next pandemic will occur. It may have started two weeks ago and we just don't know it yet, or it may not come for twenty years. But for at least the last five hundred years, pandemics have occurred three to five times a century, with the greatest duration between pandemics of 42 years. We are now at 37 years and counting.

Pandemics do not need air travel to spread. In the 1690s, when it took six to eight weeks to cross the Atlantic, influenza crossed from England to the colonies. In Virginia one report said "the people dyed . . . as in a plague." In Massachusetts Cotton Mather wrote, "All conditions of persons were attacked . . . The sickness extended to almost all families. Few or none escaped, and many dyed especially in Boston, and some dyed in a strange or unusual manner, in some families all weer sick together, in some towns almost all weer sick so that it was a time of disease."

We have substantial information only about the last four pandemics, which occurred in 1889, 1918, 1957, and 1968. Of these, by far the most lethal was the one in 1918, but there are some indications that similarly lethal influenza outbreaks occurred in the past as well. In 1580, according to one account, some Spanish cities reportedly were "nearly entirely depopulated by the disease."

No one knows with certainty how many people died in the 1918 pandemic, but according to Nobel laureate Frank MacFarlane Burnett, that pandemic killed at least 50 million people, and possibly 100 million. It did this in a world whose population was only 28 percent as large as today's. That is the equivalent of 175 to 350 million today. Yet even without adjusting for population and using Burnett's lower estimate, the 1918 influenza pandemic killed more people in 24 weeks than AIDS has killed in the 24 years that disease has been known. Well over half the deaths occurred in an incredibly short span of about 10 weeks, between late September and early December, 1918.

In the developed world, the overwhelming majority of victims suffered what we would today regard as a typical attack of the disease. For example, the case mortality rate in the United States was no more than 2 percent. But influenza attacks so many people that the U.S. death toll was an estimated 675,000, the equivalent of about 1.8 million today.

We were of course at war when the pandemic erupted, and some people have theorized that the war contributed to the lethality of the disease. This reminds me

of what Thomas Huxley called the great tragedy of science, when a beautiful theory is slain by an ugly fact. This theory is entirely inconsistent with the actual course of the disease.

There are several other points worth making about 1918. Influenza normally behaves like a bully, killing people with the weakest immune systems, particularly the elderly and the very young. This is true not only with the endemic disease that occurs every year, but in the 1889, 1957, and 1968 pandemics.

This was not true in 1918. The people most likely to die in 1918 were healthy young adults, aged 20 to 35, people with the strongest immune systems.

Symptoms could be horrific. People turned so dark blue from lack of oxygen a physician reported he had difficulty distinguishing between black and white patients. Victims could bleed from their mouth, nose, ears, and eyes.

The impact on society was immense. Part of the problem came from false reassurances from all levels of government. The Surgeon General said, "There is no cause for alarm."

There was cause for alarm. Every city, town, and village ran out of coffins. People could die less than 24 hours after their first symptoms. This enormous disconnect between what people saw for themselves and what they were being told destroyed all trust in authority. People became alienated. In city and country victims starved to death "not from lack of food but because the well are afraid to help the sick." Streets emptied. In Philadelphia in a city of almost two million people, one medical student who was in charge of an emergency hospital saw so few cars on his way home every night over a drive of 12 miles that he started counting them; one night he saw not a single other car on the road, and wrote, "The life of the city has almost stopped." Doctors and nurses were kidnapped. A confidential Red Cross report noted "a fear and panic akin to the terror of the Middle Ages of the plague." One sober scientist, not given to overstatement, wrote that if the epidemic had continued "for a few more weeks, civilization could disappear from the face of the earth."

But as I said before, a 1918-like scenario is not needed to justify the full attention of the government to influenza. A best case scenario serves well enough.

This is because in recent years, despite antibiotics would cut deaths from complicating secondary bacterial infections, we have become more vulnerable to influenza, not less vulnerable, both in its economic impact and in the death toll.

Ironically, medical science has increased our vulnerability by its enormous advances that have increased the number of people living with impaired immune systems. These include not only many more elderly, but cancer survivors who have undergone chemotherapy or radiation therapy—which weakens the immune system—transplant recipients, people infected with HIV, and others.

As a result, a mild virus would kill more Americans than in the past, not less. The 1968 influenza pandemic was the mildest that we know of, with approximately 34,000 deaths in the United States, equivalent to about 55,000 in today's population. By comparison, the CDC projects that a pandemic caused by even such a mild virus would today most likely kill between 89,000 and 207,000 in the United States alone.

Deaths are, however, only one measure of the impact of a pandemic. A pandemic will also cause massive economic losses and social disruption. Increased efficiencies and just-in-time inventory management in business and health care have both cut into the surge capacity to make needed goods and exposed much of the economy to supply disruptions.

There is however one bright spot. Although in past decades, the nation has paid too little attention to influenza, and therefore we have made little progress on improving our ability to make vaccines, or in finding real solutions that can only come from basic research, such as developing a vaccine that works against conserved portions of the virus, or in finding effective anti-viral drugs. But if we pay attention to influenza now, even in the relatively short term of the next few years, it may be possible to improve our vaccine production capacity enough to make a real difference.

Influenza pandemics seem to come in waves. Certainly that was the case in 1889, 1918, 1957, and 1968. The first wave, which in 1918 probably lasted six to eight months, was mild. In 1957 the first isolate was identified in February, and the pandemic did not really erupt until September. In 1968 there seems to have been a year between identification of the first isolate as a new virus and serious pandemic disease. And in the 1889–1890 pandemic, the third wave was the most deadly.

So a window of opportunity does exist. If surveillance and vaccine production capacity improve enough, we do have a chance to intervene successfully and cut the death toll significantly.

How much our ability to fight this disease improves is largely up to the appropriations committee.

Thank you.

Senator SPECTER. Thank you very much for joining us, Mr. Barry. What are your time constrictions?

Mr. BARRY. I need to leave about 10:25, I think.

#### PENNSYLVANIA PLAN

Senator SPECTER. Okay. We will proceed, then, with 4 minute rounds.

When you mentioned Pennsylvania, a couple items of your testimony attracted my specific attention: "Pennsylvania" and "chemotherapy." Let me start with Pennsylvania.

When they won't reveal the plan, do you think there's the slightest suggestion that they either don't have one, or it would be embarrassing to be revealed?

Mr. BARRY. Well, I have no details on this, other than, as I said, I talked last week at the Pennsylvania Public Health Association, and they told me this. They said that the State considers it, sort of, a national security issue, which—it just seems very odd to me.

#### CHEMOTHERAPY PATIENTS

Senator SPECTER. Well, we'll pursue that. We had a little trouble getting the plan of our own administration, so maybe it's not out of line.

When you talk about the people who have had chemotherapy, as I say, that rings a bell close to home. Immune systems down. Any special advice for that category of individual?

Mr. BARRY. Not that I know of. When you undergo either chemotherapy or radiation therapy, it takes a long time for the immune systems to fully rebound.

Senator SPECTER. How long?

Mr. BARRY. It can be years. In some cases, never. It, sort of, depends on the course of chemotherapy and your own individual body. So, any individual can consult his physician as to what kind of shape their immune system is.

#### VACCINE DEVELOPMENT

Senator SPECTER. When you say the first wave is not too bad, so that there's a window of opportunity, what window of opportunity to do you see here, where we are so far behind on developing a vaccine?

Mr. BARRY. Well, by "window," I meant that you do have some time once the virus surfaced.

Senator SPECTER. Well, you have some time, too, before—

Mr. BARRY. That—right.

Senator SPECTER [continuing]. Before it surfaces.

Mr. BARRY. Right, exactly.

Senator SPECTER. Where we are now.

Although you can't really tell how much it has surfaced.

Mr. BARRY. I applaud, you know, your earlier amendments, and I am glad that the administration is now spending the money. You create a vaccine infrastructure that is capable of responding within a matter of months, with a new vaccine. If your surveillance is good enough, you will likely catch it very soon after it becomes a



human virus. These past four pandemics have shown between 6 months and 1 year before that virus becomes serious. So, depending on how much investment, how well things go, it is plausible that—3 years from now, 5 years from now—that in 6 or 8 months we might well be able to produce large doses of vaccine. We certainly could not do that today, but you are making the investment. This committee, of course, has a lot to say over what the investment is—in creating just the infrastructure that will allow us to respond. Again, whether it would take 3 years or 10 years before we are really ready, that depends on how long it takes to develop the cell culture techniques.

#### FEDERAL, STATE, AND LOCAL COMMUNICATION

Senator SPECTER. Let me interrupt you, Mr. Barry, because I have one more question and my time is about to expire. Your full statement will be made a part of the record. As you saw Secretary Leavitt put, high on the list, communications. This subcommittee would be interested in your expertise on what ought to be communicated, and how. For example, your suggestions on radiation or chemotherapy. If you could supplement your testimony with what you think we ought to do about communications, we'd appreciate it.

[The information follows:]

Dear Senator Specter: Thank you for the opportunity to testify, and for your graciousness in accommodating my travel schedule. I'm writing now to reply to the two questions you asked me to address.

The first involved the effect of chemotherapy and radiation therapy on the immune system. Chemotherapy is the most common cause of immunosuppression (a weakened immune system) and myelosuppression (insufficient production of blood cells) in people receiving cancer treatment. It's impossible to generalize about how severe these impacts will be, since they depend on the drugs used, the dosage, the schedule, previous treatments for cancer, age, nutritional status, type of cancer, and the stage of the cancer. White blood cell production tends to be most sensitive to chemotherapy drugs. Radiation therapy has a similar impact. How long it takes a person's immune system to recover depends on many factors as well.

No doubt you would prefer a better answer than the generalities above. In that case, may I suggest you contact Dr. Steven Rosenberg, chief of the Surgery Branch at the National Cancer Institute, whom you may know since he has often testified. Dr. Rosenberg is best known for being the first to develop a way to stimulate the immune system to cure a cancer, and his combined expertise on clinical medicine, laboratory research, immunology, and cancer make him one of the best people in the world to answer your question in greater detail.

Your second question involved something closer to my own area—communicating with the public. I have studied in considerable detail what are probably two of the three greatest natural disasters (the 1927 flood and the 1918 influenza pandemic) ever to strike the country, and, given that my home is in New Orleans, have lived through the third, Katrina. I hope I have learned something from those experiences.

I believe firmly that the first responders are not firemen or health care workers or police, but the public. This means that considerable effort should be expended to get information to the public sooner rather than later, and people should be given more information—even if incomplete—rather than less. Information of course is power, and when people have information they have some control and can make their own informed decisions. Some of those decisions, even when fully informed, will be bad ones. But without information, both bad individual decisions and panic are more likely to ensue.

On influenza specifically, I'm not sure of the best way to get information out in advance of an actual outbreak. A highly skilled writer might be able to put useful information into a brief public service announcement (or some notice on mass transit), while simultaneously referring people to places where they could get more facts about the disease itself, its progress, what individuals and their families should do,

and on what's being done. People should be able to easily access this information, and they should be able to go deep into the subject if they choose to.

The most obvious place for the kind of thing I am suggesting is a website; that's necessary but insufficient since too many people don't have access to them. Perhaps pamphlets for distribution not only in doctors' & dentists' offices, etc., but in churches and temples, movie theaters and schools. (This of course means the information has to be out there well in advance of any decisions to close public places.)

Again, since the real first responders are the public, the more the public knows, the better off everyone is. Should a pandemic actually strike, we need the most forthright statements. The parts of the book that Secretary Leavitt took most to heart related to the false reassurances given to the public, which caused the loss of trust and threatened the very fiber of the society. I would not even issue such statements as: "Don't panic," or "Stay calm." I believe that most people's natural response is, "Wow. I didn't know things were that bad."

The message also has to fit the pandemic. If the pandemic is like 1968, that calls for one message. If it looks like it will resemble 1918, it requires another. In the latter case, I think the message should resemble Churchill's "blood, sweat, and tears" speech. "This is serious. Many Americans will die no matter how well we respond. But we will do all that is humanly possible, it will pass, and we will get through this."

To keep public trust, we need to hold nothing back from either the general public or the media. Holding information close is almost as destructive of trust as lying. People usually think you know more than you are saying anyway. We need to fight that preconception by flooding people with information. Get everything out. Explain that we don't know when we don't know, and explain why we don't know—we're conducting tests x,y,z, and part x takes 14 hours for a result, part y takes 22 hours, etc.

In terms of the course of the disease, if we don't know we should perhaps give a range of the most likely scenarios, from best case to worst case. The idea that we somehow best protect the public by keeping bad news from them is counter-productive. Yes, the media will hype any statements and spark fear and even panic that might otherwise not exist. Nonetheless, in the long run I think society is better served by being told best case, worst case, and points in between, as well as what those in authority are doing about it both nationally and locally.

Thanks again for the opportunity to testify. I hope you find this a suitable reply.

Senator SPECTER. Senator Harkin.

#### HOSPITAL SURGE CAPACITY

Senator HARKIN. Thank you, Mr. Chairman.

Mr. Barry, your book, in my reading of it, brought back to—memories of my father, who was born in 1886, died in 1967. But during my formative years growing up, he talked about his early years. The two things that made the biggest impression on his lifetime, I think, was the flu of 1918, which I never really thought about that much, in which many members of his own family and communities died, and the Great Depression. I thought, how could those two be equal? But, in reading your book, I can see now that the great flu really was kind of equivalent in its impact on people's lives.

Now, having said that, one of the things I said to Secretary Leavitt before he left was—had to do with hospital surge capacity not addressed. In your book, you talk about some of these scenes, about 4,000–8,000 cases coming into these hospitals, they are in the corridors, and you describe, in your book, the accounts of the nurses and others about what was happening. Talking about what you see out there today, I mean, are we—what would happen today if this kind of pandemic were to hit, and we are looking at millions of people in America seeking hospital help?

Mr. BARRY. Well, I think that is part of our increased vulnerability. Hospitals, like everything else, have become more efficient.

There are no vacant, or much fewer vacant, beds than there used to be. Even in 1957, I have seen photographs of, essentially, emergency hospitals, like 1918, basically look like airplane hangars filled with cots. Back in 1957, I do not know the exact numbers of hospital beds compared to population, but I would, offhand, guess that there were more than there are today. So, that is a very real problem, and a very good question for you to ask. Of course, I'm not capable of answering it, but I—it is a good question.

Senator HARKIN. But it's your sense, your feel, that—

Mr. BARRY. I mean, yeah, we would be overwhelmed. The healthcare system today, without any question, would be overwhelmed by a major pandemic. I mean, even in the normal course of a flu season—I was on a book tour in Kansas City, and I turn on the news, and eight hospitals closed their emergency rooms because of influenza season, just normal influenza. A pandemic is multiplied many-fold.

Senator HARKIN. Thank you.

Thank you, Mr. Chairman.

Senator SPECTER. Thank you, Senator Harkin.

Senator Cochran.

Senator COCHRAN. Well, welcome, Mr. Barry. It is a pleasure to get to see you here before our subcommittee.

Mr. BARRY. Thank you.

Senator COCHRAN. I think "Rising Tide" was one of the most interesting books I have ever read.

Mr. BARRY. Thank you.

Senator COCHRAN. I congratulate you for that, and I will have to read "The Great Influenza." I will.

But, thank you for being here today and helping us get the big picture on the impact that such an influenza outbreak in our country would have and the things we can do to prepare for it.

You have looked at the request that the administration has submitted, in terms of the priorities, better international surveillance, domestic surveillance, vaccines, anti-virals, developing of greater capacity for production, communications, and State and local preparedness. Is there anything that you think that the administration has failed to request, in terms of emergency funding, that we should also consider?

Mr. BARRY. No, I think the basics of the plan are sound. I would share the comments about the idea that the States have to put out money when they are already pressed, as compared to smallpox or some of the other things. But, basically, you know, it is a sound plan and a very good place to begin.

Senator COCHRAN. In your research for—

Mr. BARRY. Of course, I have not seen any details. I mean, like you—

Senator COCHRAN. Yes. Sure.

Mr. BARRY [continuing]. I mean, all I have heard was the Secretary's testimony.

Senator COCHRAN. Sure. In your research for the book, "The Great Influenza," did you come across any parallel with the bird flu and the question of whether or not transmission, instead of just going between birds and humans who have had close contact,

whether there is a natural evolution for man-to-man communication of a disease like that?

Mr. BARRY. Actually, in the full prepared comments, I mention that all influenza viruses are bird viruses. All of them are. Historically, it is one of the most rapidly mutating viruses in existence, and that gives it the opportunity to jump species. It can do that one of two ways, either directly mutating a virus, a bird virus becoming a human virus, which happened in 1918, or it can do it indirectly. A bird virus can infect the same cell that an existing human virus that, once upon a time, was a bird virus also infects, and then they trade genes and create a new virus. That happened in 1957 and 1968.

There very recently has been some scientific work that confirmed 1918 was completely a bird virus that went straight to man through mutation, and they have tracked and identified several points of mutation, and they are comparing that to H5N1 right now. There are some points of similarity, where H5 has seemed to make progress along those lines. It does give us a good way to monitor H5, but we are not certain that even if it makes all those mutation points similar to what happened in 1918, that does not automatically mean it will become a human virus.

Senator COCHRAN. Well, thank you very much for being here. You have added to our hearing, and we appreciate your cooperation with our subcommittee.

Mr. BARRY. Thank you very much.

Senator SPECTER. Thank you, Senator Cochran.

Senator DeWine.

Senator DEWINE. Mr. Barry, thank you very much. You describe some horrible symptoms in 1918, the flu. Would the symptoms of today's bird flu be similar in any way, or can you tell?

Mr. BARRY. Some of them are. I have read pathology reports from H5 victims and, in fact, noted that in those pathology reports, they say, "These findings have never before been described in influenza." In fact, all of those findings had been described in 1918. Chiefly, that the virus can get into other organs besides the lung, including the brain, which is quite unusual, but—normally, in birds, it is an intestinal virus, and, in people, normally it is respiratory virus. But both the 1918 flu and—I believe H5 variety can infect other organs and cause other symptoms.

Senator DEWINE. In your book, you state that, in 1918, members of the American medical research community really expected such a situation, but thought they were prepared for it.

Mr. BARRY. Right.

Senator DEWINE. Any similarities between now and then, you know, that we think maybe we're prepared, or we're getting prepared, and that we are not?

Mr. BARRY. Well, I don't think—

Senator DEWINE. You've touched on this a little bit already, but—

Mr. BARRY. I don't think anyone—and I think Secretary Leavitt would be among the first to tell you—I don't think anybody thinks we're prepared today. Again, it would have been nice if this had happened a few years ago, but it would have been even nicer if, in the last 40 years, a lot more energy had been devoted to influenza,

in which case maybe we would have the virus against the concerned portion—I mean, the vaccine against the concerned portions of the virus, one vaccine that worked against all influenza viruses. But for—you know, a few years ago, we were spending more on West Nile than we were spending on influenza, and West Nile, this year, has killed about 55 people. If we had not spent a penny on West Nile this year—in my opinion, this year, it would have killed about 55 people. Whereas, influenza is killing 36,000 Americans a year anyway. I mean, every year.

Senator DEWINE. Every year.

Mr. BARRY. Yeah. Yeah.

Senator DEWINE. Yeah.

Mr. BARRY. So, it had—it has been a disease that has not been taken seriously over a long time. Now it is being taken seriously. We don't know when the next pandemic is going to come. If it comes next year, we are in serious trouble. If it waits 10 years, chances are pretty good we will be able to handle it, certainly a lot better than we could today.

Senator DEWINE. Good. Thank you very much.

Thank you, Mr. Chairman.

Senator SPECTER. Thank you, Senator DeWine.

#### CONCLUSION OF HEARING

Thank you very much, Mr. Barry. Your book is certainly a big red flag and something we need. If you would follow up with some specific suggestions on communications, you have got a background to give us some special expertise and insights on that.

I thank you all very much, and that concludes our hearing.

[Whereupon, at 10:25 a.m., Wednesday, November 2, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]