DRAFT
PANDEMIC INFLUENZA PREPAREDNESS AND RESPONSE PLAN

Department of Health and Human Services

Core Document
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Comments on this draft plan should be forwarded to:

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Executive Summary

An influenza pandemic has a greater potential to cause rapid increases in death and illness than virtually any other natural health threat. Planning and preparedness before the next pandemic strikes – the inter-pandemic period – is critical for an effective response. This Draft Pandemic Influenza Preparedness and Response Plan describes a coordinated strategy to prepare for and respond to an influenza pandemic. It also provides guidance to state and local health departments and the health care system to enhance planning and preparedness at the levels where the primary response activities in the U.S. will be implemented.

Influenza causes seasonal epidemics of disease resulting in an average of 36,000 deaths each year. A pandemic – or global epidemic – occurs when there is a major change in the influenza virus so that most or all of the world's population has never been exposed previously and is thus vulnerable to the virus. Three pandemics occurred during the 20th century, the most severe of which, in 1918, caused over 500,000 U.S. deaths and more than 20 million deaths worldwide. Recent outbreaks of human disease caused by avian influenza strains in Asia and Europe highlight the potential of new strains to be introduced into the population. Recent studies suggest that avian strains are becoming more capable of causing severe disease and that these strains have become endemic in some wild birds. If these strains reassort with human influenza viruses such that they can be effectively transmitted between people, a pandemic can occur.

Characteristics of an influenza pandemic that must be considered in preparedness and response planning include: 1) simultaneous impacts in communities across the U.S., limiting the ability of any jurisdiction to provide support and assistance to other areas; 2) an overwhelming burden of ill persons requiring hospitalization or outpatient medical care; 3) likely shortages and delays in the availability of vaccines and antiviral drugs; 4) disruption of national and community infrastructures including transportation, commerce, utilities and public safety; and 5) global spread of infection with outbreaks throughout the world.

The Department of Health and Human Services (HHS) continues to make progress in preparing to effectively respond to an influenza pandemic. This has been done through programs specific for influenza and those focused more generally on increasing preparedness for bioterrorism and other emerging infectious disease health threats. Substantial resources have been allocated to assure and expand influenza vaccine production capacity; increase influenza vaccination use; stockpile influenza antiviral drugs in the Strategic National Stockpile (SNS); enhance U.S. and global disease detection and surveillance infrastructures; expand influenza-related research; support public health planning and laboratory; and improve health care system readiness at the community level.

Additional preparation is also ongoing in several critical areas. Vaccination is the primary strategy to reduce the impact of a pandemic but the time required currently to develop a vaccine and the limited U.S. influenza vaccine production capacity represent barriers to optimal prevention. Enhancing existing U.S. and global influenza surveillance networks can lead to earlier detection of a pandemic virus or one with pandemic potential. Virus identification and

the generation of seed viruses for vaccine production is a critical first step for influenza vaccine development.

In addition to expanding the number of global surveillance sites and extending existing sentinel surveillance sites to perform surveillance throughout the year, there has been a concomitant enhancement of laboratory capacity to identify and subtype influenza strains. Vaccine research and development can be accelerated during the inter-pandemic period by preparing and testing candidate vaccines for influenza strains that have pandemic potential, conducting research that will guide optimal vaccine formulation and schedule, and assessing techniques that can enhance manufacturing yields using current and prospective production methods. Plans are in place to increase U.S. influenza vaccine manufacturing capacity through a partnership with industry to assure that vaccine can be produced at any time throughout the year. In addition the Centers for Medicare and Medicaid Services (CMS) and the Centers for Disease Control and Prevention (CDC) are working to increase demand for annual influenza vaccine in high risk groups. Increasing demand for annual influenza vaccines will not only improve annual influenza prevention and control but will also strengthen the vaccine delivery system and expand manufacturing capacity to meet this increased demand. Enhanced planning by the public and private health care sectors to assure the ability to distribute vaccine, targeting available supply to priority groups, and monitoring vaccine effectiveness and adverse events also are critical to meet pandemic response goals.

Early in a pandemic, especially before vaccine is available or during a period of limited supply, use of other interventions may have a significant effect. For example, antiviral drugs are effective as therapy against susceptible influenza virus strains when used early in infection and can also prevent infection (prophylaxis). In 2003, the antiviral drug oseltamivir was added to the SNS. Analysis is ongoing to define optimal antiviral use strategies, potential health impacts, and cost-effectiveness of antiviral drugs in the setting of a pandemic. Results of these analyses will contribute to decisions regarding the appropriate type and quantity of antiviral drugs to maintain in the SNS. Planning by public and private health care organizations is needed to assure effective use of available drugs, whether from a national stockpile, state stockpiles or in private sector inventories.

Implementing infection control strategies to decrease the global and community spread of infection, while not changing the overall magnitude of a pandemic, may reduce the number of people infected early in the course of the outbreak, before vaccines are available for prevention. Travel advisories and precautions, screening persons arriving from affected areas, closing schools and restricting public gatherings, and quarantine of exposed persons may be important strategies for reducing transmission. The application of these interventions will be guided by the evolving epidemiologic pattern of the pandemic.

Planning by state and local health departments and by the health care system and coordination between the two is critical to assure effective implementation of response activities and delivery of quality medical care in the context of increased demand for services. Guidance included in this plan and from other organizations, as well as technical assistance and funding are available to facilitate planning. Coordination in planning and consistency in implementation with other emergency response plans, such as those for bioterrorist threats and SARS can improve

efficiency and effectiveness. In addition, other public health emergency programs such as the Heath Resources and Services Administration (HRSA) Hospital Preparedness Program and the CDC Public Health Preparedness and Response Cooperative Agreements are providing states with resources to strengthen their ability to respond to bioterror attacks, infectious diseases and natural disaster. For example, initiatives and funding being provided by HRSA will help states improve coordination of health care services and emergency response capacity and facilitate preparedness for influenza, smallpox, SARS, as well as other public health emergencies. In FY 04, HHS introduced a cross-cutting critical benchmark for state pandemic influenza preparedness planning as part of the Department's awards to states to improve hospitals' response to bioterrorism and other diseases. The goal of this planning activity is to assure implementation of an effective response including the delivery of quality medical care in the context of the anticipated increased demand for services in a pandemic (www.hhs.gov/asphep/FY04benchmarks.html). Completing pandemic preparedness and response plans and testing them in tabletop and field exercises are key next steps. All totaled since Sept. 11, 2001, HHS has invested more than $3.7 billion in strengthening the Nation's public health infrastructure.

Preparedness for an influenza pandemic is coordinated in the office of the Assistant Secretary for Health, HHS. Response activities will be coordinated by the Assistant Secretary for Public Health Emergency Preparedness, on behalf of the Secretary in close coordination with the Department of Homeland Security as stipulated in HSPD#5. Other federal agencies will play critical roles as well.

Pandemic influenza response activities are outlined by pandemic phase, a classification system developed by the World Health Organization (WHO) in 1999. Phase 0, the inter-pandemic phase, is divided into 4 levels: Phase 0, Level 0 (with no recognized human infections caused by a novel influenza strain; Phase 0, Level 1 ("new virus alert") with a case of human infection caused by a novel strain; Phase 0, Level 2 (with two or more human cases but no documented person-to-person transmission and unclear ability to cause outbreaks; and phase 0,level 3 ("pandemic alert") with person-to-person spread in the community and an outbreak in one country lasting for more than two weeks. Progression from a new virus alert to a pandemic alert will be accompanied by response activities that include intensified U.S. and global surveillance; investigation of the virology and epidemiology of the novel influenza strain including collaboration with international partners on containment; vaccine development and clinical testing leading toward licensure of a pandemic vaccine; coordination with health departments and activation of local plans, and implementation of the communications plan which includes education of health care providers and the public.

Pandemic Phase 1 occurs with confirmation that the novel influenza virus is causing outbreaks in one country, has spread to others, and disease patterns indicate that serious morbidity and mortality may occur. In Phase 2, outbreaks and epidemics occur in multiple countries with global disease spread. Response activities during these phases depend, in part, on the extent of disease internationally and in the U.S. Community-level interventions and travel restrictions may decrease disease spread. Once vaccine becomes available, immunization programs will begin. At this phase, antiviral prophylaxis and therapy targeted to maximize impact, local coordination of hospital and outpatient medical care and triage, and activation of emergency

response plans to preserve community services also will occur. Federal agencies and personnel will support response activities, monitor vaccine effectiveness and adverse events following vaccination and antiviral drug use, conduct surveillance to track disease burden, and disseminate information.

Phase 3 signals the end of the first pandemic wave and may be followed by a second seasonal wave in Phase 4. A pandemic will end in Phase 5, as population immunity to the pandemic strain becomes high due to disease or vaccination, the virus changes, and/or another influenza strain becomes predominant. Phase 3 activities include recovery, assessment and refinement of response strategies, ongoing vaccine production and vaccination and restocking supplies such as antiviral drugs. Greater vaccine availability, experience with and improved strategies for a pandemic response, and increased immunity to the pandemic strain should decrease the impact of the second pandemic wave.

Synopsis

A. Purposes of the Pandemic Influenza Preparedness and Response Plan

- To define and recommend preparedness activities that should be undertaken before a pandemic that will enhance the effectiveness of a pandemic response.
- To describe federal coordination of a pandemic response and collaboration with state and local levels including definition of roles, responsibilities, and actions.
- To describe interventions that should be implemented as components of an effective influenza pandemic response.
- To guide health departments and the health care system in the development of state and local pandemic influenza preparedness and response plans.
- To provide technical information on which recommendations for preparedness and response are based.

B. Components of the Pandemic Influenza Preparedness and Response Plan

- The Plan includes this core section and twelve annexes.
- The core plan describes coordination and decision making at the national level; provides an overview of key issues for preparedness and response; and outlines action steps to be taken at the national, state, and local levels before and during a pandemic.
- Annexes 1 and 2 provide information to health departments and private sector organizations to assist them in developing state and local pandemic influenza preparedness and response plans.
- Annexes 3-12 contain technical information about specific preparedness and response components. They include a description of influenza disease and pandemics; surveillance; vaccine development and production; vaccine use strategies; antiviral medication use strategies; strategies to decrease transmission of influenza; communications; research; observations and lessons learned from the 1976 swine influenza program; and comparisons between planning for an influenza pandemic and Severe Acute Respiratory Syndrome (SARS) outbreaks.

C. Pandemic Plan Development Process

- The first national pandemic influenza plan was developed in 1978, shortly after the swine influenza cases and vaccination campaign in 1976.
- In 1993, a U.S. Working Group on Influenza Pandemic Preparedness and Emergency Response was formed to draft an updated national plan. This group included representatives from the HHS agencies (CDC, FDA, NIH, HRSA and others) and coordinated by the National Vaccine Program Office (NVPO).
- Comments and input on specific issues included in the plan has been obtained from a wide range of groups in the public and private sectors; and from other pandemic influenza preparedness plans (see web links) or planning guides (such as the Association of State and Territorial Health Officials [ASTHO]).

- Recent developments that have influenced the influenza pandemic planning process include experience gained through planning for bioterrorist events and other health emergencies such as the international response to SARS and the national responses to anthrax cases and the implementation of a the US smallpox vaccination program.
- Ongoing enhancements in public health and communications infrastructure and development of new technologies, for example in vaccine development and production, are likely to influence portions of the plan. Therefore, it is envisioned that the Plan will be an evergreen document, which will be modified as new developments warrant. Supporting materials (such as educational materials, fact sheets, question and answer documents, etc.) will be added to the Plan or modified as needed.

D. Goals of a Pandemic Response

- Limit morbidity and mortality of influenza and its complications during a pandemic.
- Decrease social disruption and economic loss.

E. Key Pandemic Preparedness and Response Principles

- Detect novel influenza strains through clinical and virologic surveillance of human and animal influenza disease.
    - Global surveillance networks identify circulating influenza strains informing recommendations for annual influenza vaccines in the U.S. and around the world.
    - Surveillance also has identified novel strains that have caused outbreaks among domestic animals and persons in several countries.
    - Given the speed with which infection may spread globally via international travel, effective international surveillance to identify persons who have influenza illness coupled with laboratory testing to determine the infecting strain is a critical early warning system for potential pandemics.
    - Effective U.S. surveillance systems also are fundamental in the detection of influenza disease and the causative strains, and for monitoring the burden of morbidity and mortality.

- Rapidly develop, evaluate, and license vaccines against the pandemic strain and produce them in sufficient quantity to protect the population.
    - The time from identification of a new influenza strain to production, licensure, and distribution is approximately six to eight months. In contrast to the protracted timelines in the development, licensure and use of other vaccines, the accelerated timeline for the annual influenza vaccine reflects active collaboration and coordination of the World Health Organization, HHS agencies and influenza vaccine manufacturers.
    - Use of new molecular techniques to develop high-yield vaccine reference strains (the "seed" viruses that will be prepared by public sector labs and provided to vaccine manufacturers) and production of monovalent vaccine containing only the pandemic strain could shorten the timeline to initial availability of a pandemic vaccine.

- Currently, three manufacturers produce influenza vaccine that is licensed for the U.S. market, two with all or part of the production process located in the U.S. The amount of pandemic influenza vaccine produced depends on the physical capacity of the manufacturing facilities, the growth characteristics of the pandemic virus in embryonated chicken eggs used for vaccine production, and the amount of influenza virus protein (antigen) that is included in each dose to achieve optimal protection. The number of available doses also is limited by manufacturing capacity for filling and labeling vials or syringes. In 2004, HHS worked with industry to assure year-round supply of eggs for vaccine production. In addition HHS is supporting the expansion of production capacity and diversification of influenza manufacturing technology, particularly the development of influenza vaccines made in cell culture.

- Implement a vaccination program that rapidly administers vaccine to priority groups and monitors vaccine effectiveness and safety.
  - In contrast to the childhood immunization program, the distribution and administration of influenza vaccine during the annual seasonal epidemic occurs largely through the private sector.
  - In a pandemic, vaccine supply levels will change over time.
    1) When a pandemic first strikes vaccine will likely not be ready for distribution. Because of this, antiviral drug therapy and preventive use in those not infected (prophylaxis), quality medical care, and interventions to decrease exposure and/or transmission of infection will be important approaches to decrease the disease burden and potentially the spread of the pandemic until vaccine becomes available.
    2) Vaccine will require six to eight months to produce. Once the first lots of vaccine are available, there is likely to be much greater demand than supply. Vaccine will need to first be targeted to priority groups that will be defined on the basis of several factors. These may include: the risk of occupational infections/transmission (e.g., health care workers); the responsibilities of certain occupations in providing essential public health safety services; impact of the circulating pandemic virus on various age groups; and heightened risks for persons with specific conditions. Although the priority groups for annual influenza vaccination will provide some guidance for vaccine priority-setting for a pandemic, the risk profile for a pandemic strain and the priorities for vaccination may differ substantially and therefore will need to be guided by the epidemiologic pattern of the pandemic as it unfolds.
    3) Later in the pandemic, vaccine supply will approximate demand, and vaccination of the full at-risk population can occur.
  - Given the time required for vaccine development and vaccine production capacity, shortages may exist throughout the first pandemic wave.
  - In recent years when influenza vaccine was delayed or in short supply for annual influenza epidemics, many persons were vaccinated who were not in recommended priority groups, vaccine distribution was inequitable, and a gray market developed in response to increased demand, with high prices being paid

for some vaccine doses. During a pandemic, increased demand for vaccine could exacerbate these problems.

- Several options exist for purchase and distribution of influenza vaccine during a pandemic. The Federal government could purchase all available pandemic influenza vaccine with *pro rata* distribution to state and local health departments; there could be a mixed system of Federal and private sector purchase; or the current, primarily private system could be utilized. It should be noted that the Federal government already finances a substantial portion of influenza vaccine, including that purchased for eligible children under the Vaccines for Children (VFC) program and reimbursement for doses administered to persons 65 years of age or above under the Medicare Modernization Act. In a mixed system with public and private vaccine supply, the proportion in each sector may change as target groups and available vaccine supply change during the course of a pandemic response. The range of options is currently being considered by HHS.

- Determine the susceptibility of the pandemic strain to existing influenza antiviral drugs and target use of available supplies; avoid inappropriate use to limit the development of antiviral resistance and ensure that this limited resource is used effectively.
  - The objective of antiviral prophylaxis is to prevent influenza illness. Prophylaxis would need to continue throughout the period of exposure in a community. The objective of treatment is to decrease the consequences of infection. For optimal impact, treatment needs to be started as soon as possible and within 48 hours of the onset of illness.
  - Two classes of drugs are used to prevent and treat influenza infections.
    - *Adamantines* (amantadine and rimantadine) are effective as prophylaxis and have been shown to decrease the duration of illness when used for treatment of susceptible viruses. However, resistance often develops during therapy. The adamantines are available from proprietary and generic manufacturers.
    - *Neuraminidase inhibitors* (NI; oseltamivir and zanamivir) also are effective for prophylaxis and treatment of susceptible strains. New data suggests that NI treatment can decrease complications such as pneumonia and bronchitis, and decrease hospitalizations. The development of antiviral resistance, to date, has been uncommon. The NIs are produced by European manufacturers. The U.S. supply of NIs is limited as demand for these drugs during annual influenza outbreaks is low. Zanamivir supply is limited in the U.S.
  - The available supply of influenza antiviral medications is limited and production cannot be rapidly expanded: there are few manufacturers and these drugs have a long production process. In 2003, oseltamivir was added to the SNS. Analysis is ongoing to define optimal antiviral use strategies, potential health impacts, and cost-effectiveness of antiviral drugs in the setting of a pandemic. Results of these analyses will contribute to decisions regarding the appropriate antiviral drugs to maintain in the SNS. Planning by public and private health care organizations is needed to assure effective use of available drugs, whether from a national stockpile, state stockpiles or the private sector.

  - Developing guidelines and educating physicians, nurses, and other health care workers before and during the pandemic will be important to promote effective use of these agents in the private sector.

- Implement measures to decrease the spread of disease internationally and within the U.S. guided by the epidemiology of the pandemic.
  - Infection control in hospitals and long-term care facilities prevents the spread of infection among high-risk populations and health care workers.
  - Because influenza strains that cause annual outbreaks are effectively transmitted between people and can be transmitted by people who are infected but appear well, efforts to prevent their introduction into the U.S. or decrease transmission in the community are likely to have limited effectiveness.
  - If a novel influenza strain that is not as efficiently spread between people causes outbreaks in other countries or the U.S., measures such as screening travelers from affected areas, limiting public gatherings, closing schools, and/or quarantine of exposed persons could slow the spread of disease. Decisions regarding use of these measures will need to be based on their effectiveness and the epidemiology of the pandemic.

- Assist state and local governments and the health care system with preparedness planning in order to provide optimal medical care and maintain essential community services.
  - An influenza pandemic will place a substantial burden on inpatient and outpatient health care services. Because of the increased risk of exposure to pandemic virus in health care settings, illness and absenteeism among health care workers in the context of increased demand will further strain the ability to provide quality care.
  - In addition to a limited number of hospital beds and staff shortages, equipment and supplies may be in short supply. The disruptions in the health care system that result from a pandemic may also have an impact on blood donation and supply.
  - Planning by local health departments and the health care system is important to address potential shortages. Strategies to increase hospital bed availability include deferring elective procedures, more stringent triage for admission, and earlier discharge with follow-up by home health care personnel. Local coordination can help direct patients to hospitals with available beds and distribute resources to sites where they are needed.
  - Health care facilities may need to be established in non-traditional sites to help address temporary surge needs. Specific challenges in these settings such as infection control must be addressed.
  - Not all ill persons will require hospital care but many may need other support services. These include home health care, delivery of prescription drugs, and meals. Local planning is needed to address the delivery of these and essential community functions such as police, fire, and utility service.

- Communicate effectively with the public, health care providers, community leaders, and the media.
  - Informing health care providers and the public about influenza disease and the course of the pandemic, the ability to treat mild illness at home, the availability of

vaccine, and priority groups for earlier vaccination will be important to ensure appropriate use of medical resources and avoid possible panic or overwhelming of vaccine delivery sites. Effective communication with community leaders and the media also is important to maintain public awareness, avoid social disruption, and provide information on evolving pandemic response activities.

F. Coordination of a Pandemic Response

An influenza pandemic will represent a national health emergency requiring coordination of response activities. As outlined in Homeland Security Presidential Directive 5 (http://www.fema.gov/pdf/reg-ii/hspd_5.pdf), the Department of Homeland Security (DHS) has primary responsibility for coordinating domestic incident management and will coordinate all nonmedical support and response actions across all federal departments and agencies. HHS will coordinate the overall public health and medical emergency response efforts across all federal departments and agencies. Authorities exist under the Public Health Service Act for the HHS Secretary to declare a public health emergency and to coordinate response functions. In addition, the President can declare an emergency activating the Federal Response Plan, in accordance with the Stafford Act, under which HHS has lead authority for Emergency Support Function #8 (ESF8)

- HHS response activities will be coordinated in the Office of the Assistant Secretary for Public Health Emergency Preparedness in collaboration with the Office of the Assistant Secretary for Public Health and Science and will be directed through the Secretary's Operations Center. The Operations Center will maintain communication with HHS agency emergency operations centers and with other Departments.
- HHS agencies will coordinate activities in their areas of expertise. Chartered advisory committees will provide recommendations and advice. Expert reviews and guidance also may be obtained from committees established by the National Academy of Sciences, Institute of Medicine or in other forms.

G. Preparedness Activities

- During the inter-pandemic period many activities can be pursued to assure that the government is as prepared as possible for a pandemic. These include:
    - Expand manufacturing capacity for influenza vaccine, develop surge capacity for a pandemic vaccine production, and assess potential approaches to optimize vaccine dose, and diversify manufacturing.
    - Strengthen global surveillance – human and veterinary – leading to earlier detection of novel influenza strains that infect humans, cause severe disease and are capable of person-to-person transmission such that they have a high probability of international spread and assess the susceptibility of the pandemic virus to antiviral drugs. Enhanced surveillance infrastructure also will strengthen detection of other respiratory pathogens – as occurred with SARS. In addition to coordination between HHS and USDA, building and strengthening a global veterinary surveillance network will complement the existing clinical laboratory network organized by WHO.
    - Strengthen U.S. surveillance by expanding to year-round surveillance for influenza disease and the viral strains that cause it. Develop hospital-based

surveillance for severe respiratory illness (e.g., influenza and other infectious agents) and identify methods to rapidly expand the current sentinel physician surveillance system during an influenza pandemic or other health emergency.

- Conduct research to better understand the pathogenic and transmission potential of novel influenza viruses in order to improve predictions about the strains that could trigger an outbreak that could lead to a pandemic.
- To shorten the timeline to vaccine availability in a pandemic, develop collections (libraries) of novel influenza strains that may cause a pandemic; prepare reagents to diagnose infection and evaluate candidate vaccines; and develop high-growth reference strains that can be used for vaccine production.
- For selected novel influenza strains, develop investigational vaccine lots and perform clinical studies to evaluate immunogenicity, safety, and whether one or two doses are needed for protection. In the determination of the optimal vaccine dose, studies should also be performed to assess whether adding an adjuvant – a substance to enhance the immune response to vaccination – or alternative vaccine administration approaches will lead to improved protection and/or the ability to protect more people with the available amount of vaccine virus and effectively expand the vaccine supply.
- Conduct research to develop new influenza vaccines that are highly efficacious, are easier to administer, or that are directed against a constant portion of the influenza virus and thus potentially sidestep the need to develop a new vaccine every year to match the predominant viral strains that are most likely to cause disease. With this approach it may be possible to create an influenza vaccine stockpile in the future.
- Continue efforts to expand annual influenza vaccine use and provide appropriate incentives to strengthen the vaccine delivery system. Increase vaccine use and encourage manufacturers to increase overall capacity.
- Improve capacity to monitor influenza vaccine effectiveness and to track vaccine distribution and coverage.
- Periodically assess the appropriateness of the types and quantities of antiviral drugs included in the SNS.
- Promote planning and provide guidance to groups that will have the lead role in a pandemic response such as state and local health departments, the public and private health care organizations, and emergency response groups; and review, test and revise the plans, as needed.
- Evaluate the potential impacts of interventions to decrease transmission of infection such as travel advisories, school closings, limiting public gatherings, and quarantine and isolation.
- Develop materials for various audiences that will inform and educate them about influenza and pandemic influenza.

Pandemic Influenza Preparedness and Response Plan

SECTION ONE: BACKGROUND AND OBJECTIVES

I. Introduction

A. Background

The first pandemic of the 20th century, the "Spanish flu," began in 1918 and, by the time it ended the following year, by conservative estimates, this pandemic had caused more than 500,000 deaths in the U.S. and more than 20 million deaths worldwide. Later pandemics in 1957 and 1968 caused far fewer deaths in the U.S. (104,000 collectively), but still posed a substantial burden on the health care system, and resulted in substantial economic costs and social disruption.

Influenza is one of the most common causes of febrile and respiratory illness. In the U.S., yearly influenza activity can occur as early as October or November through March or April; peak activity has occurred most often in February. During the average epidemic season, more than 36,000 deaths and 114,000 hospitalizations occur. The risk of severe illness and/or death is higher among adults ≥65 years old; among persons of any age with underlying chronic diseases including lung or heart disease, metabolic diseases, and immunosuppression; and among children <2 years old. Vaccination represents the major strategy to reduce the impact of influenza and is recommended for high-risk persons 6-23 months of age; all persons aged 50 years or older; and persons who live with or care for those at high risk, including health care workers. Despite these recommendations influenza vaccine is underused. For example, in 2002, only 38% of persons aged 50-64 years and 68% of persons aged 65 years and older were vaccinated against influenza.

Influenza viruses circulating in the population are continuously evolving, which requires that vaccines be redesigned and produced annually to provide the best match to the influenza strains that are expected to be circulating. Generally, the changes in influenza viruses (antigenic drift) are not large, and persons who have experienced influenza or had been vaccinated previously retain some immunity. However, occasionally and unpredictably, significant changes can occur in the influenza virus (antigenic shift). Pandemics occur when novel influenza A viruses bearing new surface proteins (new hemagglutinin [HA] and/or neuraminidase [NA] surface antigens). These viruses may be derived from animal or avian influenza viruses and develop the ability to spread effectively among people. By definition pandemics involve the circulation of strains for which most or all of the world's population lack preexisting immunity, therefore, global and national spread of infection and severity of illness would be expected to be much greater than during the annual influenza season.

B. Impact of an Influenza Pandemic

It is impossible to predict the overall impact of an influenza pandemic on the U.S. and global community. Improved medical care, vaccines, and antiviral drugs will prevent deaths, hospitalizations, illnesses, and social disruption that would otherwise occur. Conversely, the increasing amount and speed of global travel and the greater proportion of the population who are elderly or have chronic underlying diseases create new vulnerabilities. The recent outbreak of Severe Acute Respiratory Syndrome (SARS) highlighted the role of international travel in disease transmission. In an influenza pandemic where infection would be expected to spread more easily from person-to-person and may be transmitted by asymptomatic persons, the potential rate and extent of spread is likely to be much greater.

The exact health care burden of an influenza pandemic on the U.S. cannot be predicted with certainty. Published estimates of the number of deaths, hospitalizations, and outpatient visits that may occur are shown in Table 1. Overall the burden of illness and the burden on the health care system will also depend on the transmission potential and virulence of the strain, the epidemiology of the specific pandemic, and the rapidity and effectiveness of the response

Table 1. Estimated excess U.S. health care burden from an influenza pandemic

	Annual influenza	**Pandemic Estimates**
Deaths	20,000-40,000	89,000 - 207,000
Hospitalizations	114,000	314,000- 733,000
Outpatient visits	~5,000,000-10,000,000	18,000,000- 42,000,000

Reference: Meltzer, et al, Emerging Infect Dis 1999;5:659-71.

C. Necessity for Planning

Planning is the key to reducing the health and social impacts of the next influenza pandemic. A U.S. pandemic influenza plan was initially drafted in 1978, after the 1976 swine influenza outbreak in New Jersey, and was revised in 1983. In 1993, a U.S. Working Group on Influenza Pandemic Preparedness and Emergency Response was formed to draft an updated national plan. Planning activities included input from the public and private sectors and resulted in a number of actions and the posting of guidance for state and local health departments on the Internet in 2001 and publication of an update in 2002 (Strikas RA, Wallace GS, Myers MG: Influenza pandemic preparedness action plan for the United States 2002 update. Clin Infect Dis 35(5): 590-6, 2002). Pandemic influenza preparedness plans also have been developed by the Association of State and Territorial Health Officials (ASTHO), the Council of State and Territorial Epidemiologists (CSTE), by other countries, regional groups, and by the World Health Organization (WHO). *(See Internet Resources for Internet links to each of these plans.)*

Several recent developments have influenced the influenza pandemic planning process. These include experience gained through planning for bioterrorist events, new communications systems, advances in vaccine development, licensure of new antiviral medications, improved surveillance infrastructure, experience from national emergency responses to anthrax cases and SARS, implementation of a smallpox vaccination program, influenza vaccine delays and spot shortages in 2000-2001 and 2003-2004, and the widespread outbreak of H5N1 avian influenza in Asia in 2004. New developments will continue to result in updates and modification to the plan. Supportive materials (such as educational materials, fact sheets, question and answer documents, and forms) will be added as they are developed. In addition, pandemic influenza planning should be considered in the context of other emergency response planning activities. Pandemic influenza plans may be useful in preparing for bioterrorist events, other infectious disease pandemics, or other health emergencies. Recognizing overlap and promoting consistency – especially at the state and local levels – will improve the planning process and increase the feasibility of implementation.

II. Goals and Objectives of Pandemic Influenza Preparedness and Response

- Ensure optimal coordination, decision-making, and communication between federal, state, and local levels
- Detect novel influenza strains through clinical and virologic surveillance of human and animal influenza disease
- Rapidly develop, evaluate, and license vaccines against the pandemic strain and produce them in sufficient quantity to protect the population
- Implement a vaccination program that rapidly administers vaccine to priority groups and monitors vaccine effectiveness and safety
- Deliver antiviral drug therapy and prophylaxis and avoid inappropriate use of these agents, which may result in antiviral resistance
- Implement measures to decrease the spread of disease guided by the epidemiology of the pandemic
- Provide optimal medical care and maintain essential community services
- Communicate effectively with the public, health care providers, community leaders and the media

III. Intent of the Plan

Planning and preparedness are essential to optimally achieve the goals and objectives of a pandemic response. Therefore, the purpose of this plan is to define the roles, responsibilities, and actions of key stakeholders before a pandemic and at each stage of a pandemic response. Specifically, the plan will:

- Describe the role of HHS in coordinating a national response to an influenza pandemic
- Provide guidance and tools to promote pandemic preparedness planning and coordination at federal, state, and local levels, including both the public and private sectors

- Provide guidance and priority research activities needed to strengthen preparedness, thereby improving the effectiveness of response
- Provide the technical background underlying recommendations

Preparedness is the key to effective response. Preparation requires planning and testing the plan as well as maintaining and strengthening key capacities and infrastructures such as surveillance, influenza vaccine research, development and production, and communications. It is important that planning be done at all levels of responding organizations – from national to local and institutional levels. Federal agencies and authorities will provide overall direction, guidance and coordination, while state and local health departments and the medical care system will form the front line with respect to management of ill persons and administration of interventions such as vaccine and antiviral medications and possibly community-level interventions such as isolation and quarantine. Thus, information and guidance provided in this plan should serve as a platform for the development of plans at the state and local levels.

Multiple stakeholders have important roles in pandemic influenza preparedness and response. Stakeholders include federal departments and agencies; public health organizations; state and local health departments and laboratories; private health care organizations; influenza vaccine and antiviral manufacturers; and vaccine distributors and vaccinators. Not every section of this plan will be immediately relevant to each of the stakeholders. The guidelines and annexes have been compiled into a single plan with the goals of enhancing understanding and improving coordination between public and private sectors and at different levels of the health care system. This structure also emphasizes that an effective response to influenza pandemic requires planning, infrastructure, and action at many levels and by many groups.

IV. Progress and Synergies in Preparedness Planning

HHS has made substantial progress in preparing to effectively respond to an influenza pandemic. This has been done through programs specific for influenza and those focused more generally on increasing preparedness for bioterrorist and other health threats. Substantial resources have been allocated to assure and expand influenza vaccine production capacity;[1] increase influenza vaccination coverage and acceptance; stockpile influenza antiviral drugs in the Strategic National Stockpile (SNS); enhance U.S. and global disease detection and surveillance infrastructures; expand influenza related research; support public health planning and laboratory capacity; and improve health care system readiness at the community level.

Several of these programs take advantage of synergies that exist between preparedness for an influenza pandemic and for bioterrorist health threats, as well as synergies with existing immunization programs.

[1] President Bush requested $100 million in his 2004 and 2005 budget submissions for pandemic vaccine preparedness. Congress provided $50 million in 2004. The 2005 request is pending.

The Continuation Guidance for Budget Year Four of the Bioterrorism Cooperative Agreement (http://www.bt.cdc.gov/planning/continuationguidance/index.asp) and the 2004 Immunization Continuation Grant Application Guidance both describe synergies between planning for bioterrorism and for other infectious disease threats and identifies pandemic influenza preparedness as a key activity. Health departments have been encouraged to program funding from these sources for pandemic influenza planning. HRSA is providing funding to states under the National Bioterrorism Hospital Preparedness cooperative agreement to strengthen health care capacity and coordination which also are key issues for pandemic influenza response. Resources are available from the CDC to strengthen public health laboratories – a critical component of surveillance. Funding support from the VFC program and from Medicare reimbursement for vaccination of older adults also helps support expanding influenza vaccine coverage. In addition to resources, activities by multiple groups and stakeholders in the public and private sectors will be needed to effectively respond to an influenza pandemic at national, state, and local levels.

V. Pandemic Phases

An influenza pandemic is defined by the emergence of a novel influenza virus, to which much or all of the population is susceptible, that is efficiently transmitted person-to-person, and causes disease outbreaks in multiple countries. Influenza pandemics during the 20th century were caused by viruses with novel antigenic characteristics (possessing hemagglutinin antigen types that had not been identified previously or had not recently circulated among people). The influenza virus strain responsible for the 1918 pandemic was one of the most deadly and was notable for causing serious illness among young adults. The reason for the increased severity in the 1918 pandemic has not been established. Pandemics in 1957 and 1968 were less severe but still caused markedly increased disease and mortality compared with annual influenza epidemics.

However, not all novel influenza types that are transmitted person-to-person result in pandemics. The swine influenza strain, which infected military personnel at Fort Dix, New Jersey, in the spring of 1976, did not reappear in the subsequent fall. And avian influenza strains that caused infections in Asia 1997, 1999, 2003 and 2004, and in the Netherlands in 2003 did not spread widely because they were not well adapted to person-to-person transmission and were contained by a vigorous public health response.

The World Health Organization, in 1999, defined six pandemic phases under which preparation and response can be organized (Table 2). Most of the activities defined as preparedness would be done during the inter-pandemic period, Phase 0, Level 0. A "Novel virus alert" (Phase 0, Level 1) would signal the beginning of a transition from preparedness to response that should be in place by the time of a "Pandemic alert" (Phase 0, Level 3). Before declaring a pandemic alert, WHO will convene an international task force to ensure that the assessment of the new virus's pandemic potential includes an assessment to determine whether the situation could represent either an unusual ecological situation of an

animal vector spreading the virus to persons in different locations or whether it could represent bioterrorism.

These phases provide a framework for planning, however, specific actions may not be needed at every phase or level for each component of preparedness or response. In addition, actions may be different if infections caused by a novel influenza virus (Phase 0, Level 2) occur in the U.S. or another country or if person-to-person transmission of a new strain (Phase 0, Level 3) is slow and limited or is widespread. For example, the U.S. response to avian influenza outbreaks in Hong Kong in 1997 and 2002 (Phase 0, Level 2) was limited because the virus did not spread well between people and was contained by public health measures such as culling infected chicken flocks. The 2003 Netherlands outbreak of avian-influenza also was contained by culling infected flocks, as well as vaccinating and providing antiviral therapy and prophylaxis to infected persons and contacts in the area without a significant U.S. response.

Table 2. WHO influenza pandemic phases

Phase	Level	Definition
0 *Inter-pandemic Phase*	*0*	Epidemic influenza viruses circulate in human populations causing yearly outbreaks; no evidence that a novel influenza virus has infected humans
	1	*Novel Virus Alert*: Identification of a novel influenza virus in a person
	2	Confirmation that the novel influenza virus has infected two or more people, but the ability of the virus to spread rapidly person-to-person and cause multiple outbreaks of disease leading to epidemics remains questionable.
	3	*Pandemic Alert:* Confirmation of person-to-person spread in the general population with at least one outbreak lasting for more than 2 weeks in one country
1		Confirmation that the novel influenza virus is causing several outbreaks in one country and has spread to other countries, with consistent disease patterns indicating serious morbidity and mortality is likely in at least one segment of the population
2		Outbreaks and epidemics are occurring in multiple countries and spreading across the world
3		End of the first wave of the pandemic
4		Confirmation of a second or later wave caused by the same novel virus strain
5		Confirmation that the pandemic has ended

SECTION TWO: INFLUENZA PANDEMIC PREPAREDNESS

VI. Federal Coordination and Activities

Preparedness activities during the inter-pandemic period (Phase 0, Level 0) are the key to an effective pandemic response. Within HHS, pandemic preparedness activities will be overseen by the Assistant Secretary for Health (ASH).in coordination with the Assistant Secretary for Public Health Emergency Preparedness The National Vaccine Program Office (NVPO) will oversee and be responsible for periodic revisions and updates to the pandemic influenza plan and will assure integration with other emergency preparedness and response plans.

HHS offices, agencies, and advisory committees have important roles both for pandemic preparedness and response. Lead roles and responsibilities for preparedness activities are highlighted in Table 3.

Table 3. Summary of major pandemic preparedness roles of HHS agencies, offices and advisory committees

HHS Agencies and Components	Roles
Office of Assistant Secretary for Health (ASH)	• Coordinates HHS pandemic preparedness activities and monitors progress
Office of the Assistant Secretary for Public Health Emergency Preparedness	• Coordinates HHS pandemic response activities
National Vaccine Program Office (NVPO)	• Coordinates development and revisions of the pandemic influenza preparedness and response plan • Coordinates and monitors preparedness activities during the inter-pandemic period, reporting to the ASH • Via the Interagency Vaccine Group (IAVG) coordinates HHS agencies on vaccine issues
Office of the General Counsel	• Advises on legal authorities related to key pandemic response activities
Office of the Assistant Secretary of Public Affairs (ASPA)	• Develops communications plan including messages and materials
Office of Global Health Affairs (OGHA)	• Oversees interactions with other governments and international organizations related to pandemic preparedness

HHS Agencies and Components	Roles
CDC	• Director acts as lead in communications with states and other public health organizations, and with WHO • Conducts viral and disease surveillance in the U.S. and globally; characterizes influenza viral strains; identifies potential vaccine reference strains; and develops and distributes reagents globally for novel virus identification. • Develops reference strains (seed viruses) necessary for the development of pandemic vaccine candidates. Conducts research to better understand transmission and pathogenicity of influenza viruses with pandemic potential • Develops, evaluates and modifies disease control and prevention strategies • Promotes and supports influenza vaccination programs • Investigates outbreaks, defines epidemiology of disease and monitors the impact of influenza • Assesses the effectiveness and safety of vaccination and other influenza control strategies through surveillance and epidemiological studies • Stockpiles antiviral drugs and other essential materials
Food and Drug Administration (FDA)	• Regulates and licenses vaccines and antiviral agents through the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research, respectively • Develops influenza viral reference strains and reagents and makes them available to manufacturers for vaccine development and evaluation
National Institutes of Health (NIH)	• Conducts research on influenza virus biology, pathogenesis, immunology • Conducts research to improve methods for vaccine development and production • Supports virologic surveillance of animals and characterizes infecting strains • Conducts clinical evaluation of candidate pandemic vaccines including immunogenicity and safety of different formulations and dosing schedules through contract Vaccine Treatment and Evaluation Units • Supports the development of influenza viral reference strains and reagents and makes them available to manufacturers for pandemic vaccine development • Establishes collection of novel influenza isolates with pandemic potential and develops vaccine reference strains and reagents • Supports antiviral drug development and evaluation • Conducts genomic sequencing of novel strains

HHS Agencies and Components	Roles
HRSA	• Oversees the National Vaccine Injury Compensation Program • Coordinates planning for health care and hospital surge capacity and emergency preparedness
Centers for Medicare and Medicaid Services (CMS)	• Promotes and supports influenza vaccination for Medicare patients • Fosters improved delivery of influenza vaccination to hospitalized pneumonia patients
HHS Advisory Committees	**Roles**
National Vaccine Advisory Committee (NVAC)	• Advises the Assistant Secretary for Health (ASH) on pandemic preparedness from perspectives of the multiple stakeholders included in the committee membership
Advisory Committee on Immunization Practices (ACIP)	• Advises the CDC Director and Secretary of HHS on use of vaccines and antiviral agents during a pandemic including priority groups for these agents when supply is limited
Vaccine and Related Biological Products Advisory Committee (VRBPAC)	• Determines which influenza strains will be included in the influenza vaccine on a yearly basis • Advises the Commissioner, FDA, on the safety and efficacy of influenza vaccines submitted for U.S. licensure.
Advisory Commission on Childhood Vaccines (ACCV)	• Advises the HRSA Director and the HHS Secretary on vaccines included in the National Vaccine Injury Compensation Program

Although HHS has the lead role in preparing for an influenza pandemic, other federal agencies also contribute to preparedness and planning. The Department of Homeland Security has overall authority for emergency response activities and will coordinate interventions to maintain community services during a pandemic. The Department of Defense and the Department of Veterans Affairs may be in a position to provide surge capacity for medical care. The Department of Agriculture conducts surveillance for influenza in domestic animals. Other Departments (e.g., the Department of Energy and Department of Transportation) will be responsible for maintaining infrastructure during a pandemic. Although plans and activities by these agencies are likely to be similar for pandemic influenza as for other health emergencies, a critical difference is that a pandemic is likely to present substantial needs for health care and infrastructure simultaneously throughout the country, limiting the ability to shift resources from unaffected to affected communities.

Key Decisions for Pandemic Preparedness

In addition to planning, a series of key decisions are needed to guide response to the emergence of a new influenza strain and a pandemic and to facilitate planning by state and local health departments and the health care system. Options for these decisions currently are being considered by HHS and are outlined below.

- Vaccine purchase and distribution – Approximately 85 % of annual influenza vaccine doses distributed in the U.S. are purchased by the private sector. Federal funding reimburses providers for vaccine and administration costs for most doses administered to Medicare and Medicaid patients. The proportion of federally purchased vaccine is likely to increase with inclusion of influenza vaccine in the VFC program and universal vaccine recommendations for children 6 to 23 months old beginning with the 2004-2005 influenza season. Private sector providers and mass vaccinators effectively deliver more than 80 million doses of vaccine during a several month period in the fall preceding the annual influenza season. However, this primarily private vaccine purchase and delivery system may not be optimal in a pandemic. In this setting, targeting limited vaccine supply to priority groups will be needed to optimally reduce morbidity and mortality, and will be important as one way to address current limitations in the system that may be a barrier to equitable distribution of vaccine.

In a pandemic, vaccine purchase and distribution options include: public sector purchase and distribution of all pandemic influenza vaccine; a mixed public-private system where public sector supply may be targeted to specific priority groups (e.g., health care workers and those providing essential public safety services) and those who may be underserved by the current system; or maintenance of the current, largely private system. Important considerations include: 1) whether vaccine purchase recommendations will apply only to a pandemic and will not alter existing vaccine purchase and distribution mechanisms for annual influenza vaccination; 2) how decisions may differ depending on the severity of the pandemic; 3) how Federally purchased vaccine can be distributed to local communities and administered by private sector organizations and providers, as described in state and local pandemic influenza preparedness plans; and 4) what the Federal role in vaccine purchase and distribution should be. This role may change over the course of the pandemic with greater federal involvement early in the pandemic when vaccine is in short supply.

- Stockpiling of influenza antiviral medications – Influenza-specific antiviral medications, when administered as prophylaxis, can be effective at preventing influenza and, as treatment, in reducing complications, hospitalization, and death. U.S. and global antiviral drug production capacity and supply are limited – particularly for the newer neuraminidase inhibitors. Oseltamivir, a neuraminidase inhibitor, has recently been purchased for the SNS, however, the amount available is limited relative to potential demand. Factors that will be considered include feasibility of public sector distribution during a pandemic; potential impacts, costs, and cost effectiveness of a larger stockpile; and the shelf life of stockpiled drug and other logistical issues.

- Priority groups for vaccine and antivirals when supply is limited relative to potential demand – When vaccine and antiviral medications are in short supply, focusing their use within priority groups can help achieve the goals of reducing health, social, and economic impacts of a pandemic. An initial list of suggested priority groups consistent with achieving these public health goals outlined above is being developed by HHS. The Department is soliciting public comment in identifying priority groups in the event that resources are limited. Many of these groups are likely to be similar to those recommended for intervention following other natural and bioterrorist health threats.

In addition, there are decisions that cannot be made until a pandemic is imminent and surveillance and epidemiological data are available to determine transmission patterns, the geographic spread of disease, and segments of the population that are at highest risk of infection and complications. Nevertheless, knowledge of the types of decisions that will be needed can promote planning, facilitate development of options, and guide infrastructure development and data collection to support decision-making. For example, one key decision will be when to produce a vaccine against a novel influenza strain and whether that product should be made *in lieu* of or in addition to a vaccine for the strains anticipated to cause the annual epidemic.

Some of the major decisions that will be needed to guide a pandemic response are highlighted in Table 4.

Table 4. Key decisions for pandemic influenza response.

Pandemic Response	Key decisions
Vaccine	• When should manufacturers produce a vaccine directed at a novel strain? • Should this vaccine be produced with or instead of vaccine for annual epidemic strains? • Should vaccine be administered as rapidly as possible or more slowly to better assess adverse events and efficacy?
Antiviral therapy and prophylaxis	• How should limited supplies of antivirals be used? What should be the balance between prophylaxis and therapy? • Should additional antiviral drugs be purchased by the public sector when a pandemic is imminent, beyond what is maintained in the SNS?
Actions to decrease spread of a pandemic	• Should travelers from countries with outbreaks be screened and should travel be restricted? • Should exposed persons be quarantined? • Should public gatherings be restricted or schools closed?

Understanding existing legal authorities and potential gaps also is important for planning and preparedness. While no law specifically addresses pandemic influenza, numerous federal and state statutes authorize relevant public health actions. An understanding of these authorities and strategies for addressing any limitations will be essential for planning and implementing an effective response to influenza pandemic. Key preparedness issues include resolving any intellectual property issues; making decisions regarding liability concerns of manufacturers and vaccinators; and assuring that needed authorities exist to support outbreak containment activities

VII. State and Local Health Department Planning

A major difference between an influenza pandemic and natural disasters such as a tornado or hurricane, or intentional release of a biological, radiological, or chemical agent, is that a pandemic is likely to cause both widespread and sustained effects and is thus likely to stress the resources of every state. This broad resource strain will make it difficult to shift resources between states and reinforces the need for each state to develop a plan, reflecting a substantial degree of self-reliance.

This draft plan provides a framework for overall preparation, direction and coordination related to a pandemic. However, influenza pandemic preparedness planning at state and local levels is important for effective implementation and to ensure that the response can be tailored to local needs and conditions. Because pandemic influenza planning issues substantially overlap with planning issues related to other health threats, many of the components of this plan should be the same as those contained in plans for bioterrorism or other health emergencies. However, there are unique aspects to planning for an influenza pandemic that would benefit from the formation of a planning committee and the development and distribution of a separate plan specific to pandemic influenza (*See Annex 1: Planning Guidance for State and Local Health Departments.)*

There are several key steps in the state and local planning process. Many states have suggested that planning should start with the formation of a planning committee that includes persons both from the health sector (public and private) and the emergency response sector. Because of the importance of identifying relevant state laws and authorities, including a legal representative could be very useful. Important stakeholders should be brought into the process at an early stage. Meeting with a range of public and private sector groups can help build awareness; will increase understanding regarding the role each group may play in a pandemic response; and will lead to greater involvement in the process. Stakeholders include groups involved in the annual influenza vaccination process and those that provide emergency assistance, maintain community services, keep public order, and provide communications.

Principal elements of the pandemic plan should include

- Command, control, and management procedures including legal authorities
- Surveillance
- Vaccine management including distribution and administration

- Acquisition and use of antiviral agents
- Use of pneumococcal vaccine and antibiotics, respectively, to prevent or treat complications of influenza
- Appropriate use of personal protective equipment
- Appropriate implementation of community level control measures (e.g., travel restrictions, school closings, isolation and quarantine)
- Emergency response including delivery of medical care, providing social services, and maintenance of essential community services
- Communications – internal and external.

Organizing the plan around these elements and pandemic phases may be a useful conceptual approach, although the rapid evolution of events during a pandemic will mean that phases may overlap. Particular attention should be devoted to activities occurring during the inter-pandemic period. In most instances, this is the only period during which key components of the public health infrastructure can be developed or strengthened. It is also a period during which health care providers and organizations can be educated, and coordination and response practiced in tabletop and field exercises. Efforts to improve use of influenza and pneumococcal vaccines during the inter-pandemic period may contribute to pandemic preparedness. For example, increasing influenza vaccination use may stimulate increased vaccine production by manufacturers to meet demand, enhance the vaccine delivery infrastructure, and increase acceptance of influenza vaccine, as well as decreasing the annual health impact of influenza. Lessons learned regarding vaccine delivery and acceptance among racial and ethnic minorities might also improve ability to vaccinate hard-to-reach populations at the time of a pandemic. Pneumococcal vaccination protects against one of the most severe bacterial complications of influenza infection. Given a single U.S. manufacturer for both the pneumococcal polysaccharide and conjugate vaccines, inter-pandemic vaccination consistent with existing recommendations also is important to prevent shortages associated with increased demand when a pandemic occurs.

VIII. Health Care System and Private Sector Planning

Access to and provision of quality medical care are among the most important strategies to decrease morbidity and mortality during a pandemic, particularly during the period before vaccine becomes available. Severe influenza seasons can severely strain current medical care systems. In a pandemic, higher disease rates are likely to stress outpatient and inpatient care further, and this situation is likely to be exacerbated by high rates of absenteeism among health care workers who are likely to be at increased risk of exposure and illness or who have to care for ill family members during a pandemic. In addition to managing infections contracted in the community, it will be important to control the spread of infection among vulnerable populations in hospitals and long-term care facilities such as nursing homes. To address health care issues, representatives of health care organizations should be included in state and local health department pandemic planning activities. In addition, health care organizations should review existing plans and guidelines that may be relevant during a pandemic and, where appropriate, develop plans specific to an influenza pandemic. (*See Annex 2: Planning Guidance for the Health Care System.*)

If the medical care system is to respond to increased demands for care during a pandemic, it will be necessary to protect medical care providers from becoming infected or developing illness. Since vaccine and antiviral supplies likely will be limited, health care organizations should define critical staff and establish priority levels for preventive interventions to assure continued operations. Health care workers should be educated regarding appropriate infection control practices to prevent the spread of influenza and guidelines should be strictly enforced. Strategies for enhancing staffing and hospital bed capacity will need to be developed. If the need for hospitalization exceeds available capacity, care delivery in non-traditional settings, such as hotels and schools, may be required.

Delivery of care to persons who are ill but do not require hospitalization is also an important consideration that will relieve some of the stress on the health care system. Public-private coordination will be essential to assure that medical care and support (such as meals) are provided. Organizations such as the Red Cross, community volunteer groups, or home health care agencies may play key roles. Volunteers to FEMA also provide an important resource at the community level that should be considered as preparedness and response plans are developed.

Influenza outbreaks in hospitals and long-term care facilities such as nursing homes occur each season. This problem will be exacerbated during a pandemic. Because persons in long-term care facilities are usually elderly or have underlying chronic medical conditions, this population is among those with highest risk for developing life-threatening complications from influenza infection. Planning for institutional settings should focus on strategies to reduce the introduction of infections, to rapidly detect and respond to outbreaks, and to provide care and decrease the spread of infection.

IX. Community Response Planning

In addition to its impact on delivery of health care and the health care system, an influenza pandemic may have substantial impacts on the need for and delivery of other community services. Persons who are ill but do not require hospitalization may need home health care services as well as other community support such as delivery of prescription medications and, possibly, meals. States may wish to work with community-based organizations to develop plans. These services may be especially important for older adults who are likely to be most impacted by pandemic influenza. Providing a range of home care services also will be important if isolation and quarantine are implemented as strategies to decrease the transmission of infection. Plans should be developed at the local level through a process that involves public health and emergency preparedness groups along with groups that can provide community services. Community support strategies already may have been developed as part of preparedness for other public health emergencies – either natural or as a result of a bioterrorist attack.

Other vital community services also will be affected by an influenza pandemic. A moderate pandemic could infect one-third of the population. Thus, essential services such as fire and police, utilities, waste disposal, and transportation systems are likely to experience personnel shortages and potential disruption. Work absenteeism because of a need to care for ill family

members or concern about potential contact with infectious persons in the workplace may exacerbate the problem. Reluctance to travel to affected areas may impact the delivery of food supplies and other essential materials in some communities. Coordination with emergency response agencies, including FEMA and development of local strategies which are common to other emergency response plans should be encouraged.

X. Surveillance

Surveillance for influenza requires global and national monitoring both for virus strain and disease activity. Timely identification of circulating or novel virus strains, including those from avian and animal sources, is important for pandemic detection and vaccine preparation. Monitoring influenza disease activity is important to facilitate resource planning, communication, intervention, and investigation. An analysis of the viral strains referred to WHO's global influenza laboratory network leads to recommendations for annual vaccine production. As novel strains are identified, such as the avian H5N1 or H7N7 strains that were implicated in human infection in 1997 and 2003 and 2004, reference strains and seed viruses appropriate for manufacturing can be developed, candidate vaccines can be produced, and appropriate reagents can be prepared for diagnostics and vaccine evaluation.

A. U.S. Virus and Disease Surveillance in Humans

CDC coordinates national influenza surveillance. The U.S. national influenza surveillance system consists of four components: laboratory surveillance, outpatient influenza-like-illness (ILI) surveillance, pneumonia and influenza related mortality surveillance, and assessment of influenza activity in individual states. Traditionally, influenza surveillance has been conducted from October through mid-May. However, efforts are underway to move toward year-round reporting in recognition that unusual outbreaks and pandemic influenza can occur at anytime. In 2004, a subset of laboratories and health care providers will report influenza data to CDC year round for the fourth year in a row. Enhancing this system by increasing the number of sites that obtain specimens for laboratory testing and strain identification would improve the likelihood that new influenza strains are rapidly detected.

Table 5: Current U.S. Influenza Surveillance System

Surveillance Objective	Existing Infrastructure	Data Elements
Determine when, where, and which influenza viruses are circulating	*WHO and National Respiratory and Enteric Virus Surveillance System Collaborating laboratories:* network of state and local public health labs, hospital labs, and commercial labs that test specimens collected as a part of routine patient care, targeted surveillance, and outbreak investigations	*Weekly reports:* ▪ number of specimens tested ▪ number positive for influenza by type/subtype Labs send a subset of influenza isolates to CDC for further testing

Surveillance Objective	Existing Infrastructure	Data Elements
Determine the impact of influenza on outpatient morbidity	*U.S. Influenza Sentinel Provider Surveillance Network:* a collaborative effort between CDC, state health departments, and primary health care providers	*Weekly reports:* ▪ number of patients with ILI by age ▪ number of patients seen for any reason Providers collect respiratory specimens from a subset of ILI patients for influenza testing at the state laboratory
Determine the impact of influenza on mortality	*122 Cities Mortality Reporting System:* vital statistics offices of 122 U.S. cities	*Weekly reports:* ▪ number of death certificates with influenza or pneumonia as underlying or contributing cause of death ▪ Total number of death certificates filed
Influenza activity at the state level	*State and Territorial Epidemiologists Report:* State health departments report the overall level of influenza activity in the state based on defined criteria	*Weekly reports of influenza activity*: ▪ None ▪ Sporadic ▪ Local ▪ Regional ▪ Widespread

Current influenza surveillance will provide the foundation for surveillance during a pandemic. Recent enhancements include updating data transmission systems to provide real-time reporting and data feedback to state health departments, analysis of mortality and illness data by age, and developing outbreak detection algorithms to detect changes in levels of ILI. Future enhancements will include exploring use of existing electronic datasets to increase the flexibility of the existing system to respond to emergencies, exploring hospital based surveillance for severe respiratory syndromes that may be caused by influenza but also may be related to SARS or other agents, and continuing to work with states to increase participation in the sentinel provider and laboratory influenza surveillance so more accurate and reliable estimates of influenza can be made at the state and local levels. While the existing system provides a broad overview of influenza activity, none of the current systems are population-based; therefore, they are not readily able to provide case or death rates.

B. Veterinary surveillance

A pandemic influenza virus strain is likely to arise from reassortment of animal and human influenza viruses. Therefore, coordination of surveillance with the U.S. Department of

Agriculture (USDA) is critical, given USDA's responsibility to conduct influenza surveillance in domestic animals. Recent outbreaks in domestic poultry in Asia and Europe associated with cases of human disease highlight the importance of coordinating these surveillance activities. Surveillance for influenza viruses in poultry in the U.S. has increased substantially since the outbreak of highly pathogenic avian influenza (HPAI) in Pennsylvania and surrounding states in 1983 and 1984. Individual states are generally responsible for the development and implementation of surveillance programs that are consistent with the size and complexity of the resident poultry industry. Although there is considerable variation among states regarding the number and source of samples tested, the samples are derived from a wide range of sources, one of which is the investigation of suspected cases of avian influenza. Investigations may be conducted by state animal health officials, USDA-accredited veterinarians, university personnel, or members of the poultry industry. Samples from affected flocks are routinely submitted to state laboratories for diagnosis. If importation of HPAI is suspected, a Foreign Animal Disease Diagnostician will conduct an investigation and submit samples directly to the National Veterinary Services Laboratories (NVSL) in Ames, Iowa.

Other sources of surveillance samples from poultry come from monitoring for serum and egg yolk antibodies at processing plants, routine testing of game birds, qualifying birds for export, and testing prior to interstate movement. In addition, the USDA's Animal and Plant Health Inspection Service (APHIS) has been monitoring live bird markets in the northeastern region of the U.S. since 1986 for the presence of avian influenza viruses that may pose a threat to commercial poultry.

Most birds submitted for entry into the United States must be quarantined in USDA approved quarantine facilities. During quarantine, avian influenza virus isolation is attempted on samples collected from all dead birds and some live birds. Birds with documented HPAI are not released from quarantine.

Reagents for serologic monitoring for avian influenza are provided free of charge by the NVSL. In addition, suspected isolates of avian influenza and samples positive for influenza antibodies may be submitted to the NVSL for confirmation, subtype identification, and assessment of pathogenicity. Documented outbreaks and infections are reported each year in the Proceedings of the U.S. Animal Health Association Annual Meeting.

Several programs exist for surveillance in wild birds in North America. NIH supports annual surveillance of influenza viruses in wild migrating birds in North America. Collaborations exist with the Canadian Wildlife Service to isolate influenza viruses from migratory birds. Results obtained after analysis of the virus isolates from wild birds are published periodically.

Surveillance in the U.S. for influenza viruses in swine and horses is considerably less systematic than in poultry. While no requirement exists for USDA notification when cases or outbreaks of influenza occur in these animals, considerable interest exists in understanding the viruses that are circulating among them. It is clearly recognized that swine influenza viruses are endemic in pigs in the U.S. and that outbreaks may occur each year. In general,

only outbreaks in swine of unusual severity or duration are likely to be investigated and reported. On the other hand, surveillance for influenza viruses causing disease in horses has practical utility because data generated from analysis of equine influenza viruses can be used to guide equine influenza vaccine formulation. The Animal Health Trust, Newmarket, U.K. has taken the lead in organizing a program for equine influenza surveillance and reporting, primarily in Europe and the United States. Based on this surveillance, an annual report is published (http://www.aht.org.uk).

C. Global Surveillance

Global collaboration, under the coordination of WHO, is a key feature of influenza surveillance. WHO established an international laboratory-based surveillance network for influenza in 1948. The network currently consists of 112 National Influenza Center (NIC) laboratories in 83 countries, and four WHO Collaborating Centers for Reference and Research of Influenza (one is located at CDC). The primary purpose of this surveillance network is to detect the emergence and spread of new antigenic variants of influenza, to use this information to update the formulation of influenza vaccine, and to provide as much warning as possible about the next pandemic. This system provides the foundation of worldwide influenza prevention and control.

The CDC maintains frequent communications with WHO headquarters in Geneva, with the other three WHO Collaborating Centers, and with NICs worldwide. The WHO Collaborating Center located at CDC (in collaboration with the Center for Biologics Evaluation and Research, FDA) annually produces and distributes worldwide the WHO influenza reagent kits needed to identify the influenza viruses that are expected to circulate. This center also conducts comparative serologic and molecular studies of representative and unusual influenza viruses sent from NICs around the world. Results of these studies are used by the Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee (VRBPAC), in selecting influenza strains for annual U.S. influenza vaccines

In 2004, HHS made additional contributions to WHO with the goal of strengthening regional capacity for early detection of novel influenza viruses that pose a pandemic threat in Asia. Recognition that the expense of shipping viral isolates is a barrier to their timely analysis, these funds will also support shipping costs for laboratories.

Finally, this support will also foster the development of a strategic plan to establish a voluntary global animal influenza surveillance network. The recent decision by the UN Food and Agriculture Organization (FAO) to establish a veterinary surveillance network in Southeast Asia will build on an existing effort to begin limited systematic influenza surveillance in swine. Together, these programs will improve the quality of diagnosis and epidemiological data. In addition to enhancing the evaluation of viruses causing illness in animals, this system will help countries to assess the effectiveness of their control programs (http://www.fao.org). The Office International des Epizooties (OIE) has established reference laboratories for avian and equine influenza. These laboratories provide diagnostic testing including virus characterization, reagents, and training. The OIE member countries report outbreaks of avian, equine and swine influenza, and the OIE prepares a yearly

summary of these reports. Finally, in response to the first known transmission of highly pathogenic avian influenza viruses from birds to man in 1997, NIH has supported an animal influenza surveillance program in Hong Kong and plans to expand coverage into other parts of Asia.

XI. Vaccine Development and Use

The annual development, regulation and production of influenza vaccine is a complex process that requires close coordination between the public and private sectors under tight time restrictions imposed by the need to have a current vaccine available in time for the influenza season. The public health sector is primarily responsible for surveillance, strain selection, development of reference viruses to be used in manufacturing, regulatory approval, and safety evaluation and monitoring. The private sector (vaccine manufacturers) work with vaccine seed strains to optimize growth characteristics, and produce and distribute vaccine. The interdependence between public and private sectors in vaccine development underscores the need for a strong public sector capacity and infrastructure.

A. Development

Vaccination with a pandemic strain-specific vaccine is likely to be the most important strategy for preventing morbidity and mortality from pandemic influenza. Therefore, during the inter-pandemic period it is important to ensure that resources are in place so that a pandemic vaccine can be developed as quickly as possible once a novel strain is identified. .

Licensed influenza vaccines use virus grown in embryonated chicken eggs. In preparation for annual influenza seasons, vaccine development, regulation and production include the following steps:

- Flocks of chickens are hatched in the previous summer and begin laying eggs that can be used for manufacturing vaccine for the Northern Hemisphere.
- In meetings during January /February, global and national viral and epidemiological surveillance data are reviewed by WHO and FDA's Vaccine and Related Biological Products Advisory Committee (VRBPAC). Based on an analysis of the viral strains that were referred to the WHO Collaborating Centers, recommendations are made regarding the three strains that are to be included in the vaccine for the following fall/winter influenza season in the northern hemisphere. Analogous meetings are held by WHO in September/October to make influenza vaccine strain recommendations for the Southern Hemisphere.
- Reference viruses for each of these three strains are prepared by HHS agencies and global laboratories from surveillance isolates and are assessed for their potential to be used as seed viruses in manufacturing based on their growth characteristics and immunogenicity. These reference viruses may be further adapted by manufacturers into working seeds that are evaluated and approved by FDA.
- Manufacturers grow viruses in eggs and purify them to produce vaccines for investigational and commercial use.
- FDA evaluates candidate vaccines based on potency testing and limited immunogenicity and safety data. By contrast with annual influenza vaccines, for a

pandemic vaccine, additional clinical testing may be sought before licensure, depending on whether clinical studies had been done during the inter-pandemic period for similar candidate vaccine strains. Also, licensure of new influenza vaccines, such as those containing an adjuvant or a vaccine manufactured in cell culture would require more extensive clinical studies to demonstrate safety and efficacy.

- Large-scale vaccine manufacture occurs with vaccine generally becoming available in August – November, about six to eight months after recommendation of the vaccine components (note that time to manufacture of a monovalent pandemic vaccine may be shorter than for the annual trivalent vaccine).

There are several steps in this process that must proceed in a timely manner or bottlenecks could occur. Manufacturers must ensure that the supply of embryonated eggs is adequate for production needs. Although in most years, old flocks are destroyed in summer months to make way for the establishment of new flocks, it has been possible to delay the flock cull in order to extend the egg harvest and inoculation process and produce additional doses of vaccine, when needed. In addition, because manufacturers may be producing influenza vaccine for the southern hemisphere, additional flocks may be acquired to accommodate year-round influenza vaccine production. The ability to rapidly produce vaccine against a pandemic strain may be limited by the availability of eggs. The available egg supply may have already been used to prepare vaccine for the annual vaccine production or may be unexpectedly affected by weather or infections. In addition, many wild-type influenza strains grow poorly in eggs. Therefore, time must be spent to develop high growth reassortants that increase the yield of vaccine virus per egg over the wild type virus. Because of the increased virulence of some influenza strains, especially those of avian origin, initial modification of the virus may require facilities with high levels of laboratory safety (Biosafety Level 3), which are not widely available, and select agent regulations may restrict shipment of such viruses between countries and laboratories. Reagents needed to evaluate candidate vaccines take time to produce and could delay the process but generally are produced concurrent with manufacturing activities leading to the formulation of the final vaccine. Finally, industrial capacity to produce vaccine and to fill and label vials or syringes may not be sufficient to meet national needs during a pandemic.

Several enhancements can be made to the vaccine development infrastructure during the inter-pandemic period that will lead to more rapid availability of vaccine against a novel influenza strain during a pandemic. *(See Annex5: Vaccine Development and Production)*

- Libraries of reassortant influenza viruses that would be suitable as reference strains for vaccine production can be prepared from avian influenza parent strains – including those identified as causing human infection – and reagents to assess their immunogenicity developed. The availability of these materials may shorten the time for vaccine development and evaluation depending on the similarity between a strain in this library and a pandemic strain.

- New molecular techniques such as “reverse genetics” can be used to more reliably, and possibly more rapidly, produce high-growth reassortant viruses.

- Programs are underway to assure the year-round availability of eggs for vaccine production and to promote the development, U.S. licensure, and production of influenza vaccines using cell culture technology. The latter will diversify the manufacturing base, reduce the vulnerabilities associated with egg-based production, increase the amount of vaccine produced, and lead to generation of surge capacity for production in response to extraordinary needs.

- Evaluation and licensure of an influenza vaccine that includes an adjuvant – a substance that improves the immune response and is a component of many current commercially available vaccines – or alternative delivery strategies that may increase the number of people who could be protected by available vaccine by allowing manufacturers to include less influenza virus antigen in each vaccine dose.

B. Vaccine Supply

Currently, three manufacturers produce licensed influenza vaccine for the U.S. market. Aventis-Pasteur supplies the majority of U.S. doses; Chiron (formerly Powderject) supplies vaccine produced in the U.K; and MedImmune, in June 2003, received FDA approval for a live-attenuated influenza vaccine administered intranasally to healthy persons 5 to 49 years of age; part of the vaccine production process, including filling and labeling vials occurs in the U.S.

Despite public health recommendations for annual influenza vaccination that include over 185 million persons less than half of all Americans who should receive the vaccine are immunized. During the 2003-2004 influenza nearly the entire vaccine supply of over 87 million doses was used. For 2004-2005 the manufacturers are planning on producing approximately 100 million doses.

Because a pandemic influenza vaccine would likely include only a single virus strain (monovalent) rather than the three strains included in the annual influenza vaccine (trivalent), the number of doses available would be expected to be triple that produced annually. This assumes that the antigen necessary to produce a sufficient immune response (15 micrograms) remains the same as the annual vaccine. At 2003-2004 production levels this translates to 270-300 million monovalent vaccine doses – enough to vaccinate the entire U.S. population.

However, this amount of vaccine may still be insufficient since a two-dose vaccine schedule (a priming dose followed by a booster dose) may be needed for an inactivated vaccine in a pandemic because the population will be immunologically naïve. Whether a live attenuated influenza vaccine approach to a pandemic vaccine would require one or two doses has not been evaluated.

Implementing strategies to increase annual vaccine demand and use during the inter-pandemic period will encourage manufacturers to respond with increased supply, thus increasing production capacity which will contribute directly to pandemic preparedness. In addition, clinical studies that evaluated the immunogenicity of influenza vaccine containing a reduced antigen dose suggest that lower levels of antigen might be sufficiently immunogenic

for some groups of people. By including less antigen in each vaccine dose, existing production may be able to make more doses and additional people could be protected. The use of an adjuvant or an alternative approach to vaccine administration may also increase immunogenicity and permit a reduced antigen dose. Licensed Influenza vaccines do not currently include an adjuvant; therefore, including an adjuvant in the vaccine's formulation could complicate the licensure process and delay vaccine availability in the setting of a pandemic.

Vaccine supply during a pandemic

Initially, when a pandemic influenza strain first infects people in the U.S., there will likely be no or very limited amounts of vaccine available. This period could last for up to six months depending on when the pandemic strain is detected and how rapidly it spreads to the U.S. and on how rapidly vaccine development and production proceed. Previous 20th century pandemics began in the U.S. within weeks of the initial disease outbreak and/or virus identification. In the absence of vaccine, primary response strategies include interventions to slow the spread of infection, antiviral therapy and prophylaxis, and quality medical care. After vaccine becomes available, for some period, vaccine availability will be far less than national demand, requiring prioritized usage of vaccine to optimally decrease morbidity and mortality. As vaccine production increases and with some of the population already having been vaccinated in the initial targeted program, supply will become adequate to meet demand. This may lead to changes in strategies for vaccine distribution and administration because there may no longer be a need to limit vaccine only to those in designated priority groups. Tracking vaccine production, delivery, and use will be important to guide appropriate vaccination strategies and use.

C. Vaccine Safety

Carefully monitoring for vaccine safety is important to assure that the benefits of vaccination exceed the risks and, to assess the etiology of adverse events that occur following vaccination, and to maintain confidence in the vaccination program. Influenza vaccine – like all other vaccines – occasionally causes local reactions at the site of injection and may cause mild systemic symptoms such as headache or fever. The association of swine influenza vaccine (1976) with Guillain-Barre syndrome (GBS), a condition marked by progressive muscle paralysis which may result in a need for mechanical ventilation, was an unusual but highly prominent event.

In the U.S., routine national surveillance for adverse events following immunization is conducted through the Vaccine Adverse Event Reporting System (VAERS), which is managed jointly by CDC and FDA. The vaccine safety monitoring infrastructure also includes a network of Clinical Immunization Safety Assessment (CISA) centers where events occurring after vaccination can be thoroughly investigated; and the Vaccine Safety Datalink which consists of vaccination and medical records from several large managed care organizations that can be analyzed to assess whether specific health events are associated with vaccination. During a pandemic, these systems would provide ongoing and real-time assessments of adverse events. In addition, they would be supplemented by additional safety studies, such as clinical studies of specific adverse events, and active surveillance for all

events occurring in specific segments of the population. These safety surveillance infrastructures and additional studies were used successfully in the intensive monitoring of the recent smallpox vaccination program.

D. Vaccine Delivery and Administration

Since all or most of the population will be susceptible to infection with the pandemic strain, vaccination of the entire U.S. population may be recommended. Once vaccine becomes available, supply will be limited.

Several options exist regarding purchase and distribution of pandemic influenza vaccine. Currently, approximately 90 million Americans are vaccinated each year. Increasing the proportion of public sector purchase for a pandemic may improve the ability to target priority groups and to reach those who may be underserved by the current system. Related to, but separate from, the approach to purchasing vaccine is the decision regarding how vaccine will be administered. For example, private sector groups under contract to state and local health departments with experience in vaccine administration may serve an important role. Systems to monitor vaccine delivery will need to be developed in order to assess whether available doses are being delivered to targeted groups; whether racial/ethnic disparities exist in coverage; and whether two doses are being given if a multi-dose schedule is needed for protection. Expansion of existing State-based immunization registries to include influenza vaccination or development of a specific pandemic vaccine monitoring system that builds on systems being developed to respond to bioterrorism are among the approaches that could be considered. Epidemiological studies will be implemented to assess vaccine effectiveness in preventing disease and complications and vaccine safety. Annual studies to rapidly assess vaccine effectiveness against influenza should be implemented in the inter-pandemic period to build the capacity to collect these data during a pandemic.

XII. Antiviral Agents

The targeted use of antiviral agents could, as part of a response strategy to susceptible strains, decrease the health impact of an influenza pandemic. Use of antiviral prophylaxis has been up to 70% to 90% effective in preventing symptomatic influenza infection caused by susceptible strains, if prophylaxis is begun before exposure to influenza. Also, treatment with one class of agents, neuraminidase inhibitors, has been shown to decrease severe complications such as pneumonia and bronchitis and to reduce hospitalizations. These interventions may be particularly important before vaccine is available and for those in whom vaccine may be medically contraindicated. Limitations of prophylaxis and therapy include drug availability, logistics of delivery to priority groups, side effects, potential development of resistance, and cost.

The adamantine class of antiviral drugs, amantadine and rimantadine, are more widely available and less expensive than the neuraminidase inhibitors. However, they are more likely to cause side effects and induce antiviral resistance, particularly used for treatment. Therefore, their use should probably be reserved for pre-exposure prophylaxis in selected populations. Given the limited supply, prophylaxis should be limited to those who are

supporting the goal of maintaining quality public safety, providing critical response capacity, and other essential public health services. Target groups, to be defined by State health departments, might include front-line health care workers, public health personnel, those who provide essential community safety services, workers culling influenza-infected animals, and those involved in influenza vaccine manufacture who are at greatest risk of exposure.

Oseltamavir and zanamivir, both neuraminidase inhibitors, are newer and more expensive agents. A combined analysis of data from 10 randomized, placebo-controlled trials using oseltamivir showed a 30% to 50% decrease in pneumonia and bronchitis and in hospitalization, although overall study size was limited, particularly of persons at highest risk of complications. Neuraminidase inhibitors have been associated with fewer side effects than the adamantanes and, to date, appear less likely to induce antiviral resistance. The major issues with the neuraminidase inhibitors are their relatively high cost and limited availability. Because of limited demand during annual influenza epidemics, zanamivir supplies in the U.S. are extremely limited *(See Annex 7: Antiviral Drugs and Strategies)*

In 2003, CDC included oseltamivir in the SNS. Since the supply may be limited, stocks available in a pandemic should be targeted to priority groups with well-defined guidelines for prophylaxis and therapy. Since much of the available supply, under any of the proposed options, will remain in the private sector, collaboration with health care organizations and providers is crucial to assure that these drugs are used effectively. Coordination and education also are important because use of amantadine and rimantadine for therapy may induce high rates of antiviral resistance, diminishing their usefulness. State and local health departments will need to address the logistical issues of getting therapy to end-users who are in priority groups and who are within 48 hours of the onset of symptoms - the time in which the impact of treatment has been documented. Research and development leading to licensure and manufacture of new antiviral drugs may yield long term benefits in agents that are more effective, can be used against resistant strains, increase overall supply, and may have an extended antiviral spectrum which would make them a more versatile component of the SNS.

XIII. International Coordination

Influenza disease, surveillance, and response are global efforts that require a coordinated role by governments around the world and the WHO. U.S. agencies participate in global surveillance, vaccine strain selection, and outbreak investigation. CDC is one of four worldwide WHO Collaborating Centers for Influenza. Multinational vaccine manufacturers dominate influenza vaccine development and production, and antiviral drugs for influenza are produced by a handful of manufacturers in the U.S. and other countries. When a pandemic occurs, the U.S. is unlikely to experience disease in isolation, but rather along with other countries. As demonstrated by the response to the SARS epidemic, international coordination and collaboration in an influenza pandemic are both possible and essential to decrease the global and U.S. burdens of disease. Collaboration on international surveillance will lead to earlier detection of a pandemic strain, facilitating vaccine development. Investigations of initial outbreaks, which are likely to occur first outside of the U.S., will

contribute critical early information on the epidemiological characteristics of the novel influenza virus and its transmission and also offer the potential to limit or impede the spread of the epidemic. Discussions and collaborative planning with international partners in different forums have been initiated to address issues such as sharing vaccine or antiviral supply, travel advisories or restrictions, or quarantine)

SECTION THREE: PANDEMIC INFLUENZA RESPONSE

Federal public health and medical assistance during major emergencies and disasters is provided under Emergency Support Function (ESF) #8 of the National Response Plan (NRP) or independently by HHS. This assistance can be activated by a Presidential disaster declaration, by declaration of a public health emergency through the independent authority of the Secretary of HHS, or at the request of another Federal Department or Agency.

When incident demands severely challenge or exceed the response capability of affected State, Tribal and local governments (e.g., pandemic influenza), Federal resources may be called on to provide additional capacity and capabilities. If this occurs, Federal agencies and resources function in support of the State, Tribal and jurisdictional response efforts. Federal public health and medical assistance may come in the form of medical materiel, personnel, or technical assistance. These resources may provide response capabilities for the triage, treatment, and transportation of victims, infection control, mental health counseling, and other emergency response needs.

The NRP establishes the structure and process for the systematic, coordinated, and effective delivery of Federal assistance to augment State, Tribal and jurisdictional response capabilities. It describes the types of Federal resources that are available to mitigate (prevent), prepare for, respond to, and recover from major emergencies and disasters, and it outlines a methodology for mobilizing and integrating Federal assistance.

The types of direct Federal assistance that States and Tribes may need, as well as the operations support required to sustain a Federal response (e.g., transportation, communications) are organized under Emergency Support Functions (ESFs). Each ESF is coordinated by a Primary Agency designated on the basis of its authorities, resources, and capabilities in the particular functional area. Federal public health and medical assistance is provided under ESF #8 and is coordinated by HHS. As the Primary Agency for ESF #8, HHS directs the provision of Federal public health and medical resources to fulfill the requirements identified by the affected State(s), Tribe(s) and jurisdictional authorities.

Additionally, HHS has developed an internal Concept of Operations Plan (CONOPS) that provides a framework for HHS's management of public health and medical emergencies. This plan is complementary to the NRP and covers all the preparedness and response activities, whether resulting from a Stafford Act declaration, HHS's independent authority, or at the request of another Department or Agency.

SECTION FOUR SUMMARY KEY ACTIONS BY PANDEMIC PHASE

Pandemic influenza response activities differ by pandemic phase. In addition, activities may differ depending on where disease is occurring during the early phases of a pandemic – either in the U.S. or in other countries – and by the characteristics of the influenza virus, particularly the efficiency with which it spreads between people. In addition, the severity of illness varied markedly between 20th century pandemics, with mortality about 10-fold higher in 1918 compared with 1957 and 1968; thus response strategies and needs may differ based on the severity of the next pandemic. Therefore, the following summary should primarily serve as a conceptual reference or guideline to action steps. Because an influenza pandemic is likely to unfold in unanticipated ways, decision-makers must continually reassess recommendations for response activities. Preparedness activities, undertaken during the inter-pandemic period (Phase 0, level 0) are described in the previous section of this Plan. The tables describe incremental response activities that will be implemented by phase and level. Additional guidance on international activities that will be overseen by the WHO and a summary report of the April 2004 meeting: "WHO consultation on priority public health interventions before and during an influenza pandemic" can be found on the following websites:
http://www.who.int/emc-documents/influenza/docs/index.htm/sec3.htm
http://www.who.int/csr/disease/avian_influenza/consultation/en/

Phase 0, level 1: Identification of a novel influenza virus in a person (*Novel Virus Alert*)

Novel virus alerts occurred in 1997, 1999, 2003, and 2004 with avian influenza viruses causing human disease, along with widespread infections among domestic poultry. Human cases occurred in Asia and in Europe. Avian influenza H5N1 outbreaks in Hong Kong in 1997 and in several Asian countries in 2003-2004 were caused by highly pathogenic strains and the case-fatality rate among hospitalized persons was substantially greater than seen in annual influenza epidemics. However, there was no or very limited transmission of these viruses between people. No U.S. cases caused by these strains have been identified.

At this pandemic phase/level, highest priority actions are enhanced U.S. and international surveillance to identify cases and monitor the spread of disease, epidemiological investigation, collaboration with international partners to control focal disease outbreaks, vaccine development for the novel influenza virus strain, and continued planning/preparedness.

Table 6. Activities during Phase 0, level 1
N – National, S-State, L-Local

Phase 0 Inter-Pandemic Phase *Level 1* – Novel Influenza Strain in Human		
Action		**Responsible OPDIV/STAFFDIV**
Planning and Coordination	Assess preparedness status and identify immediate actions needed to fill gaps (N/S/L)	NVPO/ASH/ASPHEP

Phase 0 Inter-Pandemic Phase *Level 1* – Novel Influenza Strain in Human		
Action		**Responsible OPDIV/STAFFDIV**
	Communicate with ASPHEP to initiate transition from preparedness to response (N)	NVPO/ASH,
Surveillance, Investigation, and Containment	Prepare reagents for identification of the new influenza strain (N)	CDC, NIH, FDA
	Assist in international influenza outbreak investigations (N)	CDC
	Implement plans to enhance national surveillance (N/S/L)	CDC
	Prepare strategies to prevent spread of infection to the U.S. from affected areas (e.g., travel advisories or precautions, assessment of travelers returning from affected areas, etc.) (N/S/L)	CDC
	Assess pathogenicity, antiviral susceptibility and other characteristics of the novel influenza strain (N)	NIH, CDC, FDA
Vaccines and Antivirals	Develop vaccine reference strain and reagents for possible vaccine production and evaluation (N)	NIH, FDA, CDC
	Communicate with vaccine manufacturers to initiate production of investigational vaccine lots (N)	NVPO, ASPHEP
	Review vaccine and antiviral use strategies	ASPHEP, NVPO, CDC
Health Care and Emergency Response	Assess capacity of health care and emergency response systems to meet needs in a pandemic (N/S/L)	ASPHEP
Communications	Communicate with state and local health departments through EPI-X and the Health Alert Network (N)	CDC
	Inform stakeholders and media of the novel virus alert (N/S/L)	CDC

Phase 0, level 2: Confirmation that the novel influenza virus has infected two or more people, but the ability of the virus to spread rapidly person-to-person and cause multiple outbreaks of disease leading to epidemics remains questionable

Each of the avian influenza outbreaks, described above, met criteria for this phase/level. Response activities and the importance of continued preparedness and planning would be

similar to those at level 1. At this level, coordination of response activities would shift from the ASH to the ASPHEP.

Table 7. Activities during Phase 0, level 2

Phase 0 Inter-Pandemic Phase *Level 2* - Human Infection Confirmed		
Action		**Responsible OPDIV/STAFFDIV**
Planning and Coordination	Assess preparedness status and identify actions needed to fill gaps (N/S/L)	NVPO, ASPHEP
	Implement transition from preparedness, coordinated by the ASH, to response coordinated by ASPHEP (N)	OASH, ASPHEP
	Establish coordination of response activities through the Secretary's Operations Center (N)	ASPHEP
	Notify government officials and legislators of pandemic status and potential need for additional resources (N/S/L)	HHS, ASL
Surveillance, Investigation, and Containment	Distribute reagents to state public health laboratories and WHO National Influenza Centers for detection of the new strain (N)	CDC
	Assist in international influenza outbreak investigations and characterize disease epidemiology (N)	CDC
	Implement plans to enhance national surveillance and to identify suspect cases and/or introduction of a novel virus into the U.S. (N)	CDC
Vaccines and Antivirals	Communicate with vaccine manufacturers and distribute vaccine reference strains (N)	NVPO, FDA, CDC, NIH
	Develop and test investigational lots of vaccine to the new strain (N)	NIH
	Assess emergency use of investigational drugs (N)	FDA
	Present data on novel influenza disease, vaccine development, and proposed vaccination strategies to federal advisory committees (NVAC, AACV, ACIP, VRBPAC) (N)	NVPO, CDC, FDA, NIH
Health Care and Emergency Response	Assess capacity of health care and emergency response systems to meet needs in a pandemic (N/S/L)	ASPHEP

Phase 0 Inter-Pandemic Phase *Level 2* - Human Infection Confirmed		
Action		**Responsible OPDIV/STAFFDIV**
Communications	Update state and local health departments, other stakeholders and the media (N/S/L)	CDC
	Enhance clinician awareness of the potential for a pandemic and the importance of diagnosis and viral identification for persons with influenza like illness, especially from potentially affected areas (N/S/L)	CDC

Phase 0, level 3: Confirmation of person-to-person spread in the general population with at least one outbreak lasting for more than 2 weeks in one country (*Pandemic Alert*)

In a pandemic alert the most critical issue in assessing the potential for a pandemic is determining the efficiency with which the influenza strain is transmitted between people. Response activities undertaken during this phase/level are likely to be different depending on whether the focus for disease outbreak(s) is in the U.S. or in another country. If the outbreak is outside the U.S., important activities could include participating in the international investigation of the disease epidemiology; contributing personnel and materials (e.g., personal protection equipment, vaccine, or antiviral drugs) to support control activities implemented by affected countries and international organizations; and enhancing surveillance and implementing control activities at points-of-entry into the U.S. If the disease outbreak that defines this phase/level occurs in the U.S., implementing control strategies; enhancing surveillance to detect whether disease has spread; and accelerating vaccine development and assuring antiviral supply become the highest priorities.

Table 8. Activities during Phase 0, level 3

Phase 0 Inter-Pandemic Phase *Level 3* – Pandemic Alert - Person-to-Person Transmission Confirmed		
Action		**Responsible OPDIV/STAFFDIV**
Planning and Coordination	Declaration of a pandemic alert (N)	ASPHEP
	Update government officials and legislators on pandemic status and need for additional resources (N/S/L)	ASPHEP
	Initiate daily briefings with SCC/DEOCs (N)	ASPHEP
	Coordinate information sharing with other federal agencies including DHS, Department of State, DOD, and others (N)	ASPHEP
	Begin negotiations with manufacturers for pandemic vaccine production and purchase (N)	ASPHEP
	Assess legal authorities for pandemic response activities and limitations (N/S/L)	OGC,ASPHEP
Surveillance, Investigation, and Containment	Collaborate with international organizations to assess epidemiology of disease outbreaks and efficiency of person-to-person transmission of the pandemic strain (N)	CDC, ASPHEP
	Contribute personnel and materials to support international outbreak containment activities (N)	CDC, ASPHEP
	Implement travel advisories, precautions, or restrictions, as appropriate (N)	CDC, ASPHEP
	If the disease outbreak is in the U.S., implement intensive control measures including isolation and quarantine, antiviral therapy and prophylaxis, vaccination (if available), and control of potential reservoirs among domestic animals	CDC, ASPHEP
	Implement plans to enhance national surveillance and to identify suspect cases and/or introduction of a novel virus into the U.S. (N/S/L)	CDC, ASPHEP
	Assure availability of diagnostic reagents for pandemic influenza strain at state and local public health laboratories (N)	CDC
	Provide reference laboratory support to test clinical specimens for influenza and identify novel strain (N)	CDC
	Develop and evaluate diagnostic tests for the novel strain	FDA, CDC, NIH

Phase 0 Inter-Pandemic Phase *Level 3* – Pandemic Alert - Person-to-Person Transmission Confirmed		
Action		**Responsible OPDIV/STAFFDIV**
	Assess antiviral resistance of novel strain (N)	CDC
	Add pandemic influenza to the list of diseases for which quarantine can be implemented (N/S/L)	Secretary HHS
	Assist states, as needed, in investigating potential cases or outbreaks of influenza	CDC
Vaccines and Antivirals	Alert manufacturers to possible production and purchase of vaccine to the new strain (N)	ASPHEP, NVPO
	Review and revise, as needed, strategies for antiviral drug use and vaccination (N)	CDC, NVPO
	Conduct and evaluate clinical studies of vaccines for the new strain (N)	NIH, FDA
	Assess candidate vaccines for licensure (N)	FDA
	Assess requests for emergency use of investigational drugs (N)	FDA
	Assess antiviral availability in a stockpile or in the market (N/S/L)	CDC, FDA ASPHEP
	Review and revise, as needed, plans for distributing and administering antivirals and vaccines (S/L)	ASPHEP, CDC
Health Care and Emergency Response	Review and revise, as needed, plans for health care delivery and community support (N/S/L)	HHS, HRSA
	Assess availability of personnel, supplies and materials for infection control and clinical care of infected patients should a pandemic occur (N/S/L)	HRSA
	Disseminate infection control guidelines to hospitals, long term care facilities, and medical care providers (N/S/L)	HRSA, CDC
Communications	Update stakeholders and the media through regular briefings (N/S/L)	ASPA, CDC
	Educate health care providers through satellite broadcasts, webcasts, and other communications channels (N/S/L)	ASPA, CDC
	Enhance access to information through websites and other communications channels (N/S/L)	ASPA, CDC

Phase 1: Confirmation that the novel influenza virus is causing several outbreaks in one country and has spread to other countries, with consistent disease patterns indicating serious morbidity and mortality is likely in at least one segment of the population

As in the previous phase/level, assessment of the efficiency of person-to-person spread of the novel influenza strain is important to evaluate the potential for a pandemic. Transmission dynamics of influenza may change as strains reassort making ongoing monitoring important. Understanding the spread of infection also is critical to development of appropriate containment strategies. Other key factors to assess include the severity of influenza caused by the novel strain, the populations and age groups that are most affected and most likely to experience severe morbidity and mortality, and antiviral susceptibilities. As in the previous level/phase, the intensity and type of response activities will differ based on whether disease is occurring in the U.S.

Table 9. Activities during Phase 1

Phase 1 – Confirmation of Onset of Pandemic		
Action		**Responsible OPDIV/STAFFDIV**
Planning and Coordination	Declaration of a pandemic in the U.S.(N)	Secretary HHS
	Activate the inter-departmental working group (N)	ASPHEP
	Review and approve plans and priorities for vaccination and antiviral drug use (N)	ASPHEP
	Obtain funding, as needed, to support vaccine purchase and other costs associated with pandemic response. Consult with DHS regarding declaration of an emergency or disaster under the Stafford Act (N)	ASPHEP
	Negotiate production and purchase of pandemic vaccine from manufacturers	ASPHEP
	Mobilize Commissioned Corps Readiness Force to contribute to pandemic response (N)	OSG
	Coordinate with international organizations and governments (N)	OGA
Surveillance, Investigation, and Containment	Continue collaboration with international organizations investigate disease outbreaks, assess efficiency of person-to-person transmission, and control the spread of the pandemic strain (N)	ASPHEP,CDC
	Assess and fill gaps in U.S. sentinel surveillance and reporting sources for viral isolates, morbidity and mortality (N/S/L)	CDC
	Assess epidemiology of influenza outbreaks in the U.S. and globally and identify risk groups for infection and complications (N)	ASPHEP, CDC

Phase 1 – Confirmation of Onset of Pandemic		
Action		**Responsible OPDIV/STAFFDIV**
	Reassess containment strategies such as isolation, quarantine, travel restrictions, etc. (N/S/L)	ASPHEP,CDC
	Provide advice and support to outbreak investigations and containment activities	CDC, CCRF/OSG
Vaccines and Antivirals	Implement distribution of the antiviral stockpile; purchase additional antiviral drugs, as available, for public sector use (N/S/L)	ASPHEP, CDC,
	Begin distribution of pandemic vaccine, if available, and immunization of priority groups (N/S/L)	CDC
	Assure availability of resources and personnel for vaccine distribution and administration (N/S/L)	ASPHEP, CDC, HRSA
	Initiate enhanced monitoring of vaccine and antiviral drug safety (N/S/L)	CDC
	Monitor vaccination coverage (N/S/L)	CDC
Health Care and Emergency Response	Activate state and local plans to coordinate health care delivery and community response (S/L)	ASPHEP, HRSA,
Communications	Expand regular briefings of stakeholders and the media (N/S/L)	OPA, CDC
	Activate pandemic communications plan (N/S/L)	OPA, CDC

Phase 2: Outbreaks and epidemics are occurring in multiple countries and spreading across the world

At this phase, the pandemic will have spread to the U.S. and communities will begin experiencing outbreaks and epidemic disease. It is assumed that, at this point, the pandemic strain will be well transmitted between people, including from infected persons to others even before the onset of clinical symptoms, as occurs with annual influenza disease.

During outbreaks, community health care resources, both human and material, are likely to be severely stressed or overwhelmed, depending on the effectiveness of preparedness activities and development of surge capacity. It is likely to be difficult to shift resources within or between states because multiple areas will be affected simultaneously, and areas not yet affected will anticipate the spread of disease.

Because of their limited availability, it is likely that there will be increased demand for antiviral drugs in both the public and private sectors. When vaccine becomes available it will be in short supply relative to demand. The limited availability of preventive and therapeutic

interventions, along with possible limits to access to clinical care could lead to public concern and substantial disruption of society and commerce.

Critical response issues at this phase include the ability to maintain health care within communities; the ability to effectively communicate and implement priorities for antiviral drug and vaccine use; the ability to distribute and administer vaccine effectively and equitably; and the ability to evaluate and modify control strategies based on epidemiological investigation and surveillance data

Table 10. Activities during Phase 2

Phase 2 – Regional and Multi-Regional Epidemics		
Action		**Responsible OPDIV/STAFFDIV**
Planning and Coordination	Activate the Federal Response Plan based on the extent of the pandemic and its impact; implement ESF #8 (N), coordinating federal response activities under HHS	ASPHEP
	Coordinate pandemic response activities through the SCC (N)	ASPHEP
	Assess legal barriers related to effective implementation of containment, prevention, and treatment strategies	OGC
	Communicate and coordinate pandemic response activities with international organizations and other governments (N)	OGA
Surveillance, Investigation, and Containment	Implement strategies to control the spread of the pandemic (such as quarantine, closing schools, and limiting public activities) (N/S/L)	CDC, OGC
	Characterize epidemiology and evaluate response and control strategies (N/S/L)	CDC
	Continue to monitor disease, health outcomes, vaccination coverage and effectiveness, antiviral resistance, and vaccine safety (N/S/L)	CDC
	Provide support to state and local health departments for investigation of disease outbreaks in institutions and other special settings	CDC, OSG
Vaccines and Antivirals	Distribute antiviral drug from the SNS for prophylaxis and therapy based on accepted strategies (N/S/L)	CDC, ASPHEP
	Distribute federally purchased vaccine to state and local health departments for vaccination of priority groups based on accepted strategies (N/S/L)	CDC

Phase 2 – Regional and Multi-Regional Epidemics		
Action		**Responsible OPDIV/STAFFDIV**
	Provide guidance for use of antiviral drugs and vaccine in the private health care sector (N)	CDC, FDA
	As available and needed, review investigational new drug applications for experimental vaccines and antiviral drugs that are proposed to be studied/used under IND (N)	FDA
	Re-evaluate vaccine dose and schedule based on effectiveness data and clinical studies to assure optimal dose and schedule	CDC, FDA, NIH
Health Care and Emergency Response	As needed, establish inpatient medical care in non-traditional facilities to provide hospital bed surge capacity (N/S/L)	HRSA
	Assess quality of health care and emergency services (N/S/L)	HRSA
Communications	Continue implementation of communications plan (N/S/L)	OPA, CDC
	Communicate prevention and control strategies to health departments, health care providers, the media, and the public, including rationales for vaccine and antiviral priorities	OPA, CDC
	Distribute educational materials and guidelines to health care providers and the public (N/S/L)	OPA, CDC

Phase 3: End of the first wave of the pandemic

The first pandemic wave is likely to taper off as environmental conditions change. This hiatus in pandemic disease may allow recovery to occur in communities and the health care system. At the same time, pandemic vaccine production will continue and vaccine be administered to decrease susceptibility for the next pandemic wave. Supplies and pharmaceutical stockpiles should be replenished. Also important will be a review of the effectiveness of control strategies and modification of these recommendations, if needed.

Table 11. Activities during Phase 3

Phase 3 – End of the First Wave of Pandemic		
Action		**Responsible OPDIV/STAFFDIV**
Planning and Coordination	Assess coordination during prior pandemic phases and revise plans, as needed (N/S/L)	ASPHEP, NVPO
	Implement expert review of pandemic response activities (N)	NVPO

Phase 3 – End of the First Wave of Pandemic		
Action		**Responsible OPDIV/STAFFDIV**
	Determine additional resources and authorities that may be needed for subsequent pandemic waves (N/S/L)	ASPHEP, OGC
Surveillance, Investigation, and Containment	Assess surveillance during prior pandemic previous phases and revise plans, as needed (N/S/L)	CDC
	Assess vaccine efficacy, safety and impact during the pandemic (N/S/L)	CDC/FDA
	Assess vaccine coverage and determine number of persons who remain unprotected (N/S/L)	CDC
	Assess antiviral effectiveness, safety, and cost-effectiveness (N)	CDC/FDA
	Continue enhanced surveillance to detect further pandemic waves (N/S/L)	CDC
Vaccines and Antivirals	Assess vaccine and antiviral distribution and use during prior pandemic phases and revise plans, as needed (N/S/L)	CDC, NVPO
	Determine potential vaccine formulation changes to improve efficacy or supply (N)	NIH, FDA
	Continue administering vaccine to persons not previously protected (N/S/L)	CDC
	Encourage manufacturers to expand production of pandemic vaccine; and expand acquisition of antivirals, as feasible (N/S/L)	ASPHEP
Health Care and Emergency Response	Assess effectiveness of health care and service delivery during prior pandemic phases and revise plans, as needed (N/S/L)	ASPHEP, HRSA
Communications	Assess effectiveness of communications during prior pandemic phases and revise plans, as needed (N/S/L)	ASPA CDC
	Communicate with health care providers, the media, and the public about the likely next pandemic wave	ASPA, CDC

Phase 4: Confirmation of a second or later wave caused by the same novel virus strain

Based on past experience, a second wave of outbreaks may occur within 3-9 months of the initial epidemic. Subsequent waves are likely to be less severe because a large portion of the population will be less susceptible having had disease or having been vaccinated during the previous season. Vaccine supply is likely to be greater given ongoing production and higher

yields as manufacturers optimize methods. This greater supply may lead to different strategies for vaccination, possibly including greater reliance on delivery by the private sector as occurs during annual influenza epidemics. Specific response activities implemented during Phase 4 will be similar to those in Phases 1 and 2.

Phase 5: Confirmation that the pandemic has ended

Decreased susceptibility to the pandemic virus and continued changes in the influenza virus result in the end of the pandemic and return to the inter-pandemic phase. An official declaration will be made by the WHO. As in Phase 3, key activities at this phase include review of the pandemic response and incorporation of lessons learned into the pandemic influenza preparedness and response plan to guide planning activities for the next pandemic.

Abbreviations and Acronyms

ACIP.....Advisory Committee on Immunization Practices, CDC
ASH .....Assistant Secretary for Health
ASPA/HHS.....Department of Health and Human Services, Office of the Assistant Secretary for Public Affairs
ASPHEP/HHS ..... Department of Health and Human Services, Office of the Assistant Secretary for Public Health Emergency Preparedness
ASTHO.....Association of State and Territorial Health Officials
CDC.....Centers for Disease Control and Prevention
FDA .....Food and Drug Administration
FEMA.....Federal Emergency Management Administration
HA.....hemagglutinin (a protein on the surface of the influenza virus)
HHS .....Department of Health and Human Services
HRSA .....Health Resources and Services Administration
ICS.....Incident Command System
ILI.....influenza-like-illness
IOM .....Institute of Medicine
NA.....neuraminidase (a protein on the surface of the influenza virus)
NI .....neuraminidase inhibitors
NIC .....National Influenza Center
NIH .....National Institutes of Health
NVPO/HHS.....Department of Health and Human Services, National Vaccine Program Office
OPHEP/HHS .....Department of Health and Human Services, Office of Public Health Emergency Preparedness
OGA/HHS.....Department of Health and Human Services, Office of Global Affairs (HHS)
PHS.....Public Health Service
SARS .....Severe Acute Respiratory Syndrome
VRBPAC.....Vaccine and Related Biological Products Advisory Committee, Food and Drug Administration
WHO .....World Health Organization

Internet Resources on Pandemic Influenza

The links listed below were active as of May 2004. However, because Web sites can change without notice, no site can be guaranteed active or accurate indefinitely.

U.S. Federal Departments

Department of Defense - http://www.defenselink.mil/
Department of Education - http://www.ed.gov/
Department of Energy - http://www.energy.gov/engine/content.do
Department of Health and Human Services - http://www.hhs.gov/
National Vaccine Program Office http://www.dhhs.gov/nvpo
Office of the Assistant Secretary for Public Health Emergency Preparedness (ASPHEP) – http://hhs.gov/asphep
Department of Homeland Security - http://www.dhs.gov/dhspublic/index.jsp
National Disaster Medical System- http://ndms.dhhs.gov/index.html
Federal Emergency Management Agency (FEMA) - http://www.fema.gov/
Department of Justice - http://www.usdoj.gov/
Department of State - http://www.state.gov/
Department of Transportation - http://www.dot.gov/
Department of Veterans Affairs - http://www.va.gov/

U.S. Government Agencies

CDC – www.cdc.gov
Food and Drug Administration (FDA) - http://www.fda.gov/
HRSA - http://www.hrsa.gov/
National Institute of Health (NIH) - http://www.nih.gov/
NIH, National Institute of Allergy and Infectious Diseases - http://www.niaid.nih.gov/

Organizations

Association of State and Territorial Health Officials (ASTHO) - http://www.astho.org/
Infectious Disease Society of America www.idsociety.org
National Foundation for Infectious Diseases www.nfid.org
Institute of Medicine (IOM) - http://www.iom.edu/
World Health Organization (WHO) – www.who.org

Influenza Background Information

CDC - Presents information on the symptoms, treatment, and complications of the disease, prevention and control, the types of influenza viruses, questions and answers on symptoms, vaccinations and myths. http://www.cdc.gov/flu/index.htm

National Vaccine Program Office – Presents a historical overview of pandemics that occurred throughout the past century (Spanish Flu, Asian Flu, Hong Kong Flu), and three influenza scares (Swine Flu, Russian Flu, and Avian Flu). www.dhhs.gov/nvpo/pandemic

World Health Organization – Defines an influenza pandemic, explains how a new influenza virus can cause a pandemic, presents the consequences of an influenza pandemic,

explains the global surveillance systems, and provides links to other pandemic plans from other nations. http://www.who.int/csr/disease/influenza/pandemic/en/

Additional Response Resources

HRSA Bioterrorism and Emergency Preparedness Grants and Cooperative Agreements – Provides information about HRSA programs for bioterrorism and emergency preparedness activities available for state and local jurisdictions. www.hrsa.gov/bioterrorism.htm

The Public Health Preparedness and Response Capacity Inventory - Provides a resource for State and local health departments undertaking comprehensive assessments of their preparedness to respond to bioterrorism, outbreaks of infectious disease or other public health threats and emergencies. http://www.phppo.cdc.gov/od/inventory/index.asp

CDC Cooperative Agreements on Public Health Preparedness – Provide funding to state and local public health jurisdictions for preparedness for and response to bioterrorism, other outbreaks of infectious diseases, and other public health threats and emergencies. http://www.bt.cdc.gov/planning/continuationguidance/index.asp

Epidemic Information Exchange – Provides a secure, web-based communications network for information exchange among CDC, state and local health departments, and other public health professionals. http://www.cdc.gov/mmwr/epix/epix.html

Centers for Public Health Preparedness – Is a national system for competency-based training tool for the public health workforce. http://www.cdc.gov/mmwr/epix/epix.html

National Pharmaceutical Stockpile – Provides information on the availability and rapid deployment of life-saving pharmaceuticals, antidotes, other medical supplies, and equipment necessary to counter the effects of nerve agents, biological pathogens, and chemical agents.http://www.bt.cdc.gov/stockpile/index.asp

Smallpox Response Plan and Guidelines (Version 3.0) – Presents the most current criteria for implementation of CDC smallpox response plan; notification procedures for suspected smallpox cases; CDC and state/local responsibilities and action in the event of a smallpox outbreak; vaccine mobilization and deployment; and CDC personnel mobilization and deployment http://www.bt.cdc.gov/agent/smallpox/response-plan/index.asp

FDA, Center for Drug Evaluation and Research – Discussion of influenza antiviral drugs and related information. http://www.fda.gov/cder/drug/antivirals/influenza/default.htm

Annexes

Annex 1 Planning Guidance for State and Local Health Departments
Annex 2 Planning Guidance for the Health Care System
Annex 3: Overview of influenza illness and pandemics
Annex 4: Surveillance
Annex 5: Vaccine development and production
Annex 6: Vaccine strategies, monitoring, and safety
Annex 7: Antiviral strategies and use
Annex 8: Strategies to limit transmission
Annex 9: Communications
Annex 10: Research
Annex 11: Observations on the 1976 swine influenza program: lessons for pandemic planning
Annex 12: Synergies and differences in preparedness and response for influenza and other infectious disease threats