



Department of Health and Human Services

Pandemic Planning Update III

A Report from Secretary Michael O. Leavitt

November 13, 2006



“Our country has been given fair warning of this danger to our homeland — and time to prepare. It’s my responsibility as President to take measures to protect the American people from the possibility that human-to-human transmission may occur.”

— President George W. Bush

November 1, 2005

Message from the Secretary

“We are in a race. A race against a fast moving, virulent virus with the potential to cause an influenza pandemic.”

- Secretary Mike Leavitt, HHS
March 13, 2006

A year ago, few Americans had heard of avian flu. Today, awareness is high. There has been a deluge of news reports, and we've had not one, but two made-for-TV bird flu movies. This past year, a nearly forgotten word, pandemic, re-entered our vocabulary. And then the media moved on.

There is a danger that as avian flu slips from the headlines, people will believe the threat is no longer real. But the race against bird flu has not slowed, and we are continuing to prepare. In fact, the highly pathogenic H5N1 avian flu virus continues to change, to probe our defenses. The virus has been confirmed in birds in 55 nations. A year ago, it had been reported in only sixteen. As this report is being written, 256 people in ten nations have been infected and 159— 59 percent—have died. The number will likely have increased by the time you read these words.

It has been one year since the President called the nation to action. I can report that the response has been unprecedented and the progress considerable. We are building a national stockpile of pandemic vaccines, antiviral drugs and other supplies needed to respond to a potential pandemic, and we are subsidizing state efforts to purchase antivirals. Thirty-three states have already placed orders.

In June, Congress passed the President's funding request of \$2.3 billion for the second year of the HHS Pandemic Influenza Plan. This funding allows HHS to continue to develop a vaccine for the US population within six months of the first sign of a pandemic, come closer to our goal of antiviral coverage of 25% of the population, and enhance domestic and international public health infrastructure and preparedness. The President's FY 2007 request also includes \$352 million for HHS agencies to build on the implementation of the Pandemic Influenza Preparedness

Plan through the following activities:

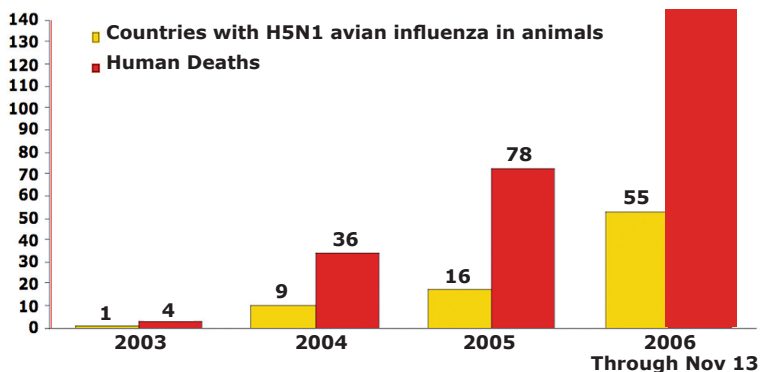
- Expanding domestic and international surveillance and detection capabilities;
- Improving pandemic preparedness and response capabilities;
- Establishing a vaccine registry to assess vaccine distribution, safety, and efficacy and;
- Improving our Nation's ability to contain a potential pandemic influenza outbreak.

Vaccine research continues at a frantic pace. Vaccines have been developed for the two known variants of H5N1 and we have already stockpiled enough vaccine to treat more than some 3 million people. We are working with

industry and other countries to increase vaccine production capacity at home and abroad.

State and local planning has been ubiquitous. We have held pandemic planning summits with broad cross-sections of leadership in every state. Every state has drafted a pandemic plan. Many have taken their planning to county and local levels. Indiana, for example, recently announced that all 92 counties had completed local pandemic influenza response plans.

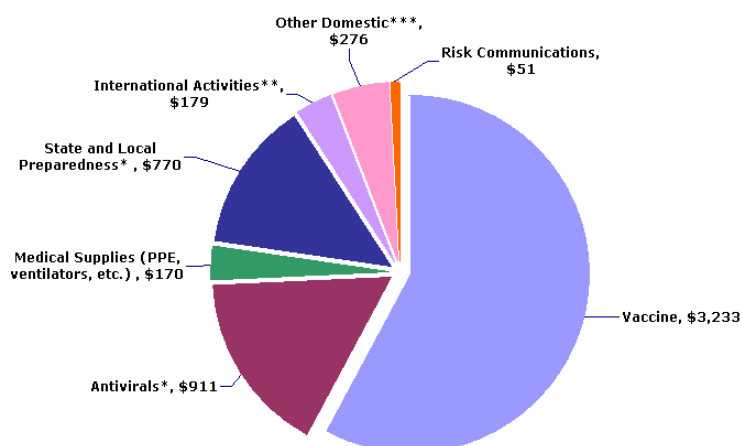
Countries with H5N1 Avian Influenza and Human Deaths (both cumulative)



Message from the Secretary (cont.)

In August, the Department of Health and Human Services (HHS) released an additional \$225 million to the states to enhance preparedness, further regional planning and hold planning exercises. In June 2006, Congress appropriated an additional \$250 million for state and local preparedness. A portion of this funding will be awarded on a competitive basis for innovative approaches to preparedness.

HHS FY 2006 Pandemic Influenza Supplemental Budget (Dollars in Millions)



*State and local preparedness includes funding for state subsidies of antiviral drugs.
 **International Activities Includes: International Preparedness, Surveillance, Response, and Research.
 ***Other Domestic Includes: Surveillance, Quarantine, Lab Capacity, Rapid Tests.
 ****This chart does not include \$30 million in supplemental funding that was transferred to USAID.

International cooperation has been extraordinary. At the urging of the President, more than 93 countries and 20 international organizations are participating in the International Partnership on Avian and Pandemic Influenza. The NIH is supporting a collaboration of domestic and international partners in the Influenza Genome Sequencing Project. Genetic sequences are being made available to the entire scientific community via the internet. Indonesia is sharing avian influenza virus samples and, recently, China also agreed to share virus samples.

Monitoring and surveillance remains our first defense against the emergence of a pandemic influenza virus. To date, the Departments of Interior and Agriculture and state partners have tested more than

35,000 wild migratory birds in the United States for avian flu. To date, the highly pathogenic strain of H5N1 has not been found anywhere in the Americas.

None of this should make us complacent. While there is no way to know when, or even if, the H5N1 virus will form a variant capable of widespread human-to-human transmission, we know that pandemics are inevitable and our efforts are designed to advance our preparedness to minimize the impact of the next pandemic when it comes.

A pandemic would impact every community in the nation over a very short period of time. It could last six to eight weeks and it could return in wave after wave with each wave lasting two to three months. There is no way to know how lethal an H5N1 avian influenza outbreak could be, but a catastrophic scenario — a

2004 – H5N1 vaccine reference strain created by reverse genetics from H5N1 virus isolated from Vietnam
 April 2005 – RFP for cell-based vaccine contract issued
 Summer 2005 – Preliminary results from H5N1 vaccine clinical trials in healthy adults aged 18-64 indicate an immune response predictive of protection against the H5N1
 September 2005 – International Partnership on Avian and Pandemic Influenza launched
 October 2005 – Southeast Asia fact-finding mission led by HHS Secretary and State Department
 November 2005 – WHO Global Meeting the National Strategy for Pandemic Influenza
 November 2005 – President Bush announces Pandemic Influenza Plan

Message from the Secretary (cont.)

pandemic of 1918 severity — could cause nearly two million deaths in the United States, and tens, perhaps hundreds, of millions of deaths worldwide.

Public and private leaders at all levels are grappling with the enormity of keeping our government, our economy, and our society functioning during a severe pandemic. There is much for each of us to do, at home, at school, at work, and in the community to plan and prepare for what we hope never happens.

As I wrote in my first report, “Preparation is a continuum. Each day we prepare brings us closer to being ready. We are better prepared today than we were yesterday. And we must be better prepared tomorrow than we are today.”

Monitoring and Surveillance



Picture a graceful whooper swan, lifting from a Mongolian wetland. It will carry on its back a tiny, 2.3 ounce solar-powered GPS transmitter as it wings its way across Eurasia to its western breeding grounds. On the ground, an international team of scientists from the U. S. Geological Survey, the United Nations Food and Agriculture Organization, the Wildlife Conservation Society and the Mongolian Academy of Sciences will carefully track the swan’s migration route.

With good reason: the swan may be carrying more than its GPS transmitter. In 2005, large numbers of whooper swans died in parts of Mongolia where few poultry are present. Testing of the dead swans verified the presence of the highly pathogenic H5N1 virus.

Tracking the swans is just one way scientists are trying to better understand and document links between wild birds and the spread of avian influenza.

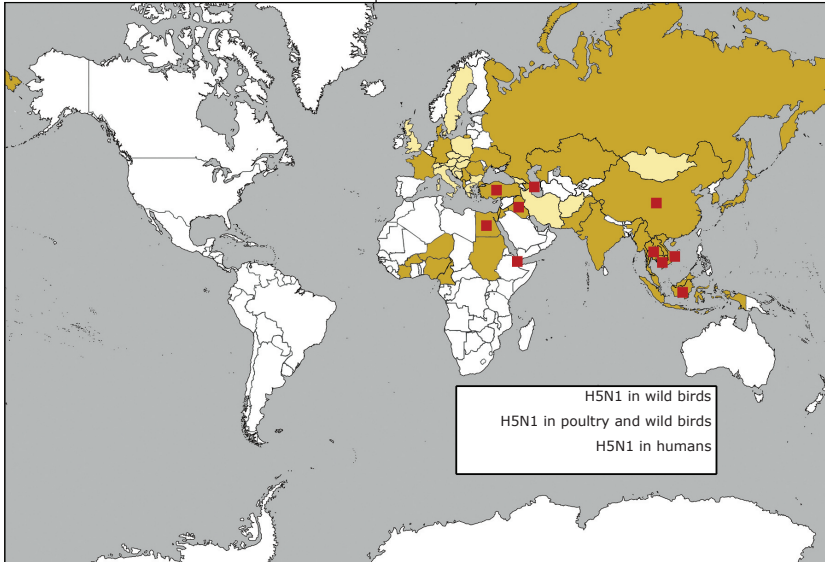
December 2005 – Passage of the Public Readiness and Emergency Preparedness Act (PREP Act)
December 2005 – Enrollment for clinical trials with H5N1 vaccine in healthy adults (>65 years of age) was completed
December 2005 – Tabletop communications exercises with US Departments and representatives from Canada and the UK
December 2005 – WHO Global Pandemic Communications Meeting in Switzerland, HHS led US delegation
December 2005 – First State Summit, Minnesota
December 2005 – Release of State and Local Pandemic Influenza Checklist
December 2005 – Convening of States Summit, in Washington, DC
December 2005 – Release of Business Pandemic Influenza Checklist

Monitoring and Surveillance (cont.)

This year, in the United States, biologists from the Departments of Interior and Agriculture and their state partners have tested more than 35,000 wild birds for the presence of H5N1.

This testing has revealed the presence of low pathogenic H5N1 and other avian viruses in several states this fall. These low pathogenic viruses are common

to wild fowl, and are very different from the highly pathogenic H5N1 circulating in parts of Asia, Europe and Africa. To date, highly pathogenic H5N1 has not been found in the Americas.



The testing is critical to provide an early warning should the highly pathogenic H5N1 virus be brought here by migratory birds. Early detection creates the opportunity to take precautions to prevent the spread of the deadly virus. Highly pathogenic avian influenza (HPAI) strains have been found and eradicated three times in the United States: in 1924, 1983 and 2004. No significant human illness resulted from any of these outbreaks.

HHS is investing resources in international surveillance and response to assist other countries in detecting a pandemic influenza outbreak early. These resources will help other countries prepare for an influenza pandemic to minimize and contain the impact of a pandemic, should one occur.

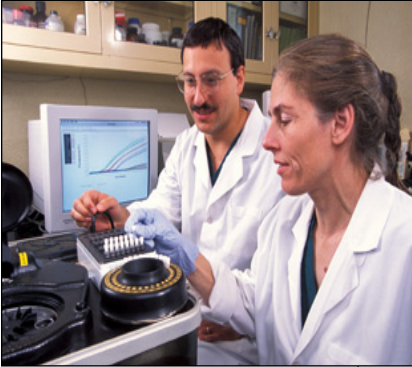
Should people become sick, it is critical to be able to quickly confirm whether or not they have been infected by the H5N1 virus. A reliable, rapid diagnostic test is needed for epidemiologic assessments, traveler screening and clinical care. The CDC is currently studying proposals for the development of such a test, and expects to award contracts later this year.

- January 2006 – RFI issued on increasing egg-based vaccine capacity
- January 2006 – Bilateral teams sent to Turkey, Armenia, Azerbaijan, Georgia, Romania, Ukraine and Nigeria to assess avian flu outbreaks
- January 2006 – Tokyo WHO conference to draft WHO pandemic plan
- January 2006 – International Pledging Conference in Beijing; \$334M in US grants and technical assistance to aid global effort
- January 2006 – 6 State Summits AZ, VT, WV, RI, GA, KY
- January 2006 – Roughly 5 million courses in SNS stockpile development of promising antivirals
- January 2006 – Release of Individuals and Families Pandemic Influenza Checklist

Research

The Armed Forces Institute of Pathology has been collecting pathological specimens since 1862. It holds some 2.5 million specimens. Exactly one of them, a lung specimen from an Army private who died in 1918, had genetic material for the virus that caused the 1918 Spanish Flu pandemic.

Applying genetic sequencing, pathologists at the Institute were able to replicate the genetic code of the deadly virus. Scientists were then able to reconstruct a virus containing all eight 1918 flu virus genes.



Unlike typical seasonal flu, which strikes hardest at the very young, the elderly and those with compromised immune function, the 1918 flu disproportionately killed young people in the prime of life. Scientists wanted to know why. Mouse studies provided clues to the answer.

“We clearly see a dramatic and uncontrolled immune response in the mouse lungs as early as one day following infection with the reconstructed 1918 virus,” said Michael G. Katze who led the research team. The virus may have turned the Army private’s immune system against him. If true, people in their prime of life, with the strongest immune systems, were most at risk.

Of particular concern is that in the limited number of human cases identified to date, we are seeing similar human mortality patterns associated with the current highly pathogenic H5N1 virus.

Genetic sequencing promises to energize the race to understand avian flu. Surveying and comparing how the virus strains circulating in poultry are changing could alert researchers to an imminent pandemic. It could also help them to select a strain to target with a vaccine. With the 1918 virus sequenced, scientists can compare genetic sequences and perhaps determine what makes one strain more lethal than another and what makes one strain more contagious than another.

The genetic sequence of each influenza virus is more than 13,000 letters long. The Influenza Genome Sequencing Project, an international collaboration supported by the National Institute of Allergy and Infectious Diseases, has set up a production line, growing different virus strains, isolating their genetic material, and then sequencing them one by one. The project’s goal is to sequence 500 to 1000 strains a year. With the sequences of over 1650 human and avian isolates made available in less than two years since its inception, the project has proven successful so far.

January 2006 – First state summit with signing of a Planning Agreement, Vermont
January 2006 – Release of Faith-based & Community Organizations Pandemic Influenza Checklist
January 2006 – Release of School Districts (K-12) Pandemic Influenza Checklist

February 2006 – Enrollment in a pediatric H5N1 vaccine clinical trial (children aged two to nine years)

February 2006 – Risk Communications Preparedness Workshop hosted by CDC in Thailand
February 2006 – Meeting with UN Coordinator for avian and pandemic influenza on how to best assist UN efforts

February 2006 – 11 State Summits CT, IA, MA, FL, OH, NV, DE, AL, MO, NE, MD
February 2006 – Laboratory assay for diagnostic testing of avian influenza A/H5 approved

Jan 2006

February 2006

Vaccines and Vaccine Production Capacity

Vaccines are the time-tested means for preventing influenza. HHS is committed to developing the technologies and creating the vaccine production capacity that pandemic preparedness requires.

First, HHS is investing in development of pre-pandemic vaccines – vaccines against currently circulating H5N1 avian influenza virus strains using conventional egg-based production methods. The situation is that the H5N1 avian influenza viruses continue to change – yielding families of closely related new strain variants, technically known as clades. The expectation is that the pre-pandemic vaccine developed from an H5N1 clade 1 virus will provide at least partial protection against new virus strains. It is, for now, the best vaccine defense we have; and so we are stockpiling it. We currently have sufficient H5N1 clade 1 vaccine courses on hand to vaccinate some three million people.

In response to the emergence of a second clade of H5N1 avian influenza viruses during 2005-2006 in Asia and Europe, HHS is moving forward with the development of H5N1 clade 2 vaccine candidates and the manufacturing of H5N1 clade 2 vaccine stockpiles. Depending on availability of vaccine seed stocks and production yield, we expect to have another five million courses of H5N1 clade 1 and clade 2 vaccines stockpiled in 2007.

Second, HHS committed over \$1 billion during 2005 and 2006 for advanced development of cell-based influenza vaccine production methods. This investment will make possible a more flexible alternative to egg-based production methods. It sets the stage for the modernization and expansion of domestic production capacity that must occur if the US is to be able to acquire 300 million treatment courses of a human vaccine within six months after the emergence of a pandemic virus.

Third, recognizing the need to expand egg-based vaccine production capacity along with cell-based capacity, HHS in July 2006 sought proposals to adapt existing egg-based manufacturing facilities for emergency production of pandemic influenza vaccine. Contracts are expected to be awarded this December.

Fourth, HHS is moving forward with advanced development of ways to make vaccines more efficient. The use of vaccine additives called adjuvants could potentially extend U.S. pandemic influenza vaccine supply several-fold and

“WHO and international experts believe that the world is now closer to another influenza pandemic than at any time since 1968, when the last of the previous century’s three pandemics began”

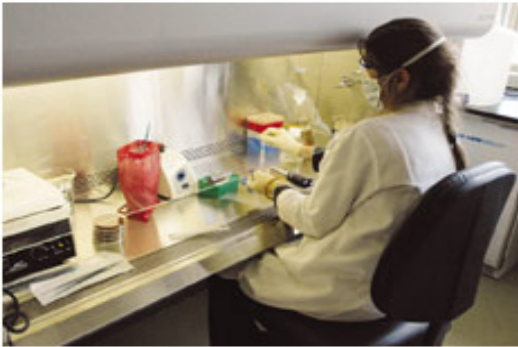
–Dr. Margaret Chan
Director-General Elect
World Health Organization
December 7, 2005

March 2006 – Release of Medical Offices and Clinics
Pandemic Influenza Planning Checklist
March 2006 – Release of Home Health Care Checklist
March 2006 – Release of Child Care and Preschool Checklist
March 2006 – 19 State Summits SC, SD, ND, WY, WI, PA, IL,
NC, VA, IN, PR, CO, UT, ID, TX, NM, OR, CA and the Virgin Islands
March 2006 – Results published demonstrated that inactivated
H5N1 vaccine induces immune responses in healthy adults
March 2006 – RFP issued for advanced
development of antigen sparing technologies
March 2006 – Pandemic flu supplemental
guidance sent to states
March-April 2006 – FDA approves
Relenza for the prevention of influenza
A and B in adults and children

Vaccines and Vaccine Production Capacity (cont.)

thus decrease the time required to achieve our manufacturing capacity target. Recently, both GlaxoSmithKline and Novartis announced results of studies demonstrating that adjuvanted vaccine produced possible protective immunity at substantially lower doses of antigen than did unadjuvanted vaccine. HHS is encouraged by these findings. Moreover, HHS currently is reviewing contract proposals for further development of such dose-sparing technologies.

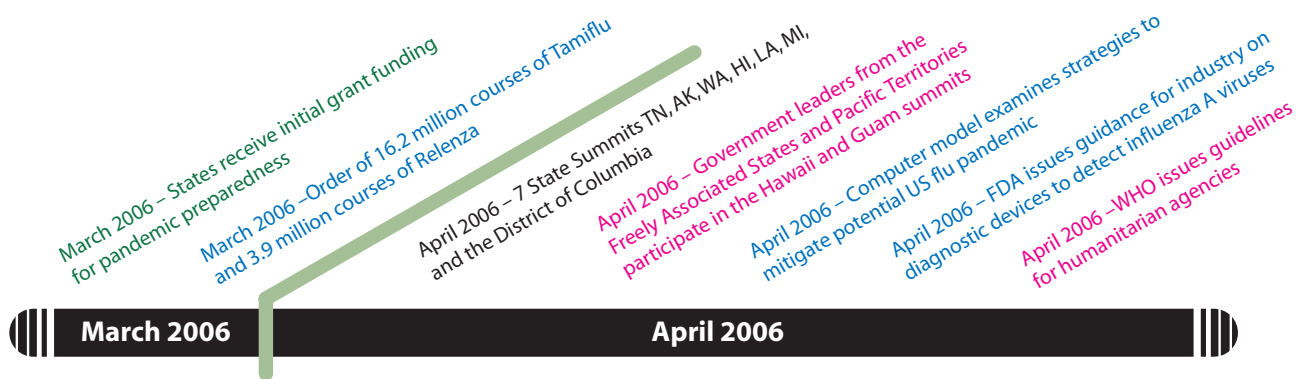
Fifth, HHS is looking to the long-term, beyond current strain-specific influenza vaccines, with a view to fostering development of a “universal vaccine” – one that provides broad-based, cross-protective immunity against multiple virus strains.



A universal vaccine would protect against viruses resulting from antigenic shift (significant changes in viral proteins) that historically have been associated with influenza pandemics as well as those resulting from antigenic drift (small changes in viral proteins) associated with seasonal influenza.

Although this is not a new concept, the prospect is receiving increased attention because new technologies have made important pre-clinical studies possible. NIH is currently working to bring such vaccine candidates through the discovery and proof-of-concept stages. Successful development of a “universal” influenza vaccine would mean that you would need only one flu shot to protect you for many years (possibly for life). This, in turn, would mean that we could stockpile the universal vaccine – thereby making influenza pandemics things of the past.

The United States is not alone in the quest to establish an adequate influenza vaccine supply. The World Health Organization (WHO) has taken a significant step forward in the global effort by publishing the Global Pandemic Influenza Action Plan to Increase Vaccine Supply. The United States has provided \$10 million to WHO to support other countries as they develop sustainable programs for vaccines to counter H5N1 or other novel influenza viruses that can infect humans.



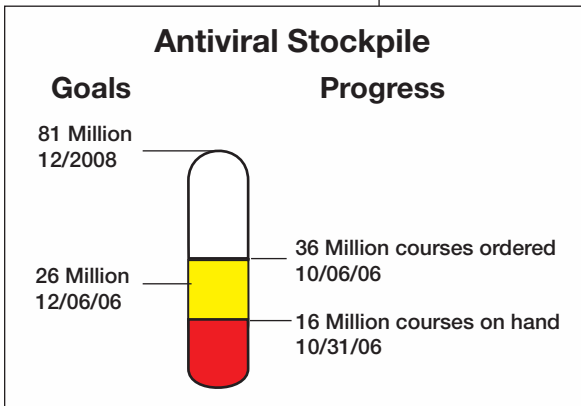
Antiviral Drugs



Antiviral medications are principally used to treat influenza infections, lessening the impact of a virus after an individual has been infected. Under certain circumstances, these drugs can also reduce transmission of the virus or even prevent infection. Two antiviral drugs are effective against the H5N1 virus in laboratory testing. Tamiflu, manufactured by Roche Laboratories, is administered as a course of capsules or liquid that is taken orally. Relenza, manufactured by GlaxoSmithKline, is administered by an inhaler. Both work by blocking the ability of the virus to multiply beyond the infected host cell.

Antivirals are an important part of our nation's Strategic National Stockpile (SNS) against pandemic flu. A total of \$782 million was allocated this year for the purchase of antivirals. The goal is to have 26 million courses of antivirals on hand by the end of 2006 and a total of 50 million courses in the SNS by the end of 2008. The Federal stockpile, in addition to State purchases of 31 million courses of antivirals, will ensure that we have enough antivirals for 25 percent of the population.

We are on target to meet those goals. Sixteen million courses of antivirals have already been warehoused, and we will have 36 million courses on hand by March 2007.



In addition to these direct purchases, HHS allocated \$170 million to subsidize state purchases of an additional 31 million courses of antivirals. These were apportioned based on population, with HHS paying 25 percent of the cost. Thirty-three states have already placed orders. Four states plan to make unsubsidized purchases above their allocation; only four states do not plan to take full advantage of the subsidy program. To date, states have ordered more than eight million courses. All stockpiled antivirals must be reserved for use in a potential pandemic; they may not be used to treat seasonal flu.

States know their delivery systems best, and are responsible for the intrastate distribution of antivirals in a pandemic. To help them, HHS joined with the Healthcare Distribution Management Association (HDMA) to develop a model distribution plan. This was completed in August, and the HDMA is now working with states to help them adapt the plan to their specific situations. Those plans will then be reviewed by HHS and the Department of Homeland Security.

April 2006 – NIH researchers model interregional spread of influenza through United States as described by virus type, size of population and commuting rates and distance

April 2006 – HHS provides assistance to Bangladesh and India to enhance planning for a potential influenza pandemic

May 2006 – Release of National Strategy for Pandemic Influenza: Implementation Plan

May 2006 – HHS awards contracts to develop cell-based influenza vaccine

May 2006 – Department of State establishes Avian Influenza Action Group to coordinate US international effort

May 2006 – Release of Long-Term Care and Other Residential Facilities Checklist

Antiviral Drugs (cont.)

Stockpiling Other Supplies

HHS has also purchased equipment for the national stockpile. Purchases to date include 73.1 million N95 respirators (with an additional 31.8 million on order) and 37.4 million surgical masks (with an additional 14.1 million on order), as well as face shields, gloves and gowns.

HHS has allocated \$25 million towards ventilator procurements. Studies are underway to determine the most appropriate types of ventilators to stockpile for response to a pandemic influenza event. SNS ventilator procurements are projected to occur in 2007-2008.

State and Local Preparedness

“The fact that New York is a major gateway to the nation and one of the world’s most densely populated cities means the possibility of a pandemic flu, however remote, is one that we must take seriously”

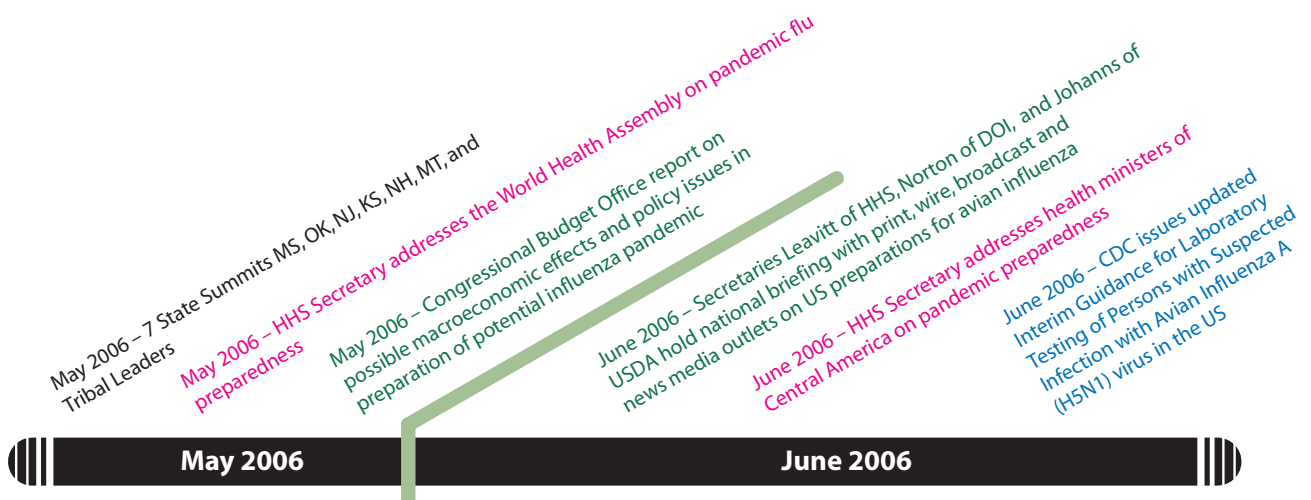
–Michael Bloomberg
Mayor, New York City

There is a video on www.pandemicflu.gov that models how a flu pandemic could spread across the United States. The model advances roughly two days per second. Forty-four seconds into day 85, virtually every county in the country is bright red, meaning more than three percent of the population is ill. If the flu is highly contagious, that happens in 64 days, and more than half the population will ultimately be affected.

What this says is that every state, every county, every community will be affected, and they could be affected over a short period of time. There would be little opportunity to shift resources from one part of the country to another, highlighting the priority of preparedness at all levels and by all sectors of society.

How you and your community will fare in a pandemic will depend in large part on planning and preparations that are put in place today at the state and local level.

That message is well understood. From Alabama, where the Poarch Band of Creek Indians and all 68 counties have conducted pandemic planning summits,



State and Local Preparedness (cont.)

to Oregon, which has conducted on-site assessments of the preparedness activities of every local health department, state and local governments are taking the threat seriously.

Every state has at least drafted a pandemic plan. The National Governors Association, with HHS funding, has launched a major initiative to help states with issues such as public health preparedness, continuity of government, and maintaining the central functions of society during a pandemic. This endeavor will include a year-long series of regional tabletop exercises. Pandemic flu exercises have already been held in more than a dozen states, and Michigan alone has held eight. Connecticut has held eight editorial board meetings to establish, as they put it, a foundation of trust between government and the media. Idaho has planned for handling garbage removal and other public works when services are not available. And so it goes.

The planning effort has been encouraged and supported by HHS. In August, based on initial state plans, I released an additional \$225 million to support these tabletop and benchmarking exercises. In addition, HHS and CDC are delivering a Crisis and Emergency-Risk Communications (CERC) course, presenting and applying proven tools and approaches to the communication of crisis information.

One of the major planning challenges surrounds community-based public health interventions such as school closure and travel restrictions, and encouraging people to stay at home, out of the way of the virus.

CERC Tabletop Assumptions

- Susceptibility to the virus will be universal
- 50% of those sickened will seek outpatient-care
- Communities should expect multiple waves of infection
- Outbreak in each community will last 6-8 weeks
- Need for credible information will be vast

With funding from HHS, the Institute of Medicine recently conducted a workshop on the role of community-based mitigation strategies during an influenza pandemic. Workshop participants were asked to assess how well existing computer models can predict the effectiveness of various community-containment procedures. They also examined how well such interventions worked during previous disease outbreaks, and discussed the potential consequences of community containment in a pandemic. Their report is expected by the end of the year.

June 2006 – Indonesia holds H5N1 influenza expert consultation

June 2006 – USAID announces \$5 million award to enhance international efforts to track avian influenza pandemic preparedness

June 2006 – Congress passes \$2.3 billion funding for influenza diagnostic testing

July 2006 – New York City Summit

July 2006 – Arkansas Summit

July 2006 – Contract awarded for \$165,943,000 in antiviral drugs

State and Local Preparedness (cont.)

“More than three-fourths of Americans say they would cooperate if public health officials recommended that for one month they curtail various activities of their daily lives.”

—Harvard School of Public Health
October 20, 2006

A Harvard School of Public Health survey released at the workshop explored potential community and personal impacts. The encouraging news was that a large majority of people surveyed said they would follow public health recommendations even if doing that requires major changes in their lives. Almost all would stay away from other people if they were infected with a pandemic flu; 85% said they would isolate the entire family if any one member became ill.

But while the survey revealed resolution, it also exposed vulnerabilities. Almost one in four (24%) said they would have no one to care for them if they were sick at home. Roughly the same number (26%) said they would experience severe financial problems if they missed even seven to ten days of work, and a majority (57%) said they would be in financial trouble if they missed one month of work.

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Communications

In early 2007, a team of pandemic flu experts and communicators will tell meetings of senior news executives that human-to-human transmission of H5N1 has been identified in a village overseas. Later in the day, they will be told the disease has spread across a region overseas. And finally, they will be told that human cases have been reported in the United States.

The announcements will be fake, part of an exercise to test how the media – and the experts – will respond should the day come when similar announcements have to be made for real. The two sides will work through the challenges of getting and reporting timely, accurate information.

One challenge is how to keep the public informed, without undue alarm, in situations where there is high interest and little new information, situations that could develop, for instance, while waiting for the results of confirmatory testing. The exercise will be repeated in six other cities, reaching national, regional, Hispanic and African-American media.

Aug 2006- Quick Diagnosis of Flu Strains Possible with New Microchip Test

Aug 2006- New York State Summit

Sep 2006- FDA Issues Guidance to Industry for Development of Call-based Viral Vaccines

October 2006- California purchases \$3.9 million courses of antivirals

