



Pandemic Influenza: Domestic Preparedness Efforts

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Summary

In 1997, a new avian influenza (“flu”) virus emerged in Asia and jumped directly from birds to humans, killing six people. The virus has since spread to more than 50 countries in Asia, Europe and Africa, where it has killed millions of birds and infected more than 270 people, killing more than 160 of them. The virus bears some similarity to the deadly 1918 Spanish flu, which caused a global pandemic estimated to have killed more than 50 million people worldwide. The current spread of avian flu raises concerns about another human flu pandemic.

Global pandemic preparedness and response efforts are coordinated by the World Health Organization (WHO). Domestic preparedness efforts are led by the White House Homeland Security Council, with the U.S. Department of Health and Human Services (HHS) playing a major role. Domestic response efforts would be carried out under the all-hazards blueprint for a coordinated federal, state and local response laid out in the National Response Plan, overseen by the Department of Homeland Security (DHS). HHS officials would have the lead in the public health and medical aspects of a response. The federal government has released several pandemic flu plans to govern federal, state, local and private preparedness activities.

There are concerns about how a domestic public health and medical response would be managed during a flu pandemic. There is precedent, under the Stafford Act, for the President to declare an infectious disease threat an emergency (which provides a lower level of assistance), but no similar precedent for a major disaster declaration (which provides a higher level of assistance). In any case, many of the needs likely to result from a flu pandemic could not be met with the types of assistance provided pursuant to the Stafford Act, even if a major disaster declaration applied.

Vaccination is the best flu prevention measure. But because of continuous changes in the genes of flu viruses, vaccines must be “matched” to specific strains to provide good protection. A pandemic flu strain would, by definition, be novel. Stockpiled vaccine would not match, so stockpiling in anticipation of a pandemic is of limited value. In addition, global and domestic capacity to produce flu vaccine is limited. The U.S. government, primarily through HHS, has launched an aggressive effort to expand domestic vaccine production capacity, and to develop technologies to support more rapid production of a matched vaccine at the onset of a pandemic.

Since matched vaccine would not be available at the outset of a flu pandemic that occurred within the next several years, planning efforts focus on measures to slow the spread of disease, and mitigate its effects. These include stockpiling of antiviral drugs to prevent or treat flu infection, planning for medical surge capacity, and continuity planning for businesses and utilities.

This report discusses pandemic flu in general, WHO and U.S. preparedness and response plans, and a number of relevant policy issues. The focus of this report is U.S. domestic public health preparedness and response planning, and the projected impacts of an influenza pandemic on Americans. This report will be updated to reflect changing circumstances.

Contents

Introduction	1
Understanding Pandemic Influenza.....	3
What Is Pandemic Influenza?.....	3
Pandemic Phases	4
Influenza Pandemics in the 20 th Century.....	5
Current Situation	6
H5N1 Avian Influenza	6
Other Flu Strains with Pandemic Potential	8
Potential Impacts of an Influenza Pandemic	8
Deaths and Hospitalizations.....	8
Economic Impacts.....	9
Pandemic Influenza Planning	10
WHO Global Influenza Preparedness Plan	10
U.S. Federal Pandemic Plans	11
National Pandemic Plans	11
Health Sector Pandemic Plans	12
Department of Defense Planning	13
Department of Veterans Affairs Planning	13
State Pandemic Plans	14
Private Sector Planning.....	14
Issues in Pandemic Influenza Planning	14
Could an Influenza Pandemic Be Stopped?	14
Who’s in Charge?.....	15
Emergency Declarations and Federal Assistance.....	17
Limited Surveillance and Testing Capability	18
Isolation and Quarantine	19
Medical Surge Capacity	21
Rationing Scarce Resources.....	21
Influenza Vaccine Supply and Use.....	23
Overview.....	23
Limited Vaccine Production Capacity.....	24
Vaccine Research and Development.....	24
Global Vaccine Availability	25
Regulatory Issues.....	25
Intellectual Property Issues	26
Vaccine Tracking and Distribution.....	27
Antiviral Drug Supply and Use.....	27
Liability and Compensation for Pandemic Countermeasures	29
Status of Current Planning Efforts	29
Smallpox Vaccine Injury Compensation.....	30
The 1976 Swine Flu Affair.....	30
Influenza as a Weapon.....	30

Tables

Table 1. WHO Pandemic Phases	5
Table 2. NVAC and ACIP Recommendations for Pandemic Vaccine Priority Groups	22

Contacts

Author Contact Information	31
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Between pathogens and humans it is a race of their genes against our wits.

—Joshua Lederberg, winner of the 1958 Nobel Prize in Medicine for his work on genetic recombination in bacteria

Introduction

The U.S. Department of Health and Human Services (HHS) defines the following influenza (flu) terms:

- *Seasonal (or common) flu* is a respiratory illness that can be transmitted person to person. Most people have some immunity, and a vaccine is available.
- *Avian (or bird) flu* is caused by flu viruses that occur naturally in wild birds. The H5N1 strain of current concern is highly pathogenic in birds, deadly to domestic fowl, and can be transmitted from birds to humans. There is no human immunity, and no human vaccine is available.
- *Pandemic flu* is virulent human flu that causes a global outbreak, or pandemic, of serious illness. Because there is little natural immunity, the disease can spread easily from person to person. Currently, there is no pandemic flu.¹

In this report, unless otherwise noted, the term *pandemic* will be used to refer to pandemic influenza.

In 1997 a new strain of *avian flu* jumped from poultry directly to humans in Hong Kong, causing several human deaths. This was the first documented occurrence of direct transmission of an avian flu virus from birds to people. Despite efforts to contain the virus through culling of poultry flocks, the virus (designated as H5N1 for specific proteins on its surface) re-emerged in 2003. It has since been reported in domestic poultry and/or wild birds in more than 50 countries in Asia, Europe and Africa.² Also since 2003, it has infected more than 270 people (and killed more than 160 deaths) in ten countries.³ As of yet the virus has not developed the ability to transmit efficiently from person to person. Were that to occur, a global influenza pandemic could ensue.

The high lethality of the H5N1 strain and its tendency to affect healthy young people remind health authorities of the deadly 1918 Spanish flu, which is estimated to have killed up to 2% of the world's population, and was a substantial cause of mortality in U.S. military personnel in World War I. The World Health Organization (WHO) says, "If an influenza pandemic virus were to appear again similar to the one that struck in 1918, even taking into account the advances in medicine since then, unparalleled tolls of illness and death could be expected."⁴

¹ Adapted from HHS, "Flu Terms Defined," at <http://www.pandemicflu.gov>.

² World Organization for Animal Health (known by its French acronym, OIE), "Update on Avian Influenza in Animals in Asia (Type H5)," at http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm. OIE is an intergovernmental organization of 167 nations and is not part of the United Nations system.

³ World Health Organization, "Confirmed Human Cases of Avian Influenza A/(H5N1)," as of Feb 19, 2007, at http://www.who.int/csr/disease/avian_influenza/country/en/.

⁴ WHO, "Global Influenza Preparedness Plan: The Role of WHO and Recommendations for National Measures before and during Pandemics," 2005, (hereafter called the WHO pandemic plan), p. 3, at <http://www.who.int/csr/disease/> (continued...)

U.S. and world health authorities believe that while periodic influenza pandemics are inevitable, their progress may be slowed, and their impacts blunted, by rapid detection and local control efforts. The added time would allow affected countries to better manage the situation, and countries not yet affected to better prepare. To realize these benefits, countries affected by avian flu must be able to track the spread of the virus in birds, and quickly detect and investigate suspected human cases. Hence, a country's capabilities in epidemiology, laboratory detection and other public health services affect the welfare of the global community as well as the country itself. This presents developed nations with novel policy challenges. For example, should they reserve scarce health resources such as antiviral drugs for themselves, or deploy them to other countries at the center of an emerging pandemic?

WHO released an updated pandemic preparedness plan in early 2005. The United States released a draft pandemic plan in August 2004, and has since released a number of documents addressing government-wide planning, public health and medical preparedness, planning for critical infrastructure readiness, and others. (See the subsequent section, "Pandemic Influenza Planning," for plans and descriptions.) States were required to prepare pandemic plans as a condition of their federal bioterrorism preparedness grants. The Administration has created a government-wide public website to disseminate information on pandemic flu preparedness and response activities.⁵

A recurring theme in planning documents and consultations is the need to engage sectors beyond healthcare and public health in planning. The Secretary of HHS, Michael Leavitt, has said, "If a pandemic hits our shores, it will affect almost every sector of our society, not just health care, but transportation systems, workplaces, schools, public safety and more. It will require a coordinated government-wide response, including federal, state and local governments, and it will require the private sector and all of us as individuals to be ready."⁶ A 1918-style pandemic could be so severe that non-health-related essential services would be impaired by high absenteeism or supply chain disruptions, and health services could be in such short supply that law enforcement protection might be required for them. Though WHO does not recommend it, except in some narrow circumstances for pre-pandemic control, countries might seal their borders or take similar measures, with impacts on trade and commerce.⁷

If a flu pandemic were to occur in the next several years, the U.S. response would be affected by the limited availability of a vaccine (the best preventive measure for flu), as well as by limited availability of certain drugs used to treat severe flu infections, and by the general lack of surge capacity within our healthcare system. The U.S. healthcare system is largely private, while the public health system is largely based in state, rather than federal, authority. This structure creates numerous challenges in assuring the needed response capacity, and coordinating the various response elements. Planning is further complicated by the fact that while periodic influenza pandemics have been seen over the years, their timing and severity have been unpredictable.

Domestic planning efforts presume that the National Response Plan (NRP), an *all-hazards* plan developed by the Department of Homeland Security (DHS), would be activated if needed to streamline the federal response to a pandemic. Pandemic flu is unlike most other threats, though.

(...continued)

[influenza/pandemic/en/](http://www.pandemicflu.gov/).

⁵ See <http://www.pandemicflu.gov/>.

⁶ Remarks of HHS Secretary Michael Leavitt on "Avian Flu," National Press Club, Oct. 27, 2005, CQ Transcriptions.

⁷ See CRS Report RS22453, *Avian Flu Pandemic: Potential Impact of Trade Disruptions*, by (name redacted).

Since flu is communicable, there is no scene to secure, and all states might be affected nearly simultaneously. Thus, while a pandemic could cause catastrophic levels of illness and death, the nation's traditional disaster response mechanisms—using geographical declarations of emergency and disaster, and state-to-state mutual aid—may be ill-suited for this threat.⁸

This report discusses pandemic influenza in general, previous pandemics and their global and domestic impacts, and the possible impacts of another pandemic caused by the H5N1 avian flu strain. It also discusses WHO and U.S. preparedness plans and their context in broader emergency preparedness efforts. Finally, the report looks at a number of policy issues in pandemic influenza preparedness and response. While reference is made when relevant to global preparedness efforts and to animal health impacts, this report focuses on U.S. domestic public health preparedness and response planning, and the projected impacts of an influenza pandemic on Americans. This report will be updated to reflect changing circumstances.

For more information on avian, pandemic and seasonal flu preparedness, see the following CRS Reports:

- CRS Report RL33219, *U.S. and International Responses to the Global Spread of Avian Flu: Issues for Congress*, by (name redacted);
- CRS Report RL33795, *Avian Influenza in Poultry and Wild Birds*, by (name redacted) and (name redacted);
- CRS Report RL33871, *Foreign Countries' Response to the Avian Influenza (H5N1) Virus: Current Status*, by (name redacted) et al.;
- CRS Report RS22576, *Pandemic Influenza: Appropriations for Public Health Preparedness and Response*, by (name redacted).
- CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by (name redacted) and (name redacted).

Understanding Pandemic Influenza

What Is Pandemic Influenza?

A *pandemic* (from the Greek, for “all of the people”) is an epidemic of human disease occurring over a very wide area, crossing international boundaries and affecting a large number of people. Though it does so with some regularity, influenza is not the only pathogen that can cause pandemics. A pandemic of the “Black Death,” which affected most of Europe in the 14th century, is generally attributed to plague (technically *Yersinia pestis*). The global spread of HIV/AIDS is often referred to as a pandemic. Literature offers numerous examples of such episodes of widespread contagion.

Influenza is a virus that causes respiratory disease in humans, with typical symptoms of fever, cough, and muscle aches, and, rarely, pneumonia and death. Though primarily a human pathogen, influenza viruses also circulate and cause illness in swine, horses, mink, seals, and domestic

⁸ For more information, see CRS Report RL33579, *The Public Health and Medical Response to Disasters: Federal Authority and Funding*, by (name redacted).

poultry, and may be carried without apparent illness in these species as well as a number of species of waterfowl. Influenza is highly contagious in humans, spreading through direct contact and airborne exposure. The virus can also persist for several hours on inanimate objects such as toys or doorknobs. In addition, influenza is infectious before symptoms appear in its victims, which also enhances its spread.⁹

Influenza viruses have a genome composed of eight segments of RNA. In addition to random mutation, flu viruses also undergo change by shuffling or *reassorting* these gene segments among different strains. Human flu viruses are of two types: Influenza A and B. Influenza A strains are further identified by two important surface antigens (proteins) that are responsible for virulence: hemagglutinin (H) and neuraminidase (N). Fifteen different H antigens and nine different N antigens have been identified in birds and mammals. Not all possible combinations of H and N antigens have been documented, and very few combinations have been shown to cause human illness. The avian flu strain causing great concern at this time is designated as H5N1 for its surface antigens.

New influenza strains typically circle the globe within three to six months of emergence. New strains circulate each year, changing slightly from prior strains (called *antigenic drift*). Each year the virus, its genome in constant flux, typically makes healthy people sick, but is generally not deadly. Healthy adults typically have partial immunity to new strains, but a newly formulated vaccine is required each year to provide full immunity. Now and then, often several times in a century, the virus changes enough through mutation or reassortment (called *antigenic shift*) that there is no partial immunity in the population. This event, an influenza pandemic, results in severe illness and death, even in healthy people. The extent and severity of illness, and the disabling impact on healthy young people, could cause serious disruptions in services and social order.

Pandemic Phases

According to WHO, the hallmarks of an influenza pandemic are: (1) the emergence of a novel influenza virus strain; (2) the finding that the strain can cause human disease; and (3) sustained person-to-person transmission of the strain. Novel influenza viruses typically acquire these characteristics in phases. **Table 1** shows the phases of an influenza pandemic as described by WHO. In the *interpandemic period*, there is no human circulation of novel viruses. During this period, there is annual circulation of common influenza viruses, which cause outbreaks each winter. In the *pandemic alert period*, a new strain is present, with increasing ability for human-to-human spread. During a *pandemic period* there is sustained human-to-human transmission of the new strain. **Table 1** also shows the public health goals WHO recommends to slow the development and spread of novel virus strains as much as possible. WHO reports the current global status at “Pandemic Alert Level 3:” a new virus is causing human cases of illness, but with no or very limited human-to-human transmission.¹⁰

⁹ David L. Heymann, *Control of Communicable Diseases Manual*, 18th ed., an official report of the American Public Health Association, 2004; and the Centers for Disease Control and Prevention (CDC) influenza home page, at <http://www.cdc.gov/flu/>.

¹⁰ WHO, Current WHO Phase of Pandemic Alert, as of February 20, 2007, at http://www.who.int/csr/disease/avian_influenza/phase/en/index.html.

Table I. WHO Pandemic Phases

Phase	Description	Overarching public health goals
Interpandemic period		
Phase 1	No new influenza virus strains have been detected in humans. A virus strain that has caused human infection may be present in animals. If so, the risk of human infection is considered to be low.	Strengthen global influenza pandemic preparedness at the global, regional and national levels.
Phase 2	No new influenza virus strains have been detected in humans. However, a circulating animal influenza virus strain poses a substantial risk of human disease.	Minimize the risk of transmission to humans; detect and report such transmission rapidly if it occurs.
Pandemic alert period		
Phase 3	Human infection(s) with a new strain, but no human-to-human spread, or at most rare instances of spread to a close contact.	Ensure rapid characterization of the new virus strain, and early detection, notification and response to additional cases.
Phase 4	Small cluster(s) with limited human-to-human transmission, but spread is highly localized, suggesting that the virus is not well adapted to humans.	Contain the new virus within limited foci or delay spread to gain time to implement preparedness measures, including vaccine development.
Phase 5	Larger cluster(s), but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).	Maximize efforts to contain or delay spread, to possibly avert a pandemic, and to gain time to implement pandemic response measures.
Pandemic period		
Phase 6	Pandemic: increased and sustained transmission in the general population	Minimize the impact of the pandemic.

Source: WHO Global Influenza Preparedness Plan, 2005, at <http://www.who.int/csr/disease/influenza/pandemic/en/index.html>.

Influenza Pandemics in the 20th Century¹¹

Historical records suggest that influenza pandemics have occurred periodically for at least four centuries. In the 20th century there were three influenza pandemics, and several “pandemic threats.”

The **1918 Spanish Flu** (H1N1) pandemic is estimated to have killed more than 50 million people worldwide, and at least 675,000 in the United States.¹² Illness and death rates were highest among adults 20-50 years old. HHS notes that “the severity of that virus has not been seen again.” Similarities between the 1918 pandemic and the current H5N1 avian flu situation have the global public health community on edge.

¹¹ Unless otherwise noted, information for this section is found on the U.S. federal government pandemic flu website, at <http://www.pandemicflu.gov/>.

¹² The U.S. population in 1918 was about one-third its current size, based on decennial census reports of more than 92 million in 1910, and more than 106 million in 1920. The U.S. population is currently slightly more than 300 million. See <http://www.census.gov>.

The **1957 Asian Flu** (H2N2) was first identified in Asia in February 1957 and spread to the United States during the summer. Health officials responded quickly and vaccine was available in limited supply by August. This pandemic killed about 69,800 people in the United States.

The **1968 Hong Kong Flu** (H3N2) became widespread in the United States in December of that year. It is estimated that 33,800 people died from this pandemic in the United States, (affecting those over the age of 65 disproportionately), making it the mildest pandemic of the 20th century.

The **1976 Swine Flu Scare**¹³ (H1N1) began when a novel virus, identified in New Jersey, was thought to be related to the Spanish flu virus of 1918 and to have pandemic potential. Federal officials mounted a vaccination campaign, and Congress provided liability protection for the manufacturer and federal injury compensation for those harmed by the vaccine. Ultimately, the virus did not spread, but the vaccine was linked with a rare neurological condition that affected more than 500 people and killed 32. The episode damaged confidence in public health officials.

The **1977 Russian Flu Scare** (H1N1) involved a virus strain that had been in circulation prior to 1957. As a result, severe illness was generally limited to those without prior immunity (i.e., children and young adults). The epidemic is not, therefore, considered a true pandemic.

In **1997, H5N1 Avian Flu**, emerged in Hong Kong and appeared to have been stamped out by mass culling of poultry. The virus re-emerged in 2003 and has spread to three continents. Global containment efforts continue.

In **1999, an H9N2** flu strain was found to have caused human illness in Hong Kong. This strain continues to circulate in birds and remains of concern to public health officials, but has not as yet shown the same lethal potential as the H5N1 strain. In August, 2004, the National Institutes of Health (NIH) awarded a contract to the Chiron corporation to produce up to 40,000 doses of an investigational vaccine against this strain, should it develop the capacity for human-to-human transmission.¹⁴

Current Situation

H5N1 Avian Influenza

WHO maintains a Web page with a cumulative count of human H5N1 cases.¹⁵ As of February 19, 2007, WHO reported 274 cases, 167 of them fatal, in 11 countries: Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Nigeria, Thailand, Turkey and Vietnam. The WHO describes pandemic influenza and the situation with H5N1 as follows:¹⁶

¹³ Sources for this section are: Richard E. Neustadt and Harvey V. Fineberg, *The Swine Flu Affair*, a report to the Secretary of Health, Education and Welfare, June, 1978; and HHS Draft Pandemic Influenza Preparedness and Response Plan, Annex 11: "Lessons Learned from 1976 Swine Influenza Program," Aug. 2004. This incident is discussed further in a later section on vaccine liability and compensation issues.

¹⁴ NIH, National Institute for Allergy and Infectious Diseases (NIAID), "H9N2 Avian Flu Vaccine Paired with Adjuvant Provokes Strong Human Immune Response at Low Doses," Sept. 25, 2006, at <http://www.nih.gov/news/>.

¹⁵ WHO, "Confirmed Human Cases of Avian Influenza A (H5N1)," at http://www.who.int/csr/disease/avian_influenza/country/en/.

¹⁶ WHO pandemic plan, p. 3.

... outbreaks ... caused by H5N1 are of particular concern because of their association with severe illness and a high case fatality. Of even greater concern is the uniqueness of the present H5N1 situation in Asia. Never before has an avian influenza virus with a documented ability to infect humans caused such widespread outbreaks in birds in so many countries. This unprecedented situation has significantly increased the risk for the emergence of an influenza pandemic.

... The risk (of a pandemic) ... remains so long as H5N1 is present in an animal reservoir, thus allowing continuing opportunities for human exposure and infection. ... Most experts agree that control of the present outbreaks in poultry will take several months or even years. ... The recent detection of highly pathogenic avian influenza in wild birds adds another layer of complexity to control.

... The world may therefore remain on the verge of a pandemic for some time to come. At the same time, the unpredictability of influenza viruses and the speed with which transmissibility can improve means that the time for preparedness planning is right now. Such a task takes on added urgency because of the prospects opened by recent research: good planning and preparedness might mitigate the enormous consequences of a pandemic, and this opportunity must not be missed.

The H5N1 strain now circulating has been especially virulent in both human and avian hosts. Studies suggest that the virus prompts an over-reaction of the inflammatory response in some human victims, causing rapid and severe damage to the lungs.¹⁷ This primary damage cannot be remedied with antibiotics or antiviral drugs. Victims may require mechanical ventilation, and may succumb despite swift and capable care. In 2004, scientists published the results of research in which they sequenced several genes from the 1918 pandemic strain. These genes, when inserted into flu viruses and used to infect mice, were found to have a similar property.¹⁸ Recently, scientists re-created and published the entire genome of the 1918 strain, reinforcing this finding.¹⁹ This property may explain the high lethality of both the 1918 and H5N1 strains in apparently healthy young people.

The H5N1 avian flu may never slip its moorings as a bird pathogen and become a serious human threat. But that possibility is a worst-case scenario for the world's public health experts. Should H5N1 become a pandemic strain, scientists are concerned that it may retain much of its virulence as it changes to a more transmissible form. In the face of such a deadly pathogen, miracles of modern medicine, unavailable in much of the developing world, may not be of much help in developed countries either. Such a scenario would challenge governments around the globe.

¹⁷ This phenomenon is often called a "cytokine storm," named after molecules in the immune system that are produced in excess. See Zhou, J, et al., "Differential Expression of Chemokines and their Receptors in Adult and Neonatal Macrophages Infected with Human or Avian Influenza Viruses," *Journal of Infectious Diseases*, vol. 194(1), pp. 61-70, July, 2006; and De Jong MD, et al., "Fatal Outcome of Human Influenza A (H5N1) is Associated with High Viral Load and Hypercytokinemia (letter)," *Nature Medicine*, vol. 12, pp. 1203-1207, Nov. 2006.

¹⁸ D. Kobasa, et al., "Enhanced Virulence of Influenza A Viruses with the Haemagglutinin of the 1918 Pandemic Virus," *Nature* vol. 431, Oct. 7, 2004, pp. 703-707.

¹⁹ See Jeffery K. Taubenberger, et al., "Characterization of the 1918 Influenza Virus Polymerase Genes," *Nature*, vol. 437, pp. 889-893, Oct. 6, 2005; and Terrence M. Tumpey, et al., "Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus," *Science*, vol. 310, Oct. 2005, pp. 77-80.

Other Flu Strains with Pandemic Potential

While H5N1 is the most worrisome, it is not the only recent flu strain with pandemic potential. Several novel strains of avian influenza associated with human transmission have resulted in pandemic alert status in the past several years. For example, in 2003 an H7N7 strain affecting commercial poultry flocks in the Netherlands resulted in 89 cases of human illness.²⁰ Most illnesses were mild, but there was one death. In 2004 in the Canadian province of British Columbia, an H7N3 avian influenza strain in commercial poultry was found to have infected at least two people. While both recovered, WHO issued a pandemic alert for the Canadian outbreak.²¹ A government worker who became ill while involved in culling flocks of poultry during a 2002 outbreak of H7N2 avian flu in Virginia was later shown to have antibodies to that strain, providing suggestive but not conclusive evidence of infection.²²

These cases demonstrate a newer understanding of the potential for direct bird-to-human transmission of avian flu viruses, and the fact that while the H5N1 strain is of special concern, public health officials can not neglect other strains. The Centers for Disease Control and Prevention (CDC) has noted several outbreaks of various strains of avian flu in North American poultry flocks in 2003 and 2004, and publishes guidance and recommendations for the protection of persons potentially exposed during such outbreaks.²³

Potential Impacts of an Influenza Pandemic

Deaths and Hospitalizations

In its pandemic flu plan, HHS estimates that about 209,000 U.S. deaths could result from a moderate pandemic, similar to those in 1957 and 1968, while 1.9 million deaths could result from a severe pandemic like that in 1918.²⁴ (CDC estimates that on average, about 36,000 die of influenza during an annual flu season.)

Estimates of impacts of a future pandemic are generally based on experience from past pandemics, which varied considerably in their severity. Trust for America's Health (TFAH), a non-profit public health advocacy group, published a report estimating deaths and hospitalizations in the United States based on mild, moderate and severe pandemic scenarios. The report presents death estimates that range from 180,000 to more than 1 million.²⁵ The report also contains estimated state-by-state health impacts.

²⁰ Bosman, et al., "Final Analysis of Netherlands Avian Influenza Outbreaks Reveals Much Higher Levels of Transmission to Humans than Previously Thought," *Eurosurveillance Weekly*, vol. 10(1), Jan. 6, 2005, at <http://www.eurosurveillance.org/index-02.asp>.

²¹ WHO, "Avian Influenza A(H7) Human Infections in Canada," Apr. 5, 2004, at <http://www.who.int/csr/don/en/>; and CDC, "Avian Influenza Infections in Humans," Oct. 17, 2005, at <http://www.cdc.gov/flu/avian/gen-info/avian-flu-humans.htm>.

²² A.J. Hostetler and Calvin Trice, "Va. Worker May Have Caught Avian Flu," *Richmond Times-Dispatch*, Feb. 28, 2004.

²³ See CDC website on avian flu outbreaks in North America at <http://www.cdc.gov/flu/avian/outbreaks/past.htm#nahumans>.

²⁴ HHS "Pandemic Influenza Plan," Part 1: Strategic Plan, p. 18, Nov. 2005, at <http://www.pandemicflu.gov>.

²⁵ Trust for America's Health (TFAH), *A Killer Flu?*, June 2005, at <http://healthyamericans.org/reports/flu/>, applies a set of assumptions and ranges of severity to a CDC-developed computer model, FluAid 2.0, to generate death, (continued...)

Predicted hospitalization rates provide an idea of the potential burden on the U.S. healthcare system, but they are prone to the same degree of uncertainty. In its final pandemic plan, HHS estimates of hospitalizations range from 865,000 to 9.9 million. TFAH estimates that U.S. hospitalizations would range from almost 800,000 to more than 4.7 million, and cites a statistic from the American Hospital Association that in 2003 there were 965,256 staffed hospital beds in registered hospitals. These projected impacts would occur over a compressed time frame of several weeks or a few months, rather than spread over a full year.

Simple extrapolations of health effects from events in 1918 do not account for advances in medical care that have occurred since then. Antibiotics are now available to treat bacterial pneumonia that often results from influenza infection, and sophisticated respiratory care is now available to treat those with severe pneumonia. Experts caution, though, that the H5N1 avian flu virus can cause severe primary damage to the lungs. If this strain were to launch a pandemic and retain this trait, large numbers of victims may require intensive care and ventilatory support, likely exceeding national capacity to provide this level of care. In any event, such specialized care is not available in most developing countries, and access to it is uneven within the United States.

Economic Impacts

An analysis published by CDC in 1999, based on the relatively mild 1968 pandemic, estimated the cost of a pandemic in the United States at between \$71.3 and \$166.5 billion.²⁶ The study modeled direct healthcare costs, lost productivity for those affected, and lost expected future lifetime earnings for those who died. Loss of life accounted for the majority of economic impact. The model did not include the potential effect of disruptions in commerce.

In December 2005, the Congressional Budget Office (CBO) prepared an assessment of the possible macroeconomic effects of a mild flu pandemic, such as those in 1957 and 1968, and a severe pandemic, such as the one in 1918. CBO estimated from the severe pandemic scenario that real Gross Domestic Product (GDP) would be about 4-1/4 percent lower over the subsequent year than it would have been had the pandemic not taken place, similar to a typical U.S. recession. From the mild pandemic scenario, CBO estimated about a 1 percent reduction in GDP, which might not be distinguishable from normal economic variation.²⁷

In November 2005, the World Bank estimated the overall U.S. economic impacts of a potential pandemic of moderate severity at \$100 to \$200 billion, and global impacts at around \$800 billion, if certain impacts were to last for a full year.²⁸ Subsequently, the International Monetary Fund commented that while the global economic and financial impacts of a severe pandemic were likely to be significant, economic activity would likely recover quickly once the pandemic had run its course.²⁹ CBO provided a synopsis of several recent studies of the macroeconomic effects

(...continued)

hospitalization and outpatient rates based on populations with different age distributions.

²⁶ M. I. Meltzer et al., "The Economic Impact of Pandemic Influenza in the United States: Priorities for Intervention," *Emerging Infectious Diseases*, vol. 5(5), Sept.-Oct. 1999.

²⁷ Congressional Budget Office, "A Potential Influenza Pandemic: Possible Macroeconomic Effects and Policy Issues," Dec. 8, 2005, revised July 27, 2006.

²⁸ The World Bank Group, "Avian Flu: Economic Losses Could Top US\$800 Billion," Nov. 8, 2005, at <http://www.worldbank.org/>.

²⁹ International Monetary Fund, "The Global Economic and Financial Impact of an Avian Flu Pandemic and the Role (continued...)"

of a possible pandemic, noting that the estimates span a wide range of effects, reflecting the considerable uncertainties involved.³⁰

There have been several studies of the economic impacts of Severe Acute Respiratory Syndrome (SARS) in 2003. One analysis showed significant short- and long-term decreases in Gross Domestic Product (GDP) in China and Hong Kong, attributing most of the losses to “the behavior of consumers and investors” rather than to actual medical costs.³¹ The World Bank economic analysis of a possible flu pandemic discusses the likely interplay between government actions, public behavior, and economic effects. Similarly, CBO notes in its assessment that government actions could either amplify or mitigate economic impacts, saying that attempts to quarantine people would probably amplify the reductions in trade, travel and tourism, but that rapid disease detection, vaccine development and deployment, and other actions, including quarantine, if effective in controlling the spread of disease, could blunt adverse economic impacts as a pandemic progressed.³²

Pandemic Influenza Planning

The United States has engaged in pandemic flu planning activities for several decades, with heightened activity in recent years in response to the threat posed by H5N1 avian flu. In addition to response efforts in the public health and medical sectors, a serious pandemic would trigger the National Response Plan (NRP), developed by the Department of Homeland Security (DHS) as a blueprint for the coordination of federal agencies during an emergency. The NRP, discussed in greater detail in later sections of this report, is an *all-hazards* plan for emergencies ranging from hurricanes to wildfires to terrorist attacks.

Described below are a number of preparedness and response plans to assist U.S. federal, state and local agencies in specific preparedness and response for a flu pandemic. U.S. plans reflect the timelines, goals and international capabilities described by the WHO in its pandemic plan. In addition, U.S. federal, state and local plans for this specific threat are intended to be consistent with the all-hazards principles in the NRP.

WHO Global Influenza Preparedness Plan

In order to guide country planning efforts, the WHO released a revised pandemic preparedness plan in early 2005.³³ The plan lays out goals and actions to be taken by WHO, as well as recommended actions for individual nations, at each of the pandemic phases (shown in **Table 1**).

(...continued)

of the IMF,” Feb. 28, 2006, at <http://www.imf.org/external/pubs/ft/afp/2006/eng/022806.htm>.

³⁰ CBO, “A Potential Influenza Pandemic: An Update on Possible Macroeconomic Effects and Policy Issues,” p. 1, May 22, 2006, revised July 27, 2006.

³¹ Warwick J. McKibben, “SARS: Estimating the Economic Impacts,” Institute of Medicine, Forum on Microbial Threats, Workshop, “Learning from SARS: Preparing for the Next Disease Outbreak,” Sept. 30, 2003, at <http://www.iom.edu/event.asp?id=14647>.

³² CBO, “A Potential Influenza Pandemic: Possible Macroeconomic Effects and Policy Issues,” p. 11, Dec. 8, 2005, revised July 27, 2006.

³³ WHO pandemic plan, at <http://www.who.int/csr/disease/influenza/pandemic/en/>.

For each phase, actions are grouped into five categories: (1) planning and coordination; (2) situation monitoring and assessment; (3) prevention and containment; (4) health system response; and (5) communications. In addition, recommended actions for individual nations are grouped according to whether the country is affected or not at a particular phase. For Phase 6 (Pandemic Phase), when it is assumed that all countries will inevitably be affected, there are recommended immediate actions for all countries, and specific actions for those affected, those not yet affected, and those for which the pandemic has subsided, noting that subsequent pandemic waves may follow the first one.

The WHO pandemic plan contains an annex of recommendations to nations for “nonpharmaceutical public health interventions,” actions such as isolation, quarantine and travel restrictions. The annex stresses the use of voluntary rather than compulsory measures, noting the lack of demonstrated utility of certain practices, or that enforcement is considered impractical for others. The annex also notes that certain practices used to control SARS, such as temperature screening at airports, are not necessarily recommended for control of pandemic influenza, depending on pandemic phase. The plan and annex also stress avoiding stigmatization of persons affected by pandemic influenza or its control measures.

U.S. Federal Pandemic Plans

In November 2005, the Administration unveiled a central federal website, run by HHS, containing interagency pandemic preparedness and response information.³⁴ The following section describes a number of government pandemic flu planning documents. Unless otherwise noted, plans discussed in this section are available on the central website, along with other information about national pandemic preparedness efforts.

National Pandemic Plans

In November 2005, the White House Homeland Security Council released the **National Strategy for Pandemic Influenza** (the National Strategy). The strategy lays out three goals: (1) stopping, slowing or otherwise limiting the spread of a pandemic to the United States; (2) limiting the domestic spread of a pandemic, and mitigating disease, suffering and death; and (3) sustaining infrastructure and mitigating impact to the economy and the functioning of society. In order to meet those goals, the strategy lays out three “pillars” of implementation activities:

- **Preparedness and Communication:** Activities that should be undertaken before a pandemic to ensure preparedness, and the communication of roles and responsibilities to all levels of government, segments of society and individuals.
- **Surveillance and Detection:** Domestic and international systems that provide continuous “situational awareness,” to ensure the earliest warning possible to protect the population.
- **Response and Containment:** Actions to limit the spread of the outbreak and to mitigate the health, social and economic impacts of a pandemic.

³⁴ See <http://www.pandemicflu.gov/>.

Finally, roles and responsibilities are laid out for the federal government, state and local governments, the private sector, individuals and families, and international partners.³⁵

In May 2006, the White House Homeland Security Council released the **National Strategy for Pandemic Influenza: Implementation Plan** (the Implementation Plan), containing more than 300 required actions—with timelines and performance measures—to be taken by federal departments and agencies, state and local governments, communities, and the private sector, to prepare for a possible pandemic. Required actions span six functional areas, as follows:

- International Efforts: Prevent and contain outbreaks abroad;
- Transportation and Borders: Slow the arrival and spread of a pandemic;
- Protecting Human Health: Limit spread and mitigate illness;
- Protecting Animal Health: Control influenza with human pandemic potential in animals;
- Law Enforcement, Public Safety, and Security: Ensure civil order during a pandemic;
- Planning by Institutions: Protect personnel and ensure continuity of operations.

The White House released a six-month status report in December 2006, stating that 92% of all actions due within six months of release of the Implementation Plan in May 2006 had been completed.

Health Sector Pandemic Plans

In August 2004, HHS released the **Draft Pandemic Influenza Preparedness and Response Plan**. The draft plan articulated steps to be taken by HHS agencies and offices, and by state and local public health authorities, in preparing for and responding to a pandemic. Specific activities discussed included surveillance, vaccine development and use, antiviral drug use, and communications. The draft plan was criticized by some as being vague, and for delegating certain critical activities—such as designating priority groups for rationing of vaccine and antiviral drugs—to states.

The draft plan was superseded by the **HHS Pandemic Influenza Plan** (the HHS Pandemic Plan), published in November 2005. The final plan built on elements in the draft plan, and has three parts: (1) a Strategic Plan, which outlines key planning assumptions and HHS agency roles; (2) a Public Health Guidance for State and Local Partners, which lays out activities on such matters as surveillance, laboratory testing, and quarantine at the borders; and (3) a part currently under development, to consist of detailed operational plans for HHS agencies involved in pandemic response. According to the plan, the HHS Secretary would direct, and the Assistant Secretary for Public Health Emergency Preparedness³⁶ would coordinate, all HHS pandemic response activities.

³⁵ With the release of the strategic plan, President Bush sent a request to Congress for \$7.1 billion in emergency spending for the departments of HHS, Agriculture, Defense, Homeland Security, Interior, State and Veterans Affairs, and the U.S. Agency for International Development. For more information, see CRS Report RS22576, *Pandemic Influenza: Appropriations for Public Health Preparedness and Response*, by (name redacted).

³⁶ This position has been redesignated as the Assistant Secretary for Preparedness and Response, pursuant to P.L. 109- (continued...)

The final plan addressed some of the gaps in the draft plan, such as the designation of priority groups to receive limited vaccine and antiviral drugs.³⁷ Other elements of the final plan received immediate criticism. For example, the section on healthcare planning focuses on individual healthcare facilities and refers to plans for surge capacity. Some experts have commented that there is little surge capacity in the healthcare sector under normal circumstances, and that officials might have to resort to the use of alternate facilities (e.g., convention centers) to care for large numbers of flu patients. The HHS Pandemic Plan does not address that contingency.

Department of Defense Planning

Shortly after the release of the HHS draft pandemic plan in August 2004, the Assistant Secretary of Defense for Health Affairs released the Department of Defense (DOD) **Pandemic Influenza Preparation and Response Planning Guidance**.³⁸ The DOD guidance follows many of the assumptions used in civilian planning, modifying them to protect a highly mobile military force during wartime. Frequent mention is made of the extremely high mortality suffered by U.S. troops during World War I as a result of the 1918 pandemic. The guidance notes that 43,000 uniformed soldiers, more than one third of all U.S. military casualties in the war, died of pandemic influenza, most of them during one 10-week period in 1918.

The DOD guidance notes that the military will use the same vaccine formulation as that developed for civilian use, though DOD will be responsible for securing its own supplies of vaccine and antiviral drugs. Priority for countermeasures in limited supply would be given to forward-deployed troops. The guidance does not set out strict tiers of priority recipients. The guidance discusses the limited utility of individual control measures such as isolation and quarantine, and suggests that larger-scale adjustments (such as extending the tour of ships at sea) could slow disease transmission. The guidance also mentions the consideration of coalition forces from other nations, and the possibility that countermeasures such as vaccine and antiviral drugs may be provided to them under certain conditions.

Department of Veterans Affairs Planning

The Department of Veterans Affairs (VA) released a comprehensive pandemic flu plan in March 2006. The plan notes that the VA owns a supply of approximately 500,000 treatment courses of the antiviral drug Tamiflu.

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417.

³⁷ Though the plan includes specific tiers of priority groups, and estimates of the number of people in each group, the designations may be modified in light of the actual behavior of a pandemic flu strain. For example, if atypical groups such as healthy young people were found to be at increased risk of severe illness, the tiers could be adjusted accordingly.

³⁸ Department of Defense, "Pandemic Influenza Preparation and Response Planning Guidance," Sept. 15, 2004, at <http://www.geis.fhp.osd.mil/GEIS/SurveillanceActivities/Influenza/fluPolicy.asp>.

State Pandemic Plans

All states were required to have submitted plans for pandemic flu preparedness to HHS (through CDC) by July 2005, as a condition of receipt of public health preparedness funding for FY2005.³⁹ This deadline pre-dated the publication of the National Strategy and the HHS Pandemic Plan. The plans of all 50 states and the District of Columbia are available on the central federal pandemic flu website. Many states continue to update their plans.

Private Sector Planning

In September 2006, the Department of Homeland Security released the **Pandemic Influenza Preparedness, Response, and Recovery Guide for Critical Infrastructure and Key Resources**. The guide provides business planners with guidance to assure continuity, during a pandemic, for facilities comprising critical infrastructure sectors (e.g., energy and telecommunications) and key resources (e.g., dams and nuclear power plants).

Domestic and global corporations have adopted specific pandemic flu plans to varying degrees. In July 2006, the Conference Board, a global business membership and research organization, reported the findings of its survey of pandemic preparedness in 553 global companies. The Board found that nearly three-fourths of respondents reported either having a pandemic plan, or being well along in developing one. But the Board commented that "... the effectiveness of business plans and the quality of relationships necessary for their successful implementation in times of extreme public, private and social stress remains open to question."⁴⁰ According to the report, "the most significant disadvantage in not conducting formal pandemic preparedness planning may be the virtually total absence of coordination with the public sector. An overwhelming 94% of participating companies report that they have not had discussions with any level of government officials about their organization's ability to provide essential services or access to facilities, equipment, or staff during a pandemic."⁴¹

Issues in Pandemic Influenza Planning

Could an Influenza Pandemic Be Stopped?

Public health experts note that vaccine, the primary measure for influenza prevention, will be available in very limited supply at the start of a pandemic. Antiviral drugs are also likely to be available in a limited supply. For both, there is limited global surge capacity for production during a pandemic. Conventional wisdom once held that there was an inevitability to the global wave of disease that a pandemic would bring, but lately this notion has been challenged. WHO and many national experts believe that scientific advances in studying and detecting flu viruses may make it

³⁹ According to cooperative agreement guidance for FY2004 funds, states were required to submit pandemic plans along with their applications for FY2005 funds. See CDC, "Cooperative Agreement Guidance for Public Health Emergency Preparedness," Program Announcement AA154, May 13, 2005, at <http://www.bt.cdc.gov/planning/guidance05/>.

⁴⁰ The Conference Board, "Most Companies Planning for an Avian Flu Pandemic, but Outcomes Remain Uncertain," press release, July 6, 2006, at <http://www.conference-board.org/utilities/press.cfm>.

⁴¹ Ibid.

possible to detect the spread of the virus early, and rein in localized clusters of infection. While not suggesting that a pandemic could necessarily be averted, they posit that if progression were slowed enough, a vaccine could be available by the time worldwide infection ensued. While there still might not be enough vaccine for everyone, if countries had at least enough for essential personnel, it would soften the impact somewhat.

Realizing this hope rests on two conditions: first, exceptional “pandemic intelligence” in countries at the epicenter of a developing pandemic; and second, an effective response in these epicenter countries. In hopes of having the best possible information in real time, WHO, along with the U.S. State Department, CDC, DOD, other U.S. federal agencies, and health officials from many other nations, are building epidemiology and lab capacity in Southeast Asia and other regions affected by H5N1 avian flu, when countries have requested assistance. The U.S. government has also participated in global pandemic response planning, through the International Partnership on Avian and Pandemic Influenza.⁴²

Who’s in Charge?

A serious flu pandemic would affect many sectors of society, not just the public health and medical communities. As such, it is useful to consider federal efforts to meet this threat across sectors, and to consider those efforts in the contexts of *preparedness* and *response*. Federal leadership may be somewhat different for each of these phases, but the nature of the threat may blur the line between them.

WHO monitors the spread of H5N1 avian flu and other novel flu viruses, and will make formal announcements of changes in pandemic threat status including, were it to occur, the onset of pandemic, defined as sustained human-to-human transmission of a novel flu virus. At that point, global response activities would ensue. However, since this threat can be anticipated, the federal government has launched a specific, comprehensive, long-term preparedness strategy. Of the more than 300 tasks in the Implementation Plan, 27 were to have been completed within three months of the plan’s publication in May 2006, while others, such as establishing domestic capacity for rapid, large-scale pandemic vaccine production, may take many years to achieve.⁴³ If a pandemic were to occur before then, unfinished preparedness activities would be completed, if appropriate, as part of the pandemic response.

WHO urges that countries plan for a pandemic as a multi-sector threat, not merely a health challenge. However, federal relationships that support state and local jurisdictions traditionally operate sector-by-sector (e.g., HHS with health services, and the Department of Transportation with transit agencies). While HHS had been the lead federal agency for pandemic planning prior to 2005, the White House Homeland Security Council appears now to be the hub through which federal preparedness activities are coordinated.

⁴² For more information, see CRS Report RL33219, *U.S. and International Responses to the Global Spread of Avian Flu: Issues for Congress*, by (name redacted). See also, Department of Defense Global Emerging Infections Surveillance and Response System (DoD-GEIS), at <http://www.geis.fhp.osd.mil/aboutGEIS.asp>.

⁴³ HHS anticipates that its efforts to establish adequate domestic surge capacity for flu vaccine production will continue through 2013. See Testimony of Gerald W. Parker, Principal Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response, HHS, hearing on “Pandemic Flu: Progress Made and Challenges Ahead,” before the U.S. Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Education and Related Agencies, 110th Cong., 1st Sess., Jan. 24, 2007.

Following release of the National Strategy and the HHS Pandemic Plan in November 2005, HHS Secretary Michael Leavitt and other federal officials hosted pandemic planning summits in all 50 states, to support states' multi-sector planning activities. Nonetheless, state plans were required as a condition of CDC grants to state health departments, and many of them remain predominantly focused on health sector preparedness. For example, many plans don't mention a possible role for the National Guard during a pandemic. Since the National Guard is a state response asset under the control of the Governor, and since a flu pandemic could be catastrophic, there has been considerable discussion of the possible role of law enforcement in pandemic response. Hence, it could be helpful if state plans specifically described how the National Guard might be used during a pandemic.

The National Response Plan (NRP), published by DHS, is a blueprint for the coordinated efforts of federal agencies during disasters.⁴⁴ In the event of a significant influenza pandemic, the NRP may be activated to coordinate federal agency activities. Responsibilities for specified activities (e.g., transportation, energy, and public works) are set out in 15 *Emergency Support Functions* (ESFs). When the NRP is activated, the Secretary of Homeland Security serves as the overall lead for a coordinated federal response, while the Secretary of HHS serves as the lead for ESF-8, Public Health and Medical Services.⁴⁵ While public health and medical activities may comprise the bulk of the federal response to a pandemic, other ESF authorities may be involved to sustain infrastructure affected by absenteeism or supply chain disruptions, requiring the coordination of other federal departments.

The National Strategy notes the federal departments designated as the lead for various aspects of a pandemic response: HHS for the medical response, the U.S. Department of Agriculture (USDA) for the veterinary response, the Department of State for international activities, and DHS for overall domestic incident management. In addition, DHS is responsible for coordinating the preparedness of privately owned critical infrastructures such as banking and telecommunications.

While pandemic influenza scenarios have been used to exercise specific elements of response, such as distribution of stockpiled medications, there has been no national exercise to test a multi-sector, multi-jurisdictional response. As a condition of receipt of \$350 million in FY2006 supplemental appropriations, Congress called on states to conduct pandemic flu exercises that would "enable public health and law enforcement officials to establish procedures and locations for quarantine, surge capacity, diagnostics, and communication."⁴⁶ The funds, awarded by CDC, are to be used by states to test three aspects of response: control of community gatherings (e.g., school closings); medical surge capacity; and mass vaccination / mass prophylaxis.⁴⁷ While no doubt useful, these exercises will be carried out state-by-state, retaining a health-sector focus. The

⁴⁴ See DHS, *National Response Plan*, Dec. 2004, hereafter called the NRP, at http://www.dhs.gov/xprepresp/committees/editorial_0566.shtm, and CRS Report RL32803, *The National Preparedness System: Issues in the 109th Congress*, by (name redacted).

⁴⁵ For more information on ESF-8, see CRS Report RL33579, *The Public Health and Medical Response to Disasters: Federal Authority and Funding*, by (name redacted).

⁴⁶ H.Rept. 109-359, to accompany H.R. 2863, Department of Defense, Emergency Supplemental Appropriations to Address Hurricanes in the Gulf of Mexico, and Pandemic Influenza Act, 2006, p. 523.

⁴⁷ CDC, "Pandemic Influenza Guidance Supplement: Phase 2," guidance for FY2006 funds, July 10, 2006, at <http://www.bt.cdc.gov/planning/coopagreement/>.

only national multi-sector pandemic exercise to date has been a table-top simulation conducted by members of the Cabinet.⁴⁸

Emergency Declarations and Federal Assistance

In the United States, public health authority rests principally with the states as an exercise of their *police powers*.⁴⁹ States play a leading role in preparing for and responding to public health threats, with HHS (primarily CDC) providing support through funding, training, technical assistance, advanced laboratory support, data analysis and other activities. The Public Health Service Act grants the Secretary of HHS the authority to declare a situation a public health emergency, which triggers an expansion of certain federal authorities.⁵⁰ Though states already have considerable power in responding to public health events, most can also declare public health emergencies and expand their powers further. In an influenza pandemic, response measures such as quarantine or prohibitions against administration of vaccine to non-priority individuals would likely be carried out, at least initially, by state rather than federal authorities.⁵¹

An influenza pandemic may disrupt services beyond the health sector. Each of the pandemic influenza plans listed earlier is written with the premise that the NRP could be triggered by a flu pandemic, thereby guiding a coordinated federal response to problems within the health sector and other affected sectors through routine, non-emergency, federal assistance mechanisms.⁵² According to the Implementation Plan, the Secretary of Homeland Security may declare a pandemic an *Incident of National Significance*, triggering the NRP, early in the event, perhaps while foreign countries were affected, but before the disease had reached the United States.⁵³

States may require additional federal assistance to maintain essential services during an influenza pandemic. Typically, such assistance is triggered by presidential emergency or disaster

⁴⁸ White House, “Press Gaggle after Avian Flu Tabletop Exercise with Homeland Security Advisor Fran Townsend, Secretary of Health and Human Services Michael Leavitt, and Secretary of Homeland Security Michael Chertoff,” transcript, Dec. 10, 2005, at <http://www.whitehouse.gov/news/releases/2005/12/20051210-2.html>.

⁴⁹ The term *police powers* derives from the 10th Amendment to the Constitution, which reserves to the states those rights and powers not delegated to the United States. Historically these have been interpreted to include authority over public health and safety.

⁵⁰ For more information, see CRS Report RL33579, *The Public Health and Medical Response to Disasters: Federal Authority and Funding*, by (name redacted).

⁵¹ For a discussion of the exercise of federal and state authorities in response to the shortage of influenza vaccine in 2004, see CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by (name redacted) and (name redacted). See also CRS Report RL33201, *Federal and State Quarantine and Isolation Authority*, by (name redacted) and (name redacted); CRS Report RL33609, *Quarantine and Isolation: Selected Legal Issues Relating to Employment*, by (name redacted) and (name redacted); CRS Report RS22219, *The Americans with Disabilities Act (ADA) Coverage of Contagious Diseases*, by (name redacted); and CRS Report RS21414, *Mandatory Vaccinations: Precedent and Current Laws*, by (name redacted).

⁵² In addition, the NRP Biological Incident Annex notes that “Actions described in this annex take place with or without a presidential Stafford Act declaration or a public health emergency declaration” by the Secretary of HHS. See NRP, Biological Incident Annex, p. BIO-1. While this annex addresses intentional bioterrorism events, it also addresses naturally occurring biological threats, and explicitly mentions pandemic influenza. In contrast, the NRP Catastrophic Incident Annex does not explicitly mention pandemic influenza. While this annex is designed to address disasters with “extraordinary levels of mass casualties” such as could occur with a pandemic, it is also explicitly focused on “no-notice or short-notice incidents of catastrophic magnitude,” a definition that would not likely apply to an influenza pandemic. See NRP, Catastrophic Incident Annex, p. CAT-1, and DHS, Notice of Change to the National Response Plan, May 25, 2006, pp. 9-10, at <http://www.dhs.gov/xprepresp/programs/>.

⁵³ Implementation Plan, p. 37.

declarations pursuant to the Robert T. Stafford Disaster Relief and Emergency Assistance Act (the Stafford Act).⁵⁴ Disaster assistance authorized by the Stafford Act includes the provision of emergency funds and supplies to stricken households, as well as aid in clearing and rebuilding damaged infrastructure. While a virus would not cause infrastructure damage directly, certain sectors may nonetheless be affected as a result of widespread absenteeism or supply chain disruptions. For example, water treatment facilities may be damaged, or may have to be shut down, if they are not adequately maintained, or if replacement parts are unavailable. Sectors that depend heavily on continuous computer support (e.g., banking) may be disrupted by absenteeism.

It is unclear whether Stafford Act major disaster assistance could be provided in response to a pandemic. Emergency declarations pursuant to the Stafford Act were made in response to West Nile virus in 2000, so there is precedent for a presidential emergency declaration, (providing a lower level of federal assistance) in response to an infectious disease threat. The matter of presidential authority to declare a major disaster (providing a higher level of federal assistance) in response to an infectious disease threat generally, and a flu pandemic specifically, is less clear. In the past, FEMA has, in the context of the national TOPOFF exercises, interpreted biological disasters as ineligible for major disaster assistance pursuant to the Stafford Act.⁵⁵ However, the Administration view is that the President's authority to declare a major disaster pursuant to the Stafford Act could be applied to an influenza pandemic.⁵⁶

Limited Surveillance and Testing Capability

The CDC coordinates domestic surveillance for seasonal flu in humans.⁵⁷ Monitoring for pandemic flu is integrated into these existing systems. Key challenges in the rapid detection of novel flu viruses in humans are the vagueness of flu symptoms, which can be seen with many other diseases, and the difficulty in distinguishing specific flu strains of interest from the background of other strains commonly in circulation.

The routine CDC system for domestic flu surveillance has seven reporting components: (1) more than 120 laboratories; (2) more than 1,000 sentinel healthcare providers; (3) death records from 122 cities; (4) reports from health departments in the states, territories, New York City and the District of Columbia; (5) influenza-associated deaths in children; (6) Emerging Infections Program sites in 10 states; and (7) laboratory-confirmed hospitalizations for influenza in young children in three sentinel counties.⁵⁸ Reporting to these systems at CDC by state and local health departments and healthcare providers is voluntary. Information is gathered and analyzed weekly during the winter flu season.

⁵⁴ See CRS Report RL33053, *Federal Stafford Act Disaster Assistance: Presidential Declarations, Eligible Activities, and Funding*, by (name redacted).

⁵⁵ See DHS, Office of the Inspector General, *A Review of the Top Officials 3 Exercise*, Office of Inspections and Special Reviews, OIG-06-07, November 2005, p. 30, at http://www.dhs.gov/xoig/rpts/mgmt/editorial_0334.shtm. The anthrax attack in 2001 also did not result in a Stafford Act declaration.

⁵⁶ Implementation Plan, Appendix C, "Authorities and References," p. 212.

⁵⁷ Another key activity is the enhanced monitoring of avian flu in birds. The H5N1 strain of concern has not yet been detected in humans or birds in the United States. For more information on domestic monitoring in birds, see CRS Report RL33795, *Avian Influenza in Poultry and Wild Birds*, by (name redacted) and (name redacted).

⁵⁸ CDC, "Overview of Influenza Surveillance in the United States," June 26, 2006, at <http://www.cdc.gov/flu/weekly/pdf/flu-surveillance-overview.pdf>.

CDC has issued recommendations to public health and medical professionals for the investigation of possible human cases of avian or pandemic flu in individuals who have a history of recent travel to a region affected by H5N1 avian flu, and who exhibit symptoms of severe respiratory disease.⁵⁹ Between February 2003 and May 2006, 59 such case reports were made to CDC by clinicians or health departments. Investigations showed no evidence of H5N1 virus infections.⁶⁰

There is not, at this time, a rapid point-of-care (bedside) test that healthcare workers or epidemiologists can use to screen a person for H5N1 flu, or any other *specific* strain of influenza. CDC recommends the use of commercial flu screening tests for initial patient evaluation. The agency cautions that commercially available screening tests cannot reliably distinguish H5N1 flu from other influenza A strains; therefore, specimens that test positive on screening should be followed up with specimens sent to the state's public health laboratory to determine which flu strain is involved. At this time, public health labs in all 50 states have the capability to test for H5N1 influenza, though there is a lag time in shipping the samples, and in test turnaround.⁶¹ The Implementation Plan calls on HHS, in coordination with DOD, VA and DHS, to support the private-sector development of reliable, rapid, point-of-care diagnostic tests for specific flu strains. CDC awarded contracts for this purpose to four companies in December 2006.⁶²

Isolation and Quarantine

Isolation and quarantine have been used for hundreds of years to prevent the spread of communicable diseases. Both methods restrict the movement of those affected, but they differ depending on whether an individual has been exposed to a disease (*quarantine*), or is actually infected (*isolation*). Persons in isolation may be significantly ill, so isolation often occurs in a healthcare setting. Persons under quarantine are, by definition, not ill from the disease in question, though they may have other health conditions that complicate the quarantine process.

In the United States, quarantine authority is generally based in state rather than federal law.⁶³ The federal government has the responsibility to prevent the introduction, transmission, and spread of communicable diseases from foreign countries, and the authority to impose quarantine on incoming travelers suspected to be infected with or exposed to certain diseases on a list of quarantinable communicable diseases. Diseases are listed by an executive order of the President, in consultation with the Secretary of HHS. On April 1, 2005, President Bush added to the list "influenza caused by novel or re-emergent influenza viruses that are causing, or have the potential to cause, a pandemic."⁶⁴ Federal quarantine is carried out by CDC's Division of Global Migration

⁵⁹ CDC, "Health Updates on Avian Influenza," June 7, 2006, and previous, at <http://www.cdc.gov/flu/avian/professional/updates.htm>.

⁶⁰ J. R. Ortiz, et al., "No Evidence of Avian Influenza A (H5N1) among Returning U.S. Travelers," *Emerging Infectious Diseases*, vol. 13(2), Feb. 2007, at <http://www.cdc.gov/EID/content/13/2/294.htm>.

⁶¹ An H5N1 influenza diagnostic test, developed by CDC, was approved by the Food and Drug Administration (FDA) and delivered to laboratories in the national Laboratory Response Network, which includes public health labs in all 50 states, many federal labs, and others, in February 2006. See <http://www.bt.cdc.gov/lrn/>.

⁶² CDC, "CDC Awards \$11.4 Million to Develop New Rapid Diagnostic Tests for Avian Influenza," press release, Dec. 4, 2006.

⁶³ For more information, see CRS Report RL33201, *Federal and State Quarantine and Isolation Authority*, by (name redacted) and (name redacted). See also: CRS Report RL33609, *Quarantine and Isolation: Selected Legal Issues Relating to Employment*, by (name redacted) and (name redacted); and CRS Report RS22219, *The Americans with Disabilities Act (ADA) Coverage of Contagious Diseases*, by (name redacted).

⁶⁴ See Executive Order: "Amendment to E.O. 13295 Relating to Certain Influenza Viruses and Quarantinable (continued...)"

and Quarantine, which operates quarantine stations at major ports, and also works closely with states to carry out quarantine activities.⁶⁵ CDC has noted that having pandemic influenza on the list assures the agency of this option for disease control, should it be felt to be worthwhile.

On October 4, 2005, in response to a question at a press conference, President Bush suggested the use of the military to enforce quarantines during a flu pandemic.⁶⁶ The comment prompted questions on two issues: the role of quarantine in controlling pandemic flu, and the role of the military in responding to domestic disasters.

While isolation and quarantine were crucial in the worldwide response to SARS, these methods are less likely to be successful in controlling influenza. Influenza has a shorter incubation period than SARS, and is often contagious in the absence of symptoms or before symptoms appear, making it difficult to identify persons who should be quarantined.⁶⁷

There has been considerable interest in recent years in studying or predicting the effects of a variety of so-called “non-pharmaceutical interventions” (NPI), including isolation and quarantine, on the potential spread of pandemic flu.⁶⁸ The Implementation Plan discusses CDC’s readiness to implement quarantines for incoming travelers, and strategies for school closures and other “social distancing” measures that may be used by local governments to slow disease spread. The Plan also notes the need for continued study of the potential impacts, both good and bad, of various approaches. The Plan makes specific reference to the practice of *geographic quarantine* (also known as *cordon sanitaire*), the “isolation, by force if necessary, of localities with documented disease transmission from localities still free of infection,”⁶⁹ saying, “The implementation of conventional geographic quarantine imposes significant opportunity costs and may result in the diversion of significant resources and assets that might be used to better effect supporting less draconian disease containment measures.”⁷⁰ In February 2007, CDC released a planning guide for the graded use of NPI—including school closures, liberal work leave policies, and teleworking strategies—matched to pandemic severity.⁷¹ The guide does not propose the use of compulsory isolation or quarantine measures, recommending that such actions be voluntary.

(...continued)

Communicable Diseases,” Apr. 1, 2005, at <http://www.whitehouse.gov/news/releases/2005/04/20050401-6.html>; and CDC, “Questions and Answers on the Executive Order Adding Potentially Pandemic Influenza Viruses to the List of Quarantinable Diseases,” Apr. 11, 2005, at http://www.cdc.gov/ncidod/dq/qa_influenza_amendment_to_eo_13295.htm.

⁶⁵ See CDC Division of Global Migration and Quarantine home page at <http://www.cdc.gov/ncidod/dq/index.htm>.

⁶⁶ Press conference with President George Bush, Federal News Service transcript, Oct. 4, 2005.

⁶⁷ Christophe Fraser, et al., “Factors that Make an Infectious Disease Outbreak Controllable,” *Proceedings of the National Academy of Sciences*, vol. 101(16), pp. 6146-6151, Apr. 20, 2004, at <http://www.pnas.org/cgi/reprint/101/16/6146>.

⁶⁸ See, for example: the Models of Infectious Disease Agent Study (MIDAS), funded by the National Institutes of Health, at <http://www.nigms.nih.gov/Initiatives/MIDAS/>; and studies of the effectiveness of measures applied during the 1918 flu pandemic, conducted by Dr. Howard Markel with funding from the Defense Threat Reduction Agency, presented to the Institute of Medicine, workshop on “Ethical and Legal Considerations in Mitigating Pandemic Disease,” Sept. 19, 2006, at <http://www.iom.edu/CMS/3783/3924/35857/37298.aspx>.

⁶⁹ Implementation Plan, p. 108.

⁷⁰ *Ibid.*, p. 109.

⁷¹ CDC, “Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States—Early Targeted Layered Use of Non-Pharmaceutical Interventions,” Feb. 2007, at <http://www.pandemicflu.gov/>.

Following the terror attacks of 2001, DOD activated a new combatant command, Northern Command or NORTHCOM, to, among other functions, provide military assistance to civil authorities in response to terrorist attacks.⁷² The NRP also articulates this role for the military in response to terrorist attacks, major disasters, and other emergencies.⁷³ There has, however, long been a prohibition against the use of federal military personnel for domestic law enforcement, except in extraordinary circumstances.⁷⁴ There were no instances in the 20th century in which federal troops were used to enforce a domestic quarantine for any disease, though there are earlier examples.⁷⁵

Medical Surge Capacity

An influenza pandemic of even limited magnitude has the potential to disrupt the normal workings of the healthcare system in a variety of ways. These may include deferral of elective medical procedures; diversion of patients away from overwhelmed hospital emergency departments and tertiary care facilities; protective quarantines of susceptible populations such as residents of long-term care facilities; and hoarding, theft or black-marketeering of scarce resources such as vaccines or antiviral drugs.

Several additional factors complicate the healthcare burden posed by pandemic flu. First, it is thought that a pandemic would spread across the United States in a compressed timeframe similar to seasonal flu, that is, over a six- to eight-week period. Second, while it is desirable that affected patients be kept in isolation, domestic isolation capacity is limited. Third, the healthcare workforce is likely to be affected by pandemic flu. Even if they are protected directly by limited vaccines or antiviral drugs, their family members may be affected and require additional care at home. Fourth, supplies of healthcare consumables such as gloves, masks and antibiotics would be stressed by a surge in global demand.⁷⁶ Even a mild flu pandemic would likely place a significant and near-simultaneous strain on the nation's healthcare system.

Rationing Scarce Resources

The WHO recommends that countries identify priority groups for vaccination and antiviral drugs, as these measures become available, and recommends that countries make these decisions before a pandemic occurs. The National Vaccine Advisory Committee (NVAC, which reports to the director of the National Vaccine Program in HHS) and the Advisory Committee on Immunization Practices (ACIP, which reports to the HHS Secretary and CDC) met in joint session in July 2005 to report to HHS Secretary Leavitt their recommendations for prioritizing vaccine and antiviral drugs for the U.S. civilian population during a pandemic.⁷⁷ The two committees put forth

⁷² CRS Report RL34342, *Homeland Security: Roles and Missions for United States Northern Command*, by (name redacted).

⁷³ NRP, "Defense Support of Civil Authorities," pp. 41 ff.

⁷⁴ CRS Report RS22266, *The Use of Federal Troops for Disaster Assistance: Legal Issues*, by (name redacted) and (name redacted).

⁷⁵ Information provided by Dr. Dale Smith, medical historian, Uniformed Services University of the Health Sciences, Bethesda, Maryland, Oct. 13, 2005.

⁷⁶ See CRS Report RS22453, *Avian Flu Pandemic: Potential Impact of Trade Disruptions*, by (name redacted).

⁷⁷ Charles M. Helms, NVAC Chairman, letter to HHS Acting Assistant Secretary for Health Cristina V. Beato, on NVAC recommendations regarding priority use of vaccine and antiviral drugs during an influenza pandemic, Aug. 10, 2005, at <http://www.hhs.gov/nvpo/nvac/documents/chairletter.pdf>.

unanimous recommendations for prioritizing pandemic flu vaccine. Their recommendations were incorporated into the HHS Pandemic Plan, and are displayed in **Table 2**.

Healthcare workers with direct patient contact and those involved in making the vaccine were given top priority by the committees. Next were those at highest risk of serious complications from flu. During seasonal flu, and during the 1957 and 1968 pandemics, those at highest risk were the very old, the very young, and individuals with certain serious chronic diseases. The committees noted that during a pandemic other groups may be shown to be at higher risk, and that tiers could be redefined according to the specific epidemiologic findings. For example, during the 1918 pandemic, healthy young people were found to be at increased risk of death when they became infected. According to the committees' estimates, more than 60% of the U.S. population, including most children, would not fall into any of the designated priority groups.

Table 2. NVAC and ACIP Recommendations for Pandemic Vaccine Priority Groups
(persons in thousands)

Group and Tier	Group total	Cumulative total
1A Healthcare workers with direct patient contact	9,000	9,000
Vaccine and antivirals manufacturing personnel	40	9,040
1B Highest risk of serious flu complications	25,840	34,880
1C Pregnant women, immunocompromised individuals, and household contacts of infants	10,700	45,580
1D Key government leaders and responders	151	45,731
2A Rest of high risk individuals	59,100	104,831
2B Most critical infrastructure and public health emergency responders	8,500	113,331
3 Other key government health decision makers, mortuary services personnel	500	113,831
4 Healthy 2- to 64-year-olds not in other groups	179,260	293,091

The proposed scheme comports with a tradition in public health practice to prioritize the most vulnerable, in this case those most vulnerable to severe complications from flu. Such a strategy does not necessarily save the most lives, though. To accomplish that when resources are scarce, resources would be given to those most likely to survive or to have better outcomes as a result, to the extent that one could determine who those people were. Conversely, treatment would be withheld from those who were unlikely to benefit, so that others may. The HHS proposal has prompted considerable debate about strategies for withholding resources during a pandemic, and shown that rationing schemes to optimize one goal (e.g., equity and fairness) may conflict with schemes to optimize another (e.g., slowing disease transmission). These are ethically complex decisions with which the civilian medical community has little experience.⁷⁸

Although HHS included recommendations for vaccine priorities in its pandemic plan, these recommendations may change. On December 14, 2006, HHS published a request for information

⁷⁸ For further discussion, see CRS Report RL33381, *The Americans with Disabilities Act (ADA): Allocation of Scarce Medical Resources During a Pandemic*, by (name redacted), and the section on Strategies for Rationing in CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by (name redacted) and (name redacted).

(RFI) in the Federal Register asking for “input on pandemic influenza vaccine prioritization considerations from all interested and affected parties....”⁷⁹ The Implementation Plan requires HHS, in coordination with DHS, to make priority recommendations for access to pre-pandemic and pandemic influenza vaccines. The recommendations are to reflect the pandemic response goals that were described in the National Strategy,⁸⁰ as well as maintaining national security. A federal interagency working group has been established to recommend priority groups, and the RFI will provide information for the working group. The working group’s draft guidance and recommendations will be published in the Federal Register for comment. HHS noted that it was particularly interested in responses to several questions concerning priorities for vaccines, including, “How can fairness, equity, efficiency and related principles be reflected in the determination of priority groupings for receipt of pre-pandemic or pandemic vaccine?” The initial deadline for responses to HHS was January 18, 2007; it was subsequently extended to February 5, 2007.⁸¹

Influenza Vaccine Supply and Use

Overview

Vaccination is considered the best preventive measure for influenza. But, because of continuous changes in the genes of flu viruses, vaccines must be “matched” to specific strains to provide good protection. Flu vaccine is currently produced in chicken eggs, using a time-consuming process with a six-month lead time. Since a vaccine could not be mass produced against a pandemic flu strain until that strain emerged, planning assumes that a matched flu vaccine would not be available for initial global pandemic control. Health officials are working to increase the speed of flu vaccine production, to increase global flu vaccine production capacity, to develop and create limited stockpiles of prototype vaccines for H5N1 and other novel flu strains, and to develop “universal” flu vaccines that don’t require strain matching for effectiveness.

On November 1, 2005, the Administration requested \$7.1 billion in emergency funding for pandemic preparedness. Congress provided FY2006 emergency supplemental appropriations of \$3.8 billion in December 2005, of which \$3.3 billion was provided to HHS. A second FY2006 supplemental appropriation in June 2006 provided HHS with an additional \$2.3 billion.⁸² The bulk of this funding has gone to support flu vaccine related activities. The Administration has established two primary vaccine goals: (1) establishment and maintenance of stockpiles of pre-pandemic vaccine adequate to immunize 20 million persons against influenza strains that present a pandemic threat; and (2) expansion of domestic influenza vaccine manufacturing surge capacity

⁷⁹ 71 *Federal Register* 75252, Dec. 14, 2006.

⁸⁰ These goals are: (1) stopping, slowing or otherwise limiting the spread of a pandemic to the United States; (2) limiting the domestic spread of a pandemic, and mitigating disease, suffering and death; and (3) sustaining infrastructure and mitigating impact to the economy and the functioning of society. National Strategy, p. 2.

⁸¹ See HHS, “Request for Information (RFI): Guidance for Prioritization of Pre-pandemic and Pandemic Influenza Vaccine,” at <http://aspe.hhs.gov/PIV/RFI/>; and CRS Report RL33381, *The Americans with Disabilities Act (ADA): Allocation of Scarce Medical Resources During a Pandemic*, by (name redacted).

⁸² See CRS Report RS22576, *Pandemic Influenza: Appropriations for Public Health Preparedness and Response*, by (name redacted).

for the production of pandemic vaccines for the entire domestic population within six months of a pandemic declaration.⁸³

Limited Vaccine Production Capacity

In 2005, there was worldwide capacity to produce at most 300 million doses of injectable *trivalent* flu vaccine, the annual vaccine that contains three different strains of influenza.⁸⁴ Only one (sanofi pasteur⁸⁵) of nine manufacturers was located in the United States. WHO reports that in 2006, worldwide capacity had expanded to 400 million doses.⁸⁶ Though production capacity can, in theory, be tripled by converting to single-strain production for a pandemic vaccine, two doses (vs. the single dose given each year) may be required to afford protection, because there is no prior immunity to be “boosted.” Furthermore, in initial trials of an H5N1 prototype vaccine, immunity was produced only by very high doses of viral antigen, which means that more capacity would be needed to make a given number of doses.

One means to increase domestic vaccine production capacity is to expand manufacturing infrastructure. In July 2006, HHS issued a solicitation for proposals to retrofit existing domestic manufacturing facilities to enable the emergency production of pandemic vaccine. HHS plans to award these contracts in February 2007. HHS plans to issue a request for proposals later in 2007 to assist in building new domestic manufacturing plants to produce of seasonal and pandemic influenza vaccines using new cell-based technologies, which may have several advantages over egg-based production.⁸⁷

Vaccine Research and Development

In addition to expanding bricks-and-mortar vaccine capacity, HHS has also used emergency supplemental appropriations to award contracts for research on improved methods of flu vaccine production. Research efforts, generally overseen by the NIH, include cell-based (rather than egg-based) production, recombinant and DNA vaccines, and so-called “antigen-sparing” approaches to boost the immune response to lower doses of virus. NIH also supports intramural and extramural research to enhance understanding of the basic nature of human immunity to influenza, and efforts to develop a universal vaccine that would provide durable immunity against diverse flu strains, eliminating the need for annual vaccination and protecting against pandemic flu strains that have yet to emerge.⁸⁸

⁸³ Implementation Plan,” p. 9.

⁸⁴ David S. Fedson, “Preparing for Pandemic Vaccination: An International Policy Agenda for Vaccine Development,” *Journal of Public Health Policy*, Vol. 26, pp. 4-29, 2005, (hereafter called Fedson article), at <http://www.palgrave-journals.com/jph/fedson.pdf>.

⁸⁵ The company does not use capital letters in its name.

⁸⁶ WHO, “WHO Reports Some Promising Results on Avian Influenza Vaccines,” press release, Feb. 16, 2007, at <http://www.who.int/mediacentre/news/notes/2007/np07/en/index.html>.

⁸⁷ See testimony of Gerald W. Parker, Principal Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response, HHS, hearing on “Pandemic Flu: Progress Made and Challenges Ahead,” before the U.S. Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Education and Related Agencies, 110th Cong., 1st Sess., Jan. 24, 2007.

⁸⁸ Ibid. See, also, testimony of Anthony S. Fauci, Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, HHS, hearing on “Pandemic Flu: Progress Made and Challenges Ahead,” before the U.S. Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, Education and Related (continued...)

Global Vaccine Availability

Some have been critical of the U.S. approach to pandemic flu vaccine development, which sets the goal of universal vaccine availability for Americans, but does not address the provision of vaccine to other countries.⁸⁹ In early February 2007, officials in Indonesia announced that they would no longer provide WHO with samples of H5N1 avian flu affecting their country, samples that are used by manufacturers to develop pandemic vaccines that would not likely be available to developing countries during a pandemic. On February 16, Indonesian officials and the WHO jointly announced an agreement whereby Indonesia would resume sending avian flu virus samples to the WHO as soon as it is guaranteed access to affordable vaccines against the disease.⁹⁰ The episode foreshadows the types of international tensions that may arise during a pandemic.⁹¹

Regulatory Issues

From a regulatory standpoint, the Food and Drug Administration (FDA) considers that a pandemic flu vaccine produced using currently-approved processes would merely represent a strain change (as with seasonal flu vaccine), not a new product.⁹² This would allow for a streamlined approval process in which a licensed manufacturer would submit additional information as a supplement to its current product license. The agency considers that virus derived by reverse genetics or grown using cell culture methods does not pose additional regulatory obstacles.⁹³ Prototype human vaccines ideally should undergo clinical trials to establish efficacy, dosage and scheduling protocols. The FDA recommends that these trials be carried out before a pandemic occurs, to the extent possible.

The HHS final plan notes that if a pandemic were to spread swiftly, pandemic vaccine may be pressed into service before standard safety and efficacy tests could be completed. Such unlicensed vaccine could be used under FDA's Investigational New Drug (IND) provisions. These include strict inventory control, record keeping, and informed consent requirements, which would pose an additional challenge for public health officials during a vaccination campaign.

Congress provided an additional mechanism, permitting the use of unapproved drugs and vaccines in an emergency, in the Project BioShield Act of 2004 (P.L. 108-276). This *Emergency*

(...continued)

Agencies, 110th Cong., 1st Sess., Jan. 24, 2007; and CBO, "A Potential Influenza Pandemic: An Update on Possible Macroeconomic Effects and Policy Issues," p. 1, May 22, 2006, revised July 27, 2006.

⁸⁹ See, for example, the Fedson article.

⁹⁰ Donald G. McNeil Jr., "Indonesia and WHO in Accord on Flu Virus," *The International Herald Tribune*, Feb. 19, 2007.

⁹¹ See "Global Solidarity Needed in Preparing for Pandemic Influenza," *The Lancet*, editorial, vol. 369, p. 532, Feb. 17, 2007; and WHO, "WHO Reports Some Promising Results on Avian Influenza Vaccines," press release, Feb. 16, 2007, at <http://www.who.int/mediacentre/news/notes/2007/np07/en/index.html>.

⁹² Presentation of Jesse L. Goodman, Director, FDA Center for Biologics Evaluation and Research, "Meeting the Challenge of Pandemic Vaccine Preparedness: An FDA Perspective," at the Institute of Medicine Symposium on Pandemic Influenza Research, Apr. 5, 2005, at <http://www.iom.edu/project.asp?id=25218>. See also Jennifer Corbett Dooren, "FDA Aims to Approve New Flu Treatments in Weeks," Dow Jones News Service, Nov. 4, 2005.

⁹³ Reverse genetics is a technique to modify viruses so they can be grown more easily for vaccine production. Cell culture is a streamlined method of growing large amounts of virus. Both techniques are explained in greater detail in CRS Report RL32655, *Influenza Vaccine Shortages and Implications*, by (name redacted) and (name redacted).

Use Authorization (EUA) permits the use of unapproved products during a declared public health emergency when alternatives are not available.⁹⁴ In early 2005, when FDA issued an EUA for an anthrax vaccine for the military, the agency noted that the statute is self-executing, and that implementing regulations were not required.⁹⁵

Intellectual Property Issues

To produce a vaccine against H5N1 or another pandemic flu strain, scientists start with a virus in circulation, and modify it for mass production. Flu virus for vaccine is grown in fertilized chicken eggs. Avian flu strains must first be weakened, or *attenuated*, or they would kill the chicken embryos, making it impossible to produce vaccine. Traditionally, flu viruses were attenuated using a cumbersome trial-and-error gene-swapping process. In developing prototype H5N1 vaccines, the virus was attenuated using a process called *reverse genetics* (RG). RG is a more efficient and reliable means of genetic modification, which removes unwanted genes and substitutes others.

RG is a patented invention. One of the patent holders, Medimmune, Inc., has waived compensation for production of prototype pandemic flu vaccines and clinical trials, saying that it had:

notified the World Health Organization in December 2003 that it would grant free access to its intellectual property to government organizations and companies developing pandemic influenza vaccines gratis for public health purposes. In addition, MedImmune, Inc., has given similar notification to NIH and (other officials) in the United States, and the National Institute for Biological Standards and Control (NIBSC) in the United Kingdom. For corporate manufacturers considering the commercial sale of pandemic influenza vaccines produced by reverse genetics, MedImmune, Inc., has sent out letters to all such manufacturers offering licenses to its intellectual property under reasonable terms.⁹⁶

In the United States, the federal government may use patented processes without consent, as long as the patent holder is appropriately compensated.⁹⁷ The situation is more complicated in other countries with vaccine plants (mainly in Europe), and would require that certain agreements among RG patent holders and governments be ironed out before mass production could begin.

⁹⁴ FDA, “Emergency Use Authorization of Medical Products,” draft guidance, not for implementation, June 2005, at http://www.fda.gov/oc/bioterrorism/emergency_use.html. This emergency use authority is somewhat broader than the Secretary’s authority to declare a public health emergency. For more information, see the Appendix, “Federal Public Health Emergency Authorities,” in CRS Report RL33579, *The Public Health and Medical Response to Disasters: Federal Authority and Funding*, by (name redacted).

⁹⁵ FDA, “Authorization of Emergency Use of Anthrax Vaccine Adsorbed for Prevention of Inhalation Anthrax by Individuals at Heightened Risk of Exposure Due to Attack With Anthrax; Availability,” 70 *Federal Register* 5452, Feb. 2, 2005.

⁹⁶ See Statement from Medimmune, Inc., regarding reverse genetics technology, in “Reverse Genetics, Intellectual Property, and Influenza Vaccination,” Institute of Medicine, *The Threat of Pandemic Influenza: Are We Ready? Workshop Summary*, p. 192 ff., Nov. 2004, at <http://www.iom.edu/CMS/3783/3924/23639.aspx>.

⁹⁷ See CRS Report RL32051, *Innovation and Intellectual Property Issues in Homeland Security*, by (name redacted). This authority is based in existing law and does not require an emergency declaration or other special circumstance.

Vaccine Tracking and Distribution

The sudden shortage of seasonal flu vaccine in the United States for the 2004-2005 season offered an unplanned exercise for pandemic preparedness, highlighting the implications of limited production capacity for vaccines and antiviral drugs, and the absence of a coordinated national system for their distribution.

In December 2006, Congress passed **P.L. 109-417**, the Pandemic and All-Hazards Preparedness Act. The act authorizes the Secretary of HHS, with the voluntary cooperation of manufacturers, wholesalers, and distributors, to track the initial distribution of federally purchased flu vaccine during a pandemic. The act also requires the Secretary to improve the effective distribution of seasonal flu vaccine, by promoting communication between state, local, and tribal public health officials and those manufacturers, wholesalers, and distributors who agree to participate in the tracking program. Vaccine distribution information submitted to the Secretary shall remain confidential in accordance with the exception to the Freedom of Information Act (FOIA) governing trade secrets and commercial or financial information, and be subject to the privacy regulations promulgated under the Health Insurance Portability and Accountability Act of 1996 (P.L. 104-191).

Antiviral Drug Supply and Use

Since pandemic flu vaccine would be unavailable in the early stages of a pandemic, governments and private parties have been interested in drugs that could treat or prevent serious illness from flu. Because influenza is a virus, antibiotics, which treat bacterial infections, are not effective in treating the direct effects of flu. Two types of antiviral drugs have been developed to treat flu: *adamantanes* and *neuraminidase inhibitors* (NIs).⁹⁸ Though both types are used to treat serious infections of seasonal influenza, the H5N1 flu strain has been shown to be resistant to adamantanes. Hence, planning efforts for a possible H5N1 pandemic have focused on NIs. Two NIs are available, and both are licensed by the FDA: oseltamivir (Tamiflu®) and zanamivir (Relenza®). The drugs can be used either for treatment when someone is severely ill with flu, or for prevention in those at risk of severe illness. When used for prevention, also called *prophylaxis*, the drug must be given for weeks (rather than the five-day treatment regime), as long the flu virus is in circulation. This has implications for stockpiling, and for the potential development of viral resistance to the drugs.

WHO has recommended that countries create stockpiles of NIs to prepare for a pandemic. Initially, the availability and cost of Tamiflu, a patented drug, were of concern to government officials seeking to acquire the drug in large amounts for their citizens. The patent holder, the Swiss pharmaceutical company Roche, Inc., has since signed agreements to manufacture the drug with more than 15 external contractors in 10 different countries.⁹⁹ Several countries have stockpiled enough Tamiflu to treat one-fifth or more of their populations.

The federal government has established two primary goals for stockpiling existing antiviral medications: (1) establishment and maintenance of stockpiles adequate to treat 75 million persons (one-fourth of the population), divided between federal and state stockpiles; and (2) establishment

⁹⁸ See CDC, antivirals for influenza, at <http://www.cdc.gov/flu/professionals/treatment/>.

⁹⁹ See CRS Report RL33159, *Influenza Antiviral Drugs and Patent Law Issues*, by (name redacted).

and maintenance of a federal stockpile of 6 million treatment courses reserved for domestic containment efforts.¹⁰⁰ States were expected to procure 31 million of the 75 million treatment courses, for which HHS would reimburse 25% of the cost. Some public health officials and Members of Congress protested the 75% state matching requirement.¹⁰¹ In an October 2006 survey of state health officials, 29 reported that they had not yet identified and put in place state funds to purchase antiviral drugs, though all but 10 of them reported that they planned, ultimately, to purchase the full amount allotted to them under the federal subsidy program.¹⁰²

Priority groups for antiviral drugs are laid out in the HHS Pandemic Plan, beginning with treatment for those who are admitted to hospitals with severe illness from flu. Priority categories are otherwise fairly similar to those for vaccine (See **Table 2.**), encompassing certain groups of high risk individuals as well as healthcare workers and other responders.

In June 2005, it was reported that farmers in China were using the flu antiviral drug amantadine (an adamantane) to treat poultry flocks to prevent avian flu, and that this may have caused the H5N1 strain to become resistant to the drug.¹⁰³ Health officials in China and elsewhere denounced the practice. Tamiflu, the more widely available of the two NIs, is generally effective against H5N1 flu, but resistance to the drug has been documented in strains of seasonal flu that circle the globe each year, and in at least four cases of H5N1 avian flu in humans. Scientists caution that resistance to Tamiflu could become a problem if the drug were pressed into service during an influenza pandemic, especially if it were used for prolonged periods for prophylaxis.¹⁰⁴ In March 2006, the FDA issued an order prohibiting the extra-label use, in poultry, of all approved human anti-influenza drugs, to help prevent the emergence of resistance, preserving the effectiveness of these drugs for treating or preventing influenza infections in humans.¹⁰⁵

Public health officials have cautioned against an over-reliance on antiviral drugs in pandemic planning. There would likely be limited availability, and drug resistance could emerge as a serious problem. Also, it has not been clearly shown that treatment with Tamiflu, for example, would actually improve survival rates in clinical settings during a potential H5N1 pandemic.¹⁰⁶ Nonetheless, given that the best pandemic response tool—vaccine—will be largely unavailable in the early going, governments can offer antiviral drug stockpiling as a tangible effort to protect their citizens.

¹⁰⁰ National Strategy, p. 9.

¹⁰¹ See Gardiner Harris, “Administration’s Flu Plan Gets Mixed Reception in Congress,” *The New York Times*, Nov. 3, 2005.

¹⁰² Association of State and Territorial Health Officials, (ASTHO), “ASTHO Survey of State and Territorial Pandemic Influenza Antiviral Purchase and Stockpiling,” Oct. 2006, at <http://www.astho.org/pubs/AntiviralSurvey121806.pdf>. Respondents included officials from all 50 states, the District of Columbia, and three territories.

¹⁰³ See, for example, Fu Jing, “Misuse of Antiviral on Poultry Must Stop,” *China Daily*, June 21, 2005, at http://www.chinadaily.com.cn/english/doc/2005-06/21/content_453023.htm.

¹⁰⁴ Q. Mai Le, “Avian Flu: Isolation of Drug-resistant H5N1 Virus,” *Nature* 437, 1108 Oct, 20, 2005; and Luciana L. Borio and John G. Bartlett, “Isolation of H5N1 Influenza Virus Resistant to Oseltamivir,” *Clinician’s Biosecurity Network Weekly Bulletin*, Oct. 18, 2005.

¹⁰⁵ 71 *Federal Register* 14374-14377, Mar. 22, 2006.

¹⁰⁶ In addition, Tamiflu may, in some people, cause adverse effects that would require that it be discontinued. See CDC, “Antiviral Medications for Influenza,” at <http://www.cdc.gov/flu/professionals/treatment/>.

Liability and Compensation for Pandemic Countermeasures

Status of Current Planning Efforts

Certain vaccines are covered under the National Vaccine Injury Compensation Program (VICP). Under VICP, an excise tax applied to vaccine sales pays for a public compensation fund. Congress enacted the program in 1986 as a no-fault alternative to the tort system for resolving personal injury claims resulting from adverse reactions to selected childhood vaccines (i.e., those that CDC has recommended be routinely administered to children.) Individuals of any age alleging injury from any covered vaccine must seek compensation through the program first, though they may decline a proposed award and then sue in court.¹⁰⁷ In the American Jobs Creation Act of 2004 (P.L. 108-357), Congress added *trivalent* flu vaccine—the annual vaccine that contains three flu strains—to the Vaccine Injury Table, a list of vaccines covered under VICP. Since the law explicitly covered trivalent vaccine, *monovalent* (or single-strain) pandemic vaccines would not be covered under this mechanism.

In December 2005, Congress passed P.L. 109-148, the Department of Defense, Emergency Supplemental Appropriations to Address Hurricanes in the Gulf of Mexico, and Pandemic Influenza Act, 2006. Division C of the act limits liability with respect to countermeasures (including vaccine) for pandemic flu and other public health emergencies. Specifically, upon a declaration by the Secretary of HHS of a public health emergency, or the credible risk of such emergency, the act would, with respect to a “covered countermeasure,” eliminate liability (except in the case of willful misconduct) for the United States, and for manufacturers, distributors, program planners, persons who prescribe, administer or dispense the countermeasure, and employees of any of the above.

On February 1, 2007, HHS Secretary Leavitt made a declaration of emergency pursuant to P.L. 109-148, saying he had “determined there is a credible risk that the spread of avian influenza viruses and resulting disease could in the future constitute a public health emergency,” triggering liability protections solely for “pandemic countermeasure influenza A (H5N1) vaccine....”¹⁰⁸ The declaration is effective from December 1, 2006 through February 28, 2010.

P.L. 109-148 also called for the establishment in the Treasury of the “Covered Countermeasure Process Fund” to provide compensation to eligible individuals for covered injuries (i.e., serious physical injury or death) directly caused by the administration or use of a covered countermeasure during a declared public health emergency, depending upon an appropriation to the fund. The act does not establish appropriations authority for the fund, however.¹⁰⁹

The Implementation Plan tasked HHS with developing a protocol and decision tools for medical countermeasures, to implement the act’s liability protections and compensation mechanism. HHS published its protocol and decision tool in December 2006.¹¹⁰

¹⁰⁷ For more information, see the National Vaccine Injury Compensation Program Home Page at <http://www.hrsa.gov/vaccinecompensation/>.

¹⁰⁸ 72 *Federal Register* 4710-4711, Feb. 1, 2007.

¹⁰⁹ For more information, see CRS Report RS22327, *Pandemic Flu and Medical Biodefense Countermeasure Liability Limitation*, by (name redacted) and (name redacted).

¹¹⁰ HHS, “Public Readiness and Emergency Preparedness Act (PREP Act) for Pandemic Influenza Medical Countermeasures Utilization Protocol & Decision Tools,” Dec. 4, 2006, at <http://www.pandemicflu.gov/plan/federal/> (continued...)

Smallpox Vaccine Injury Compensation

During implementation of the smallpox vaccination program in 2003, Congress grappled with waiving liability in order to protect the manufacturer, public officials, health providers and others who would make, recommend and deliver the product, while assuring that those who suffered adverse events resulting from the vaccine could be appropriately compensated.¹¹¹ The smallpox vaccine used for the 2003 campaign carries an unusually high risk of adverse events, and most scientists do not believe that a pandemic flu vaccine would carry a comparable risk.

The 1976 Swine Flu Affair

A 1976 vaccination campaign that was intended to protect Americans from the threat of a swine flu pandemic in 1976 is often referred to as a debacle.¹¹² In January 1976, a novel influenza strain (“swine flu”) emerged in New Jersey. In March, the Ford Administration announced a campaign to vaccinate the U.S. population by December. On August 18, Congress passed P.L. 94-380, the National Swine Flu Immunization Program of 1976. Among other provisions, the law shielded manufacturers, distributors, and public or private organizations that would administer the vaccine, from claims of injury or death that might result, and established that all such claims would be asserted directly against the United States. More than 40 million civilians were vaccinated against swine flu between October 1 and December 16. The campaign was suspended at that time due to several cases of Guillain-Barré syndrome, a potentially serious neurological condition causing paralysis and sometimes death, suspected to have been caused by the vaccine. Meanwhile, a flu pandemic never emerged. The worrisome virus from New Jersey never led to a global pandemic, or even to localized outbreaks. The federal government ultimately paid out \$93 million to individuals injured by the vaccine.¹¹³

Analysts have commented that delays in indemnifying manufacturers threatened the availability of swine flu vaccine in 1976, while delays in providing for injury compensation compromised voluntary participation in the civilian smallpox vaccine campaign in 2003. A successful emergency vaccination campaign may depend on resolving both policy concerns expediently.

Influenza as a Weapon

In the late 1990s, Congress authorized the Select Agent program to track the movement of certain bacteria and viruses that could potentially be used as biological weapons.¹¹⁴ The program, which is administered by CDC and the U.S. Department of Agriculture, was expanded in statute following the anthrax attacks of 2001. An interagency working group determines which

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¹¹¹ See CRS Report RL31960, *Smallpox Vaccine Injury Compensation*, by (name redacted).

¹¹² Sources for this section are: Richard E. Neustadt and Harvey V. Fineberg, *The Swine Flu Affair*, a report to the Secretary of Health, Education and Welfare, June, 1978; and HHS Draft Pandemic Influenza Preparedness and Response Plan, Annex 11: “Lessons Learned from the 1976 Swine Influenza Program,” Aug. 2004.

¹¹³ U.S. Department of Justice, Civil Division, Torts Branch, “Swine Flu Statistics,” Jan. 3, 1991. Overall, 4,179 claims were filed under the act. Not all claims were resolved administratively, and 1,604 claimants proceeded to file suit.

¹¹⁴ For more information, see the CDC Select Agent program page at <http://www.cdc.gov/od/sap> and CRS Report RL31719, *An Overview of the U.S. Public Health System in the Context of Emergency Preparedness*, by (name redacted).

pathogens to place on the list of Select Agents. Once an organism is listed, those individuals and facilities working with it must be registered, undergo background investigations, and follow various guidelines in facility maintenance and management, shipping, recordkeeping and other practices. The list does not include common human strains of influenza, though it does include highly pathogenic strains of avian influenza, i.e., strains which are shown to cause disease in commercial poultry. As such, H5N1 influenza is a listed pathogen. When scientists from the CDC and the Armed Forces Institute of Pathology recently re-created the 1918 pandemic flu virus, since it was a human influenza virus, it was not on the Select Agent list. It was subsequently added by HHS Secretary Leavitt on October 20, 2005.¹¹⁵ Other flu strains that typically affect humans (rather than birds) remain unregulated at this time.

When asked about the possibility that influenza viruses could be used deliberately as biological weapons, CDC Director Julie Gerberding replied, "... we recognize that influenza has some of the important characteristics of an excellent threat agent. It's easily transmissible, it's relatively easy to produce and it's very easy to modify or engineer. So it does have characteristics that if a person was intent on modifying ..., it is not beyond our imagination to consider that beyond our preparedness efforts."¹¹⁶ Dr. Gerberding also noted the natural behavior of the virus, which constantly shuffles its genes to produce new combinations, saying that "mother nature herself is a very effective terrorist."

If H5N1 avian flu were to cause a human pandemic, it would be reasonable to assume it was a natural event. Nonetheless, since influenza viruses are amenable to intentional manipulation, the Implementation Plan states that in the event of a pandemic, "The Federal Bureau of Investigation (FBI) will closely monitor events through coordination with the [CDC] and take appropriate action in the event that it is suspected that there was deliberate human intervention in the spread of the pandemic."¹¹⁷

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¹¹⁵ CDC, "Possession, Use, and Transfer of Select Agents and Toxins - Reconstructed Replication Competent Forms of the 1918 Pandemic Influenza Virus Containing Any Portion of the Coding Regions of All Eight Gene Segments," 70 *Federal Register* 61047, Oct. 20, 2005.

¹¹⁶ Testimony of CDC Director Julie Gerberding before the House Committee on Homeland Security, Subcommittee on Prevention of Nuclear and Biological Attacks, hearing on "National Biodefense Strategy," July 28, 2005, 109th Congress, 1st Sess.

¹¹⁷ Implementation Plan, p. 156.

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