

***Annex 12: Synergies and Differences in Preparedness and Response for
Influenza and other Infectious Disease Threats - Draft***

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I. Introduction

Preparedness and response planning is ongoing at national, state and local levels for a range of public health emergencies. These include pandemic influenza, bioterrorist threats and Severe Acute Respiratory Syndrome (SARS). Health also is a component of other emergency preparedness and response plans for natural disasters and terrorist attacks using non-biological weapons. To as great an extent possible, preparedness plans addressing different health threats should have common elements. This will facilitate the ability of participants to learn their roles and to practice response activities in tabletop and field exercises, leading to more effective implementation. It also increases efficiency in planning and, possibly, in development of infrastructure. At the same time, it is important that planners recognize the unique aspects of preparedness and response for different health threats and to assure that plans appropriately address these differences.

Because pandemic influenza and SARS both are infectious respiratory illnesses that spread by contact with infectious secretions, particular attention to synergies in planning has been focused on these agents. For example, some have proposed developing a generic respiratory infection preparedness and response plan with the specific features of the different agents addressed in annexes to that plan. The efficiency of such an approach depends, in part, on the extent of similarities and differences (*see Table I*). Smallpox is also considered in this document because it is a transmissible infection with respiratory spread as well as being a focus of current preparedness planning.

II. Influenza, SARS, and Smallpox: Outbreak and Disease Characteristics

A. Influenza

An influenza pandemic is likely to originate in Asia – as did two of the three pandemics during the 20th century and several of the avian strains that recently have infected humans – and to spread to the U.S. Because persons with influenza are infectious before onset of fever or respiratory symptoms, screening and restricting travel of ill persons may slow the spread, but is unlikely to stop the spread of disease. Each of the 20th century influenza pandemics swept through the U.S. and other countries with efficient person-to-person transmission, primarily through contact with infected respiratory secretions (“droplet transmission”). It is possible that a future pandemic, however, could be caused by a novel strain that is not as effectively transmitted – with transmission characteristics between those of the avian H5N1 or H7N7 strains that recently have infected people and the strains that caused previous pandemic or cause annual influenza outbreaks.

Vaccination represents the primary control strategy in an influenza pandemic. Specific influenza antiviral drugs also are available and may have significant impacts on mortality and severe morbidity, but their use would be unlikely to alter the overall course of the pandemic. Attack rates during influenza pandemics have been high, with as much as a third of the susceptible population becoming infected. Case-fatality rates are likely to be substantially less than 1 percent overall, as in the 1957 and 1968 pandemics. Although the

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case fatality rate in the 1918 pandemic exceeded 1 percent, the improvements in medical care that have occurred since that time likely would lead to a substantially lower risk of death. Whereas more than 90% of deaths from seasonal influenza epidemics occur in persons 65 years old or older, in the influenza pandemics of the last century, a greater proportion of pandemic influenza associated deaths occur in younger persons.

B. SARS

Severe Acute Respiratory Syndrome (SARS) cases also occurred first in Asia, spreading via international travel to other countries. Outbreaks occurred with transmission primarily in households and health care settings. Contaminated environmental surfaces, respiratory secretions, and airborne spread all are thought to be significant. Nevertheless, despite universal susceptibility, transmission was limited and epidemiological investigation, contact tracing, quarantine, isolation, and infection control successfully led to containment. While SARS vaccine research currently is ongoing, no vaccine was available at the time of the outbreak and use of antiviral drugs had no documented impact. Although SARS deaths did not occur in the U.S., the overall case-fatality rate was between 5 percent and 10 percent.

C. Smallpox

Many of the leading bioterrorist threat agents can cause illness after exposure to an aerosol that contains an infectious organism or toxin (such as anthrax, botulism, and tularemia); however, disease caused by these agents does not spread from person-to-person. By contrast – and similar to influenza and SARS – smallpox is transmissible and spreads by contact with infectious respiratory secretions. While the transmission of smallpox from infected to susceptible persons occurs more efficiently than for SARS, it is less efficient than for classical influenza. Because of its longer incubation period, contact tracing and quarantine of cases before they become infectious is a feasible approach to containing and controlling smallpox and can prevent exposure and transmission to susceptible persons and vaccination is a major component of a response. Contact tracing and vaccination was the primary strategy that led to the global eradication of smallpox in the 1970s

III. National, State, and Local Planning and Coordination

Separate national preparedness plans have been or are being developed for pandemic influenza, SARS, and smallpox (*see Website Resources*). Each national plan contains similar components, and each emphasizes the importance of planning at the state and local levels. Federal bioterrorism funding and immunization grant support both can be used by state and local health departments for smallpox and pandemic influenza planning. Initiatives and funding being provided by the Health Resources and Services Administration (HRSA) will help states to improve coordination of health care services and emergency response capacity and facilitate preparedness for influenza, smallpox, SARS, as well as other health emergencies. In FY '04, HHS introduced a cross-cutting critical benchmark for state pandemic influenza preparedness planning as part of the Departments' awards to states to improve hospitals' response to bioterrorism and other diseases. The goal of this planning activity is to assure effective implementation of an effective response

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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).

The Assistant Secretary for Public Health Emergency Preparedness, Department of Health and Human Services will coordinate the public health response to each of these threats. The same command and control structures will be established for pandemic influenza and other public health threats, with information from the field, federal agencies, and the emergency response community communicated to the Secretary's Operations Center, which serves as a focal point for decisions and communication. The Assistant Secretary for Public Health Emergency Preparedness will coordinate response activities. Based on the pandemic influenza phase or the extent of a SARS outbreak, some of the focus may be assigned to CDC as the lead public health agency for investigation and response. Federal advisory committees including FDA's Vaccine and Related Biological Products Advisory Committee (VRBPAC) and CDC's Advisory Committee on Immunization Practices (ACIP) will make recommendations regarding licensure and use of vaccines. Authorities for public health response activities and legal issues will be similar for influenza, SARS, and smallpox. A presidential declaration of an emergency will activate the Federal Response Plan and will be dependent on the extent and severity of disease in the U.S. Communications strategies and infrastructure are similar for the health emergencies described in this document.

IV. Surveillance

The international surveillance infrastructure for influenza and the laboratory capacity developed for that surveillance contributed to the initial detection of SARS and to tracking the spread of outbreaks. Because both influenza and SARS present as febrile respiratory illnesses, and because etiological diagnosis can be made from testing respiratory secretions, some approaches to surveillance for the two should be linked. Screening of persons hospitalized with severe febrile and respiratory illness, especially during outbreaks, is one strategy that could lead to early detection of a novel influenza subtype or SARS. Other health threats, such as inhalational anthrax, pneumonic plague, and tularemia also present as severe respiratory illness making syndromic, hospital-based surveillance a multi-purpose system. Surveillance systems focusing on illness among travelers and health care workers also may be useful for both agents, although no such system currently exists.

By contrast, smallpox is recognized as a febrile illness with a characteristic rash. Syndromic surveillance for this threat focuses on vesiculo-pustular rash and fever and an algorithm has been developed to guide laboratory testing and reporting. Laboratory capabilities used for smallpox such as viral culture, polymerase chain reaction (PCR) testing, and electron microscopy will contribute to the detection of multiple threat agents. "Multiplex" PCR tests are available to detect many of the leading respiratory pathogens (influenza; parainfluenza 1, 2, and 3; respiratory syncytial virus; and adenovirus), and can be expanded to include new threats. Rapid antigen-detection tests are available for influenza and can be used in physician offices for etiological diagnosis. This capacity does not exist yet for SARS.

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V. Response Strategies: Interventions to Prevent Disease Transmission

Controlling the spread of infection between persons is a key characteristic of the response to SARS and smallpox. Preparedness planning for these agents should include strategies such as travel alerts and screening of travelers on exit and/or entrance to another country; isolation of persons with compatible clinical illness; contact tracing and quarantine of exposed persons; and adherence to rigorous infection control. Just as during the 2003 SARS outbreak, transmission of smallpox among hospital staff and patients figured prominently in smallpox outbreaks in industrialized countries after ongoing community transmission in those areas had been interrupted. Thus, planning and coordination between state and local health departments and hospitals and other health care organizations is critical to an effective response to outbreaks caused by these pathogens.

Traditionally, interventions to slow the transmission of infection such as travel screening and restrictions, quarantine, and community control measures such as canceling school and public gatherings have not had an important role in seasonal influenza outbreaks or pandemics. Although infection control in hospitals and other health care settings is recognized as important, spread between and within countries and communities has been rapid and multi-focal, asymptomatic persons are thought to play an important role, and school closing has been tried in some areas but impact never has been formally evaluated. Because persons without symptoms may spread disease, screening travelers would be less effective in preventing spread. While future influenza pandemics are likely to spread in a similar fashion as annual influenza epidemics and prior pandemics, it also is possible that a future pandemic strain will be different. The H5N1 avian influenza strain in 1997 and the H7N7 avian influenza strain in 2002 exhibited limited person-to-person transmission (perhaps as a consequence of their being animal influenza viruses rather than animal-human reassortants and, therefore, less well adapted to cause human infections). Outbreaks of human infection caused by avian influenza strains were controlled with a vigorous public health response that included culling poultry flocks, imposing strict infection control, use of antiviral therapy and prophylaxis, and vaccination to prevent dual infection and the risk of reassortment between animal and human viral strains. The 1976 swine influenza strain, which infected several hundred people and then disappeared, also might have had different transmission dynamics compared with pandemic or annual epidemic strains. Given the possibility that interventions to decrease transmission could have an impact in some potential pandemic influenza scenarios, control strategies should be included in pandemic influenza preparedness and response plans as they are in plans for SARS and smallpox. A recent WHO consultation on priority public health interventions before and during an influenza pandemic reviewed the range of interventions that might be considered at various stages of a pandemic (<http://www.who.int>) (see *Annex 6: Strategies to Limit Transmission*).

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VI. Response Strategies: Vaccination and Antiviral Therapy and Chemoprophylaxis

A. Vaccination

Vaccination is a key element of the response to a smallpox outbreak or an influenza pandemic. No vaccine is available to prevent SARS. Smallpox response plans include both search and containment strategies, where case-contacts are identified and vaccinated, and mass vaccination. Public sector control of all smallpox vaccine has been assumed in response plans. Clinic operations, tracking systems to identify who has been vaccinated, and adverse event surveillance all are described in the national smallpox response plan (*see website resources*). Each of these components also is relevant for pandemic influenza planning. Focused vaccination of defined priority groups likely will occur early in a pandemic when vaccine supplies are limited, with mass vaccination occurring later as vaccine supply increases. Tracking who receives vaccine may be particularly important if a two-dose schedule is required for protection. Because of the need to assure that any vaccination program is designed with appropriate safety considerations careful and intensive adverse event monitoring in a sample of vaccinated persons is needed in addition to passive reporting of adverse events among all vaccinees. For the smallpox vaccination program, passive surveillance for adverse events following immunization through the Vaccine Adverse Events Reporting System was enhanced by careful follow-up of persons reporting serious reactions. In addition, active surveillance for adverse reactions in a cohort of vaccinees; analysis of databases including vaccination and health care use data; and clinical assessment of potential vaccine associated events all were implemented. Similar strategies would be enacted during a pandemic influenza vaccination campaign.

B. Antivirals therapy and chemoprophylaxis

Antiviral therapy and chemoprophylaxis can reduce mortality and morbidity during an influenza pandemic. The antiviral agents for influenza – the adamantanes and neuraminidase inhibitors – are specific to influenza and are not active against other viral respiratory pathogens. Antiviral therapy has not been shown effective against SARS. Therefore, among preparedness and response plans for SARS, smallpox and influenza, strategies for distribution and use of antiviral agents will be unique to the latter. However, there may be synergies with other preparedness and response plans, such as for anthrax, where antibiotics are maintained and distributed from the Strategic National Stockpile to state and local health departments for therapy and chemoprophylaxis. As the incidence of secondary bacterial infections may follow a primary viral infection, a supply of antibiotics that can effectively treat community acquired pneumonia should be anticipated.

VII. International Coordination

Some of the international issues that will arise in an influenza pandemic are similar to those for SARS and smallpox. In each situation, the World Health Organization (WHO) will have the primary role in coordinating the global health response (recognizing that for smallpox, an investigation of the intentional release of this pathogen will accompany public health investigations and response). Disease surveillance will be done through a range of

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existing national and international networks. Diagnostic reagents and test kits will need to be developed and distributed globally. Clinicians will need to be educated on diagnosis and management; and laboratory scientists will need to be trained to identify the etiology of clinically compatible infections. Rapid access to information, such as through videoconferences and internet materials, were important in the SARS response and are likely to be increasingly important for other global health threats.

VII. Research and Infrastructure Development for Preparedness

A. Research

Vaccine research is ongoing for influenza, smallpox, and SARS. For influenza, the foci include methods to more rapidly develop high-growth reassortant vaccine reference strains; the use of adjuvants to increase immunogenicity; and diversifying manufacturing techniques (e.g., producing vaccine both in embryonated hens' eggs and cell-culture) to increase flexibility and surge capacity. For smallpox, the primary research focus is on development of safer vaccines, particularly for those with immunosuppressive conditions who may suffer severe adverse reactions if they receive the current live-virus vaccine. SARS vaccine research is focused on development and testing candidate vaccines. Improving diagnostic testing and assessing the roles of antiviral therapy also are relevant research issues for each of the pathogens. (*See also Annex 8: Pandemic Influenza Research*).

B. Surveillance, communications, and information technology

Substantial progress in preparedness can be made in the areas of surveillance, communications, and information technology.

- *Surveillance:* Influenza and SARS both can be detected by surveillance for fever and respiratory disease. New strategies such as hospital-based surveillance and surveillance among health care workers and travelers should be considered and may be applied for both pathogens. Strengthening existing components of U.S. influenza surveillance, such as the sentinel physician network, also may provide a useful infrastructure for SARS.
- *Communications:* Communications preparedness activities include developing and testing messages and materials to be used in the event of a pandemic or emerging infectious disease outbreak, and further enhancing infrastructures to disseminate information from national to state and local levels and between the public and private sectors.
- *Information technology:* Information systems should be developed that can be used to track vaccination coverage and generate reminders for a second dose where more than one vaccination is needed for protection. Integrating such a system with state-based immunization registries will increase acceptability and usefulness. Vaccine safety infrastructures for surveillance and clinical and epidemiological investigation currently exist and should be enhanced, as needed.

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A final and critical component of preparedness is development and integration of response plans and their field-testing in tabletop and field exercises. Exercises can be multi-purpose testing components common to influenza, smallpox, and SARS such as hospital capacity and infection control. They may also be specific to one or more of these agents, for example, evaluating the ability to establish mass vaccination clinics (relevant to influenza and smallpox) or to effectively distribute antiviral agents for therapy (relevant to influenza).

Table: Comparison of outbreak characteristics, and preparedness and response activities for pandemic influenza and SARS.

The description of outbreak characteristics and consequences are based on historical experience with influenza pandemics (1918, 1957, and 1968) and on the 2003 SARS outbreak.

Characteristic	Pandemic Influenza	SARS
Outbreak Characteristics and Consequences	<ul style="list-style-type: none"> • Initial disease likely imported • Geographically widespread – entire country affected over 3 to 4 month period • Multi-focal spread with simultaneous epidemics in many areas • Attack rate of 10 percent to 35 percent of entire population • Community transmission, especially among children, predominant • High mortality among elderly; however, shift to younger ages is likely compared with seasonal epidemics • Overall case-fatality rate of 1 percent or less • Widespread disruption of transportation infrastructure • Widespread disruption of community services and economic productivity • Widespread disruption of international trade 	<ul style="list-style-type: none"> • Initial disease likely imported • Focal outbreaks in urban centers of travel and health care; many areas remain unaffected • Potential ability to track spread based on movement of infected persons or their contacts • Low overall attack rate – ability to count cases • Transmission primarily within families and health care settings • Most mortality among elderly • Overall case-fatality rate up to 5 to 10 percent • Widespread disruption of transportation infrastructure • Little disruption of community services; some disruption of economic productivity • Potential disruption of international trade
Preparedness Planning	<ul style="list-style-type: none"> • Development of national preparedness and response plan 	<ul style="list-style-type: none"> • Development of national preparedness and response plan

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Characteristic	Pandemic Influenza	SARS
	<ul style="list-style-type: none"> • Development of state and local plans, supported with CDC and HRSA's BT and immunization grant funds • Development of health care system plans encouraged 	<ul style="list-style-type: none"> • Development of state and local plans • Development of health care system plans encouraged
Surveillance and Diagnosis	<ul style="list-style-type: none"> • Large longstanding international laboratory-based surveillance networks under WHO coordination • U.S. sentinel physician network • Morbidity and mortality reporting in states and cities • Etiological diagnosis by culture, PCR, serology, and other tests • Rapid antigen detection tests available • Diagnostic testing capacity widespread (health departments, hospitals, physician offices) 	<ul style="list-style-type: none"> • <i>Ad hoc</i> international surveillance using influenza and other surveillance infrastructure under WHO coordination • Guidelines and infrastructures for U.S. surveillance being established • Etiological diagnosis by culture, PCR, serology, and electron microscopy • No rapid antigen detection tests available • Diagnostic testing capacity more limited (health departments., some hospitals)
National Coordination	<ul style="list-style-type: none"> • HHS lead • Coordination at HHS Secretary's Operations Center with input from agency Emergency Operations Centers • Most authorities for public health response and control measures exist or can be activated by a secretarial or presidential declaration 	<ul style="list-style-type: none"> • HHS lead • Coordination at HHS Secretary's Operations Center with input from agency Emergency Operations Centers • Most authorities for public health response and control measures exist or can be activated by a secretarial or presidential declaration
National and State/Local Emergency Response	<ul style="list-style-type: none"> • Emergency or disaster declaration possible with HHS role defined under ESF #8 • State level coordination defined by preparedness and response plans • FEMA personnel. National 	<ul style="list-style-type: none"> • Emergency declaration possible • State level coordination defined by preparedness and response plans • FEMA personnel, National Guard. and community

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Characteristic	Pandemic Influenza	SARS
	Guard, and community volunteers likely needed to maintain community services	volunteers may be needed to maintain quarantine and provide support
Interventions to Prevent Transmission	<ul style="list-style-type: none"> • International travel restrictions or passenger screening possible but are unlikely to prevent a pandemic • Internal U.S. travel restrictions unlikely • Quarantine unlikely • Hospital infection control useful • School closing and limits on public events possible • Chemoprophylaxis with antiviral agents in priority groups • Vaccination of priority groups 	<ul style="list-style-type: none"> • International travel restrictions possible; passenger screening likely and may prevent outbreaks • Internal U.S. travel restrictions or passenger screening likely and may prevent outbreaks • Quarantine likely to play a major role in controlling transmission and disease spread • Hospital infection control vital in controlling transmission and disease spread • School closing and limits on public events unlikely • No chemoprophylaxis available • No vaccination available
Interventions to Decrease Mortality and Morbidity	<ul style="list-style-type: none"> • Vaccination • Antiviral therapy and chemoprophylaxis • Quality medical care • Interventions to prevent disease transmission 	<ul style="list-style-type: none"> • Quality medical care • Interventions to prevent disease transmission
International Coordination and Collaboration	<ul style="list-style-type: none"> • WHO coordinated international surveillance • WHO declaration of affected countries • International sharing of diagnostic test reagents and methods • International recommendations for vaccine strain and sharing of master seed 	<ul style="list-style-type: none"> • WHO coordinated international surveillance • WHO declaration of affected countries and cities • International sharing of diagnostic test reagents and methods
Research and	<ul style="list-style-type: none"> • Research to accelerate vaccine 	<ul style="list-style-type: none"> • Research on vaccine

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Characteristic	Pandemic Influenza	SARS
Infrastructure Development in Support of Preparedness	<p>development and increase yields</p> <ul style="list-style-type: none"> • Research on use of adjuvanted vaccine • Research on vaccines against conserved antigens • Enhanced surveillance potentially at hospitals, and among health care workers and travelers • Incentives to support diversification of technology; increased speed and flexibility; and increased surge capacity of vaccine production in the U.S. 	<p>development</p> <ul style="list-style-type: none"> • Research on antiviral development • Research to define whether existing antiviral or anti-inflammatory (such as steroid) therapy is of benefit • Research to design improved, field-friendly rapid diagnostic tests