



appendix F: current HHS activities

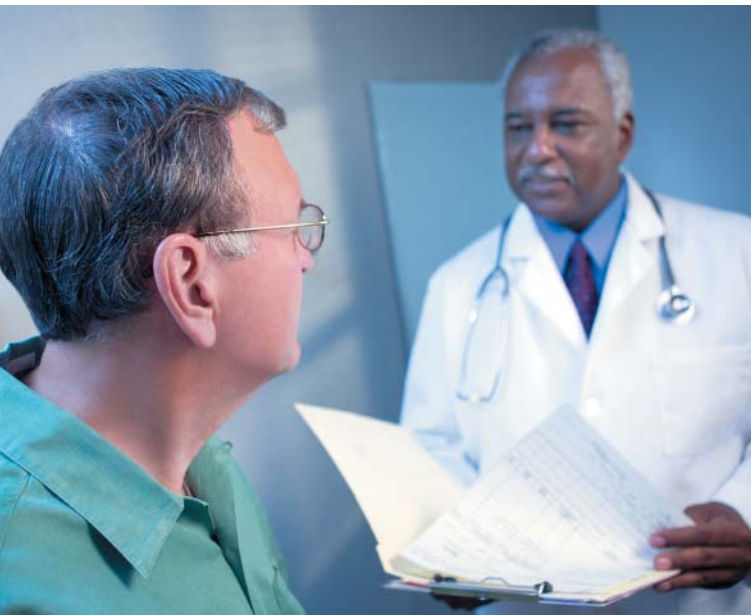
HHS is engaged in a broad array of activities to prepare for an influenza pandemic, although substantial work remains to be done to achieve the capabilities projected in this plan. Ongoing preparedness activities are summarized below.

Planning and Coordination

State and local planning. During the past several years, HHS has provided financial assistance to states to enhance their emergency preparedness activities, including pandemic influenza, through cooperative agreements. CDC provides preparedness funding annually to the public health departments of all the states, certain major metropolitan areas, and other eligible entities through cooperative agreements. HRSA, in conjunction with CDC, awards complementary cooperative agreements to provide preparedness funding annually to the same set of awardees for investment primarily in hospitals and other healthcare entities.

Part 2, Public Health Guidance for State and Local Partners, provides HHS' state partners with guidance, in the form of 11 supplements that provide information they can consider in refining and updating their plans concurrent with the release of the HHS Pandemic Influenza Strategic Plan. A major objective will be to achieve interoperability with the federal government plan and thus compliance with the principles and procedures of the National Response Plan. In particular, HHS will encourage states and municipalities to conduct drills and exercises with which to assess their readiness to respond to an influenza pandemic. HHS will assist federal, state, and local decision-makers in understanding the contents of the Plan. HHS will also work with national associations, such as the Association of State and Territorial Health Officials (ASTHO), to assist in determining their roles and responsibilities.

International collaborations. Sustained human-to-human transmission anywhere in the world will be the triggering event to initiate a pandemic response by the U.S. Because we live in a global community, a human outbreak anywhere means risk everywhere. The U.S. will pursue a containment strategy, where feasible, acting in concert with WHO and other nations as appropriate.



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HHS and the Department of State, Agency for International Development (USAID), the Department of Agriculture (USDA), and other agencies are developing a comprehensive international strategy on avian influenza and pandemic influenza. For example, HHS participates in ongoing global influenza surveillance through the CDC's WHO Collaborating Centers for Influenza. During the current pandemic alert, under the leadership of WHO, surveillance activities have been intensified and include strengthening national influenza center laboratories, training public health personnel, providing diagnostic reagents and other material support, and testing novel virus isolates from humans and animals. HHS has also contributed expertise to the WHO's influenza program and to WHO-led investigations of human cases of avian influenza in Asia. WHO has received additional funding by HHS to strengthen its Global Outbreak and Response Network (GOARN) to assist in surveillance and response worldwide and to establish a fund to ensure that laboratory specimens are shipped in a timely way to reference laboratories for further diagnostic work and confirmation.

As the pandemic threat continues, the U.S. will provide ongoing collaboration and assistance as part of the international response. During a pandemic, under the leadership of the HHS Office of Global Health Affairs (OGHA), the HHS Office of Public Health Emergency Preparedness (OPHEP), and the CDC, expertise and assistance will be provided for a coordinated international response. The U.S. is strengthening capacities in the currently affected region of East Asia and enhancing the ability of affected and high-risk countries to address the threat posed by H5N1 avian influenza. Currently, a number of bilateral and multilateral projects are underway in Asian countries to strengthen surveillance and laboratory capacity, develop rapid response capability, develop best practices for clinical case management of those infected, and develop vaccine production capability. In addition, the U.S. is working with the WHO to support international risk communication activities.

The newly formed International Partnership on Avian and Pandemic Influenza, announced by President Bush at the United Nations General Assembly on September 14, 2005, was created to improve international surveillance, transparency, timeliness, and response capabilities. Over 200 delegates from 88 countries and nine international organizations attended the first Senior Officials meeting on October 7, 2005. This initiative will strive for complete transparency, rapid response capabilities, and cooperative surveillance, and will facilitate the sharing of epidemiological data and samples among nations and with the World Health Organization (see Appendix H).



Surveillance, Investigation, and Protective Public Health Measures

Surveillance and epidemiological response. Global collaboration, facilitated by the WHO Secretariat, is a key feature of influenza surveillance. The WHO established an international laboratory-based surveillance network for influenza in 1948, which currently consists of 112 National Influenza Center (NIC) laboratories in 83 countries, and 4 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, use this information to update the formulation of influenza vaccine, and provide as much warning as possible about the next pandemic. This system provides the foundation of worldwide influenza prevention and control.

The WHO Collaborating Center located at CDC 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 NIC laboratories around the world.

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The current HHS surveillance strategy expands the geographic coverage of sentinel disease reporting sites and seeks to improve the timeliness of reporting to public health officials. Clinical and epidemiological assessment tools and investigation strategies are being developed to help guide treatment and assess risk, respectively. Finally, HHS is working to ensure real-time outbreak identification for both domestic and international events. (More information is available at www.cdc.gov/mmwr/preview/mmwrhtml/su5301a13.htm).

Diagnostics and detection. Diagnostic testing for pandemic influenza virus may involve a range of laboratory assays, including rapid antigen tests, reverse-transcription polymerase chain reaction (RT-PCR), virus isolation, and immunofluorescence antibody (IFA) assays. Currently available rapid antigen detection tests are not sufficiently sensitive to reliably distinguish influenza subtypes. In addition, capacity for molecular detection of H5N1, and other strains with pandemic potential, is available at CDC and state reference labs, but is not widely distributed. Capability for production, validation, and distribution of reagents for inclusion in WHO reference typing kits is severely limited.

HHS has augmented state and local laboratory capacity to respond to anticipated surges in laboratory needs by establishing the Laboratory Response Network (LRN). The LRN has trained laboratory personnel in the detection and characterization of novel influenza strains and will work with health departments to provide surge capacity processing and test clinical specimens from patients who meet the case definition of pandemic influenza. Health departments and LRN laboratories will also provide guidelines to clinical laboratories for the safe handling, processing, and testing of specimens. Local public health departments with laboratories not part of LRN or clinical laboratories should contact their state health department for more information regarding laboratory guidelines.

Infection control. On its website, CDC provides guidance to healthcare and public health partners on infection control measures designed to limit the spread of pandemic influenza. Guidance is included on the selection and use of personal protective equipment, such as masks, gloves, and gowns; hand hygiene and safe work practices; cleaning and disinfection of environmental surfaces; handling of laboratory specimens; and post-mortem care. The guidance also covers infection control practices related to the management of infectious patients, the protection of persons at high risk for severe influenza or its complications, personal protection in homes and in communities, and issues concerning occupational health.

CDC recommendations also outline actions that may be taken during the earliest stage of a pandemic when the first potential cases or disease clusters are detected. In this setting, individual-level containment measures (e.g., patient isolation and identification, monitoring, quarantine of contacts) may be useful in slowing the spread of pandemic influenza.

The overall HHS strategy includes a comprehensive approach to protect travelers and decrease entry of pandemic influenza into the United States. This includes: 1) issuing travel advisories and providing education to travelers to decrease their risk of acquiring pandemic influenza infection; 2) identifying persons with influenza-like illness during transit and implementing protocols to limit potential transmission to other passengers; 3) implementing point-of-entry interventions to rapidly identify persons who may have pandemic influenza; 4) isolating persons and identifying and quarantining contacts using fixed quarantine stations and other sheltering models; and 5) attempting to prevent exportation of illness from the United States to other countries and encouraging affected countries to implement similar exit screening.

HHS public health research priorities include evaluating the extent to which infection control measures, such as social distancing, mask use, and hand hygiene, prevent or minimize the spread of pandemic influenza within healthcare settings. Related to these priorities, the study of the relative clinical importance of the various modes of transmission is necessary to better define scientific rationale for various types of personal protective equipment.

Vaccines and Antivirals

Influenza vaccine. Currently, influenza vaccine for the annual, seasonal influenza program comes from four manufacturers. However, only a single manufacturer produces the annual vaccine entirely within the U.S. Thus, if a pandemic occurred and existing U.S.-based influenza vaccine manufacturing capacity was completely diverted to producing a pandemic vaccine, supply would be severely limited. Moreover, because the annual influenza manufacturing process takes place during most of the year, the time and capacity to produce vaccine against potential pandemic viruses for a stockpile, while continuing annual influenza vaccine production, is limited. Since supply will be limited, it is critical for HHS to be able to direct vaccine distribution in accordance with predefined groups (see Appendix D); HHS will ensure the building of capacity and will engage states in a discussion about the purchase and distribution of pandemic influenza vaccine.

Vaccine production capacity: The protective immune response generated by current influenza vaccines is largely based on viral hemagglutinin (HA) and neuraminidase (NA) antigens in the vaccine. As a consequence, the basis of influenza vaccine manufacturing is growing massive quantities of virus in order to have sufficient amounts of these protein antigens to stimulate immune responses. Influenza vaccines used in the United States and



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around world are manufactured by growing virus in fertilized hen's eggs, a commercial process that has been in place for decades. To achieve current vaccine production targets millions of 11-day old fertilized eggs must be available every day of production.

In the near term, further expansion of these systems will provide additional capacity for the U.S.-based production of both seasonal and pandemic vaccines, however, the surge capacity that will be needed for a pandemic response cannot be met by egg-based vaccine production alone, as it is impractical to develop a system that depends hundreds of millions of 11-day old specialized eggs on a standby basis. In addition, because a pandemic could result from an avian influenza strain that is lethal to chickens, it is impossible to ensure that eggs will be available to produce vaccine when needed.

In contrast, cell culture manufacturing technology can be applied to influenza vaccines as they are with most viral vaccines (e.g., polio vaccine, measles-mumps-rubella vaccine, chickenpox vaccine). In this system, viruses are grown in closed systems such as bioreactors containing large number of cells in growth media rather than eggs. The surge capacity afforded by cell-based technology is insensitive to seasons and can be adjusted to vaccine demand, as capacity can be increased or decreased by the number of bioreactors or the volume used within a bioreactor. In addition to supporting basic research on cell-based influenza vaccine development, HHS is currently supporting a number of vaccine manufacturers in the advanced development of cell-based influenza vaccines with the goal of developing U.S.-licensed cell-based influenza vaccines produced in the United States.

Dose-sparing technologies. Current U.S.-licensed vaccines stimulate an immune response based on the quantity of HA (hemagglutinin) antigen included in the dose. Methods to stimulate a strong immune response using less HA antigen are being studied in H5N1 and H9N2 vaccine trials. These include changing the mode of delivery from intramuscular to intradermal and the addition of immune-enhancing adjuvant to the vaccine formulation. Additionally, HHS is soliciting contract proposals from manufacturers of vaccines, adjuvants, and medical devices for the development and licensure of influenza vaccines that will provide dose-sparing alternative strategies.

Antiviral drugs. One of currently circulating H5N1 virus strains is resistant to one of two existing classes of antiviral drugs. Only the neuraminidase inhibitors, oseltamivir (Tamiflu®) and zanamivir (Relenza®) provide clinical benefit against all of the H5N1 virus strains currently circulating in Asia. As of October 2005, the Strategic National Stockpile includes 2.3 million treatment courses of oseltamivir (Tamiflu®) and 84,000 treatment courses of zanamivir (Relenza®). The Strategic National Stockpile is expecting delivery on an additional 2 million courses of Tamiflu by the end of 2005. HHS is committed to acquiring additional courses of these drugs, as stated earlier, and increasing U.S.-based antiviral production.

Further research and development. HHS plans to accelerate basic discovery in priority areas such as natural history of influenza progression, animal-to-human transmission of disease, and virus/host interaction. It plans to do this by supporting academic and private-sector research grants in priority areas that could contribute to the generation of new vaccines, drugs, and diagnostics and expanding support for multidisciplinary focus in priority areas.

HHS also plans to accelerate development of vaccines, drugs, and diagnostics by 1) supporting and accelerating the clinical testing of candidate products that are in advanced states of development (e.g. recombinant influenza vaccine and new and/or long-acting neuraminidase inhibitor antiviral drugs); 2) supporting evaluation and licensure efforts for injectable and pediatric formulations of currently licensed drugs, of new antiviral drugs, 3) supporting accelerated preclinical development including in vitro and animal model studies of promising countermeasures (e.g. siRNA and common-epitope vaccines, new immune-stimulating adjuvants, novel antiviral drugs, and genomic/proteomic microchip approaches to rapid diagnostics using surrogate markers of early infection). These will be accomplished using milestone-driven grants with private-sector partners and public/private sector collaborations; 4) supporting revised protocols and increased resources to reduce the time to prepare and qualify influenza virus reference strains used in vaccine manufacturing and to calibrate HA content in influenza vaccines for potency assays; and 5) developing accurate, rapid point-of-care diagnostic tests for clinical use during a pandemic, which will require additional investment in new technology leading both to better diagnosis of influenza and differentiation among the various respiratory infections.

Healthcare and Emergency Response

Clinical care. HHS is working with the medical community to establish clinical procedures for the initial screening, assessment, and management of patients with suspected novel influenza during a pandemic. Early recognition of illness caused by a novel influenza virus strain will rely on a combination of clinical and epidemiological features. Guidelines for the management of influenza-related complications, including community-acquired pneumonia, have also been developed.

Healthcare surge capacity. An influenza pandemic may increase the demand for hospital inpatient and intensive care unit (ICU) beds and assisted ventilation services by more than 25%. HHS is developing a deployable mass casualty capability that could be used to supplement hospitals. HHS recommends that hospitals develop their own response plans. **Supplement 3** provides guidance to hospitals on several components of a plan including hospital surveillance, hospital communication, staff education and training, triage and admission procedures, staffing and bed capacity, consumable and durable supplies, and planning for provision of care in non-hospital settings.

Psychosocial support services. HHS is focusing on the institutionalization of psychosocial support services that will help healthcare workers manage emotional stress during the response to an influenza pandemic and resolve related personal, professional, and family issues. HHS is also addressing the preparation of informational materials for employees and their families and the development of workforce resilience programs to assist families of deployed workers.

Mass fatalities and mortuary services. HHS understands that the timely, safe, and respectful disposition of the deceased is an essential component of an effective response. Pandemic influenza may quickly rise to the level of a catastrophic incident that results in mass fatalities, which will place extraordinary demands (including religious, cultural, and emotional burdens) on local jurisdictions and the families of the victims. A catastrophic incident involving mass fatalities will require federal assistance to transport, process, and store deceased victims and support final disposition and personal effects processing. Most local jurisdictions will be severely strained to handle mass fatalities or may experience profound difficulties.

If local and state fatality management capacities are exceeded, HHS, under ESF #8, will coordinate with the Department of Homeland Security (DHS) and the Department of Defense (DoD) to assist in providing mortuary services; establishing temporary morgue facilities; and processing, preparation, and disposition of human remains.

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Communications and Outreach

Risk communication. HHS is the federal government's lead agency in pandemic influenza communications. An HHS Communications and Public Outreach Strategy for Pandemic Influenza has been developed. This strategy is designed to prepare U.S. citizens and communities for a pandemic; communicate the need for local preparedness and an understanding of the implications of a pandemic; and develop consistent, clear, honest messages and materials that can be shared broadly in the U.S. and with global partners. Components of the strategy include 1) assessment of current public (or community) knowledge through ongoing surveillance of media and surveys of the public and providers; 2) development of materials such as message maps that have been developed and tested in focus groups; 3) formative audience research; 4) cross-government communication coordination; 5) facilitating community and business continuity planning by helping these sectors communicate with their constituents and prepare; 6) public engagement through forums and stakeholder meetings on such important policy issues as allocation of limited drugs and vaccines; 7) web communications development through a consolidated, centralized U.S. government website; 8) international outreach to support our global partners, in cooperation with the WHO Secretariat; and 9) continuing efforts to raise awareness about the importance of seasonal influenza vaccine and to promote increased yearly compliance of influenza and pneumococcal vaccination.

A Public Engagement Pilot Project on Pandemic Influenza was initiated in July 2005 to discuss goals for a pandemic influenza vaccination program and to pilot test a new model for engaging citizens on vaccine related policy decisions. The pilot project was sponsored by interested organizations including the Atlanta Journal Constitution, the Lounsbery Foundation, the Keystone Center, the Institute of Medicine, the University of Georgia, the CDC's National Immunization Program, the HHS National Vaccine Program Office, and the Study Circles Resource Center. To conduct this public consultation, the sponsors made use of an innovative model for engaging stakeholders from various organizations with an interest in pandemic influenza, and individual citizens-at-large from the 4 principal regions of the United States. The anticipated major benefits from this public consultation were the development of an improved plan to combat pandemic influenza and one more likely to gain public support, and a demonstration that citizens can be productively engaged in informing vaccine-related policy decisions. A complete assessment of the potential benefits from this pilot project is still underway and important potential outcomes such as improved relationships and increased trust among the participants have not been yet been measured.



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