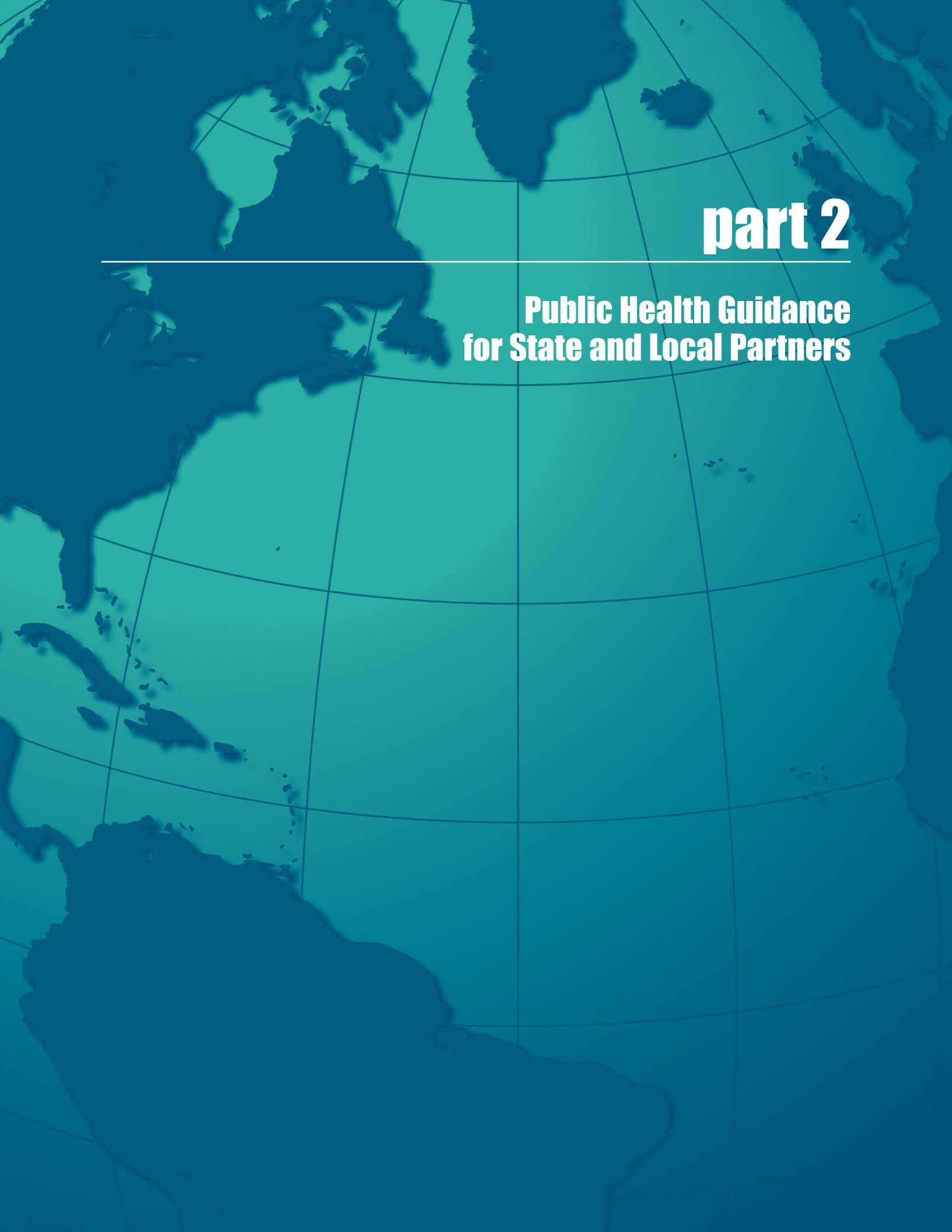

part 2

Public Health Guidance for State and Local Partners

introduction

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PART 2. PUBLIC HEALTH GUIDANCE ON PANDEMIC INFLUENZA FOR STATE AND LOCAL PARTNERS[1]

A. Introduction

An influenza pandemic may emerge with little warning, affecting a large number of people within a short space of time. During the first wave of the pandemic, outbreaks may occur simultaneously in many locations throughout the nation, preventing a targeted concentration of national emergency resources in one or two places—and requiring each locality to depend in large measure on its own resources to respond. A vaccine will not yet be available, and the supply of antiviral drugs will be limited. Local outbreaks may last for weeks or months, and widespread illness in a particular community could lead to shortages in the healthcare sector as well as in essential services.

An effective local response will depend on pre-established partnerships and collaborative planning by public health officials, hospital administrators, and community leaders, who have considered a range of best-case and worst-case scenarios. It will require flexibility and real-time decision-making, guided by epidemiologic information on the pandemic virus. It will also depend on a well-informed public that understands the dangers of pandemic influenza and accepts the potential need for control measures like self-isolation and quarantine that prevent disease spread by reducing social contact. The public must also understand and accept the rationale in prioritizing the use of limited supplies of antiviral drugs and initial stocks of vaccines.

The goal of Part 2 of the *HHS Pandemic Influenza Plan* is to help state and local jurisdictions and healthcare facilities mount an effective response to pandemic influenza. Public Health Guidance on Pandemic Influenza for State and Local Partners was developed with input from many public health and medical partners with front-line responsibility for pandemic influenza response.

Purpose and Aims

All U.S. state, local, and tribal governments must be prepared to detect the earliest cases of disease, to minimize illness and morbidity, and to decrease social disruption and economic loss. The principle aims of the *Public Health Guidance for State and Local Partners* are to:

- Provide guidance for updating state-level pandemic influenza response plans developed in fulfillment of activities under the CDC and HRSA Cooperative Agreements for Public Health Emergency Preparedness and Bioterrorism Hospital Preparedness (*www.bt.cdc.gov/planning/guidance05/index.asp* and *www.hrsa.gov/grants/preview/guidancespecial/hrsa05001.htm*).
- Help healthcare partners address the medical challenges of pandemic influenza (e.g., evaluation and management of large numbers of patients, occupational health risks, and limited supplies of antiviral medications and vaccines).
- Define the public health role in healthcare planning and preparedness for pandemic influenza.
- Strengthen linkages between public health departments and private sector partners—including healthcare facilities, community-based organizations, clinical laboratories, behavioral health experts, and first responders—to protect health and preserve essential services during a pandemic.

Many activities described in the Public Health Guidance for State and Local Partners are similar, if not the same as those required to combat other infectious diseases, such as Severe Acute Respiratory Syndrome (SARS) or intentionally-spread smallpox or plague. Topics covered in the *Public Health Guidance for State and Local Partners* may, therefore, be relevant to—or addressed in—other emergency preparedness plans. (See, for example: *Public Health Guidance for Community-Level Preparedness and Response to SARS:* www.cdc.gov/ncidod/sars/guidance/; *Smallpox Response Plan and Guidelines*: www.bt.cdc.gov/agent/smallpox/response-plan/index.asp).

[1] Through this document, the term "state and local" is inclusive of territorial and tribal governments and health authorities, as applicable.

Organization

Part 2 of the *HHS Pandemic Influenza Plan* provides an overview of

- Pandemic influenza preparedness and response planning by state and local governments (Section B)
- Community planning to support healthcare facilities on a city-wide or regional basis during an influenza pandemic (Section C)

Part 2 also includes eleven supplements that provide guidance on specific aspects of pandemic influenza planning and response:

Supplement 1: Pandemic Influenza Disease Surveillance

Supplement 2: Laboratory Diagnostics

Supplement 3: Healthcare Planning

Supplement 4: Infection Control

Supplement 5: Clinical Guidelines

Supplement 6: Vaccine Distribution and Use

Supplement 7: Antiviral Drug Distribution and Use

Supplement 8: Community Disease Control and Prevention

Supplement 9: Management of Travel-Related Risk of Disease Transmission

Supplement 10: Public Health Communications

Supplement 11: Psychosocial Workforce Support Services

The content of each supplement is summarized in Section D.

Priority activities in each Supplement are organized under the time periods laid out in the WHO classification system proposed in February 2005: the *Interpandemic Period,* the *Pandemic Alert Period,* and the *Pandemic Period.* Some of the Supplements further subdivide Pandemic Period activities according WHO pandemic phases or to local levels of disease spread that will trigger particular activities over the course of the pandemic.

To help state and local public health and healthcare partners prepare for the unexpected, the *Public Health Guidance for State and Local Partners* includes a list of cross-cutting technical resources, including exercises and drills, to facilitate the exploration of different scenarios and local concerns (see **Supplement 3. Healthcare Planning,** Appendix 1). The *Public Health Guidance for State and Local Partners* also identifies disease-control issues whose resolution will require real-time guidance during a pandemic (Box 1).

Definitions of public health terms used throughout the *Public Health Guidance for State and Local Partners* are provided in Box 3 and in the Glossary.

B. Overview of Planning by State and Local Governments

All states and localities must be prepared to coordinate the pandemic influenza response within and between their jurisdictions. State and local responsibilities include:

- Enhancing disease surveillance to ensure early detection of the first cases of pandemic influenza in their jurisdictions (see **Supplements 1 and 2**).

- Distributing public stocks of antiviral drugs and vaccines and providing local physicians and hospital administrators with updated guidance on clinical management and infection control as the situation unfolds (**Supplements 3 to 7**[2])
- Preventing local disease transmission using a range of containment strategies (**Supplements 8 and 9**)
- Providing ongoing communication with the public (about the response effort, including the purpose and duration of containment measures) (**Supplement 10**)
- Providing psychological and social support services to emergency field workers and other responders (**Supplement 11**)

As described in Part 1, the HHS will support affected states or jurisdictions during an influenza pandemic by:

- Conducting outbreak investigations, as requested
- Conducting epidemiologic and laboratory-based studies ("special studies")
- Providing ongoing information from the national influenza surveillance system on the pandemic's impact on health and the healthcare system
- Expanding supply of antiviral drugs by stimulating increased U.S. based production capacity
- Expanding U.S.-based production capacity for pandemic vaccine and working with manufacturers to ensure that pandemic vaccine is produced at full capacity
- Distributing public stocks of antiviral drugs and other medical supplies from the Strategic National Stockpile to the states
- Distributing public stocks of vaccines, when they become available
- Providing guidance on community containment strategies, including travel restrictions, school closings, and quarantine
- Communicating with the public via the news media
- Monitoring the response

Planning Process

The first step in the planning process for state and local governments is to establish a Pandemic Influenza Coordinating Committee to oversee preparedness planning and ensure integration with other emergency planning efforts. The membership of the Coordinating Committee should represent a range of disciplines and expertise in the public and private sectors (Box 2).

The Coordinating Committee should draft and formally adopt a pandemic influenza response plan that:

- Delineates the roles and responsibilities of state and local agencies and offices
- Builds on existing preparedness and response plans for bioterrorism events, SARS, and other infectious disease emergencies
- Addresses legal issues including those that affect hospital staffing, patient care, and quarantine (see below)
- Is periodically reviewed and updated

As part of the planning effort, the Coordinating Committee should:

- Help establish and promote community-based task forces that support healthcare institutions on a city-wide or regional basis (see Section C).
- Identify the authority responsible for state-level declaration of a public health emergency and for officially activating the pandemic influenza response plan.

[2] Supplements 3, 4, and 5 are primarily directed to healthcare providers and hospital administrators, while Supplements 6 and 7 are also directed to state and local health officials.

- Identify an overall coordinator to work with hospitals and communicating with medical and mental health personnel during a pandemic.
- Identify the jurisdiction's controlling authority over intrastate and interstate modes of transportation, which might be curtailed during a pandemic.
- Identify state and local law enforcement personnel who will assist in maintaining public order and enforcing control measures during a pandemic.
- Develop and reinforce relationships with local health authorities in adjoining jurisdictions.
- Make planning decisions on acquisition and distribution of antiviral drugs and vaccines, in accordance with HHS recommendations.
- Ensure that plans take into account tribal populations, where applicable.
- Conduct state-level "table top" exercises to test response capabilities.
- Encourage local jurisdictions to conduct exercises and drills.

Legal Preparedness

The Coordinating Committee should review state and local statutory provisions regarding:

- Laws and procedures for closing businesses or schools and suspending public meetings during a declared state of emergency
- Medical volunteer licensure, liability, and compensation laws for in-state, out-of-state, and returning retired and non-medical volunteers
- Quarantine laws and how they apply in a public health emergency
- Workers' compensation laws as they apply to healthcare workers and workers who provide essential services
- Reimbursement for workers placed in isolation or quarantine (if not addressed in sick leave policies)

Relevant federal law should be reviewed as well and statutes should he harmonized, as feasible.

Additional information on legal preparedness is provided in Appendices 1 and 2.

C. Overview of Community-wide Planning to Support Healthcare Facilities

Without special preparation, a large-scale pandemic could quickly overwhelm local healthcare facilities and resources. Although institutional planning by hospitals is essential (see Supplement 3), it is not sufficient. Hospitals depend on many organizations and groups—e.g., suppliers of food, drugs, and medical supplies, sanitation workers, and telephone companies—to accomplish their day-to-day tasks. If workforce illnesses and absences prevent these organizations from functioning normally during a pandemic, hospitals will be severely affected.

State health authorities should consider promoting the establishment of local pandemic influenza task forces that will ensure community readiness to provide emergency support to healthcare facilities on a city-wide or regional basis. Depending on the state, the task forces may be coordinated by municipal, county, or tribal health departments, or by regional public health offices. Task force activities should be integrated with state-wide planning efforts and should reflect common goals and principles for preparedness and response.

Each local task force should include representatives from hospitals, community service organizations, professional organizations of physicians, nurses, and pharmacists, home health care organizations, long term care facilities, federally qualified health centers (FQHC) and other healthcare safety net providers, emergency medical services (EMS), behavioral health

experts, and public health officials. The task forces should also include private sector partners who provide essential services such as food, electricity, and water. They may also include civil protection authorities such as the police, sheriff's departments, and firefighters.

During a pandemic, the task force would be responsible for coordinating health care activities within the community and should work with local health departments and hospitals to:

- Improve communication with medical care providers and health care organizations.
- Monitor local hospital resources (e.g., adult and pediatric hospital beds, intensive care unit beds, emergency department beds, medical supplies, respirators and other equipment, mortuary capacity).
- Address emergency healthcare staffing needs and other medical surge capacity issues.
- Encourage coordination among state and federal healthcare facilities, such as Veterans Administration hospitals, Indian Health Service facilities, and Department of Defense hospitals.
- Conduct contingency planning with:
  - Private sector groups that support hospital functions, to ensure continuity of operations during the pandemic. These groups may include medical supply companies, medical gas companies, companies that supply food and clean linens, and internet service providers.
  - Public utilities (water, electricity, gas, telephone, sanitation) to ensure continued service during the pandemic.
  - Local law enforcement agencies who can help maintain order if a hospital is overwhelmed by a large volume of patients (ill or worried about being ill).
  - Identify alternative care sites for patient care (child and adult) and sites for quarantine.
  - Identify community-based organizations that can provide psychological and social support to healthcare workers, public health field workers, and other emergency responders (see **Supplement 11**).

Community Planning in Rural Areas

Special efforts should be made to address pandemic planning issues in rural communities and other areas where emergency rooms and other resources for urgent care and emergency treatment are lacking. Without community-wide planning, a surge of pandemic influenza patients could force the closure of local outpatient healthcare clinics. Planning partners may include healthcare providers at outpatient clinics, federally qualified health centers (FQHCs),[3] IHS and tribal health care facilities, and other healthcare safety net providers[4] that deliver care to low-income and other vulnerable populations.

D. Public Health Guidance Supplements

The eleven Public Health Guidance supplements can be found on the following pages. An overview of each supplement is provided below.

Supplement 1. Pandemic Influenza Surveillance provides recommendations to state and local partners on virologic surveillance for influenza viruses and on epidemiologic (disease) surveillance to monitor the health impact of influenza

[3] A federally qualified health center (FQHC) is a type of provider defined by the Medicare and Medicaid statutes. FQHCs include health centers receiving grants under section 330 of the Public Health Service Act, certain tribal organizations, and clinics designated by HHS as FQHC Look-Alikes. More information may be found at: http://www.cms.hhs.gov/providers/fqhc/

[4] Health care safety net providers deliver care to low-income and other vulnerable populations, including the uninsured and those covered by Medicaid. Many of these providers have either a legal mandate or an explicit policy to provide services regardless of a patient's ability to pay (http://www.ahcpr.gov/data/safetynet/faq.htm). Major safety net providers include public hospitals and community health centers as well as teaching and community hospitals, and private physicians.

(outpatient, hospital, and mortality surveillance). The Interpandemic and Pandemic Alert Period recommendations focus on disease surveillance during regular influenza seasons, as well as on surveillance for human cases of infection with avian influenza A (H5N1) or other novel strains of influenza. They also address preparedness planning to lay the groundwork for enhanced disease surveillance during a pandemic.

The Pandemic Period Recommendations focus on surveillance activities that will be undertaken if a pandemic virus is reported overseas or if a pandemic virus emerges in or enters the United States. These activities include ongoing virologic surveillance to monitor genetic and antigenic changes in the pandemic virus, including changes in its drug susceptibilities.

Supplement 2. Laboratory Diagnostics provides recommendations to state and local public health partners on the use of diagnostic tests to detect, characterize, and monitor novel subtypes of influenza, including avian influenza A (H5N1) and other viruses with pandemic potential. The Interpandemic and Pandemic Alert Period recommendations focus on laboratory testing in support of seasonal influenza surveillance, on laboratory-based detection of novel subtypes of influenza, and on preparedness planning to support the laboratory component of the response to an influenza pandemic (e.g., detection and characterization of viruses, case reporting, specimen management, and surge capacity issues).

The Pandemic Period recommendations focus on provision of laboratory support for disease surveillance and for clinicians and hospitals. The Pandemic Period Recommendations also cover occupational health issues for laboratory workers.

Supplement 3. Healthcare Planning provides guidance to healthcare partners on developing effective institutional plans for responding to an influenza pandemic. It focuses on Interpandemic Period guidance for healthcare preparedness planning in such areas as pandemic influenza surveillance, incident management infrastructure, hospital communications, education and training, patient triage, clinical evaluation and admission, facility access, occupational health, vaccine and antiviral drug use, surge capacity, and mortuary issues. Also considered is planning for providing care in non-hospital settings including clinics, physician's offices, and the alternative care sites that will be set up if hospital-bed capacity is exceeded during a pandemic.

The Pandemic Period guidance recommendations focus on activation of institutional pandemic influenza response plans.

Supplement 4. Infection Control provides recommendations to healthcare and public health partners on basic principles of infection control for limiting the spread of pandemic influenza. These principles are common to the prevention of other infectious agents spread by respiratory droplets. Guidance is included on the selection and use of personal protective equipment, hand hygiene, safe work practices, cleaning and disinfection of environmental surfaces, handling of laboratory specimens, and postmortem 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 complications, and issues concerning occupational health.

Supplement 4 also provides guidance on how to adapt infection control practices in specific healthcare settings, including hospitals, nursing homes and other long-term care facilities, pre-hospital care (Emergency Medical Services), home healthcare, and medical offices and other ambulatory care settings. The section on hospital care covers detection of entering patients who may be infected with pandemic influenza, implementation of source-control measures to limit virus dissemination from respiratory secretions, hospitalization of pandemic influenza patients, and detection and control of nosocomial transmission. Supplement 4 also includes recommendations on infection control measures and care of pandemic influenza patients in the home, as well as in alternative care sites that may be established if local hospital capacity is overwhelmed by a pandemic.

Given some uncertainty about the characteristics of a new pandemic strain, all aspects of preparedness planning for pandemic influenza must allow for flexibility and real-time decision-making that take new information into account as the situation unfolds. If the new virus is unusual in transmissibility, virulence, or in any other way, HHS and its partners will provide state and local partners with updated infection control guidance.

Supplement 5. Clinical Guidelines focus on the initial screening and clinical assessment of patients who present from the community with fever and/or respiratory symptoms during the Interpandemic, Pandemic Alert, and Pandemic Periods. The Appendices include information on the clinical presentation and complications of influenza, the clinical features of human infection with avian influenza A (H5N1), and management of secondary bacterial pneumonia during a pandemic.

During the Interpandemic and Pandemic Alert Periods, early recognition of an illness caused by a novel influenza strain will rely on a combination of clinical and epidemiologic features. During the Pandemic Period (with a setting of high community prevalence) diagnosis will likely be more clinically oriented, as exposure history will become less helpful and the likelihood will be high that any severe influenza-like illness would be pandemic influenza.

Supplement 6. Vaccine Distribution and Use provides recommendations to state and local partners and other stakeholders on planning for the different elements of a pandemic vaccination program. The focus of the Interpandemic Period recommendations is on planning for vaccine distribution, vaccination of priority groups, adverse event monitoring, tracking of vaccine supply and administration, vaccine coverage and effectiveness studies, communications, legal preparedness, and training. The focus of Pandemic Period recommendations is on working with public health and healthcare partners to implement plans for vaccine distribution and use.

Supplement 7. Antiviral Drug Distribution and Use provides recommendations to state and local partners on the distribution and use of antiviral drugs for treatment and prophylaxis during an influenza pandemic. The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning for rapid distribution and use of antiviral drugs (e.g., procurement, distribution to priority groups, legal preparedness, training, and data collection on use, effectiveness, safety, and the development of drug resistance). The Interpandemic and Pandemic Alert Period recommendations also cover the use of antiviral drugs in management and containment of cases and clusters of infection with novel strains of influenza, including avian influenza A (H5N1) and human strains with pandemic potential.

The Pandemic Period recommendations focus on local use of antiviral drugs in three situations: when pandemic influenza is reported abroad, when there is limited transmission of pandemic influenza in the United States, and when there is widespread transmission in the United States. Recommendations for optimal use of limited stocks of antivirals will be updated throughout the course of an influenza pandemic, in accordance with new epidemiologic and laboratory data. National recommendations will also be updated as an effective pandemic influenza vaccine becomes available.

Supplement 8. Community Disease Control and Prevention provides recommendations to state and local partners on the use of disease containment strategies to prevent disease transmission at different phases of an influenza pandemic. The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning for implementation of containment measures. They 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, relatively intense individual-level containment measures (e.g., patient isolation and identification, monitoring, and quarantine of contacts) may be used without causing undue strain on limited public health and health care resources.

The Pandemic Period recommendations focus on measures that may be beneficial and practical when there is a large number of cases and extensive viral transmission. In such a setting, individual-level measures may no longer be effective or feasible (e.g., if hospital isolation beds can no longer accommodate all patients, if most contacts cannot be traced in time to prevent further exposures, or if staffing constraints make contact-tracing impractical). In that case, state and local health departments may consider measures that decrease social contact within groups or whole communities (e.g., quarantine of groups of exposed persons, cancellation of public events, snow days, self-shielding, or widespread community quarantine). Effective use of community containment measures during a pandemic will require continuous evaluation of such parameters as viral transmissibility, the number and geographic distribution of cases, the reproductive rate of epidemic propagation, and the nature and severity of illness.

Supplement 9. Management of Travel-Related Risk of Disease Transmission provides recommendations to state and local partners on travel-related containment strategies that may be employed during different phases of an influenza pandemic. These strategies range from distribution of health alert notices, to isolation and quarantine of new arrivals, to restriction or cancellation of nonessential travel. State and local health departments will implement these strategies in association with Quarantine Stations located at 11 ports of entry.

The Interpandemic and Pandemic Alert Period recommendations focus on preparedness planning, as well as on management of arriving ill passengers on international flights or cruise ships. The Pandemic Period recommendations focus on travel-related measures to prevent disease spread into, out of, or within the United States.

Supplement 10. Public Health Communications describes seven key risk communications concepts. During the Interpandemic Period, national, state, and local health communications professionals should focus on preparedness planning and on building flexible, sustainable communications networks. During the Pandemic Alert Period, they should work collaboratively to develop and disseminate consistent and accurate messages. During the Pandemic Period, they should focus on well-coordinated health communications to support public health interventions designed to help limit influenza-associated morbidity and mortality and to address related social and economic changes.

Supplement 11. Psychosocial Workforce Support Services addresses the psychological and social ("psychosocial") needs of occupational groups who participate in the response to an influenza pandemic. These groups include:

- Healthcare workers who provide medical care for the children and adults who fall ill
- Emergency field workers and other public health personnel who help control disease spread
- First responder or non-governmental organizations whose employees assist affected groups (e.g., quarantined persons or patients at home or in hospitals)
- Essential service workers whose activities maintain normal social functions and minimize social disruption
- The family members of all of these groups

Recommendations for the Interpandemic and Pandemic Alert Periods focus on institutionalization of psychosocial support services that help workers manage emotional stress and resolve personal, professional, and family issues related to the response to an influenza pandemic. They also cover preparation of informational materials for distribution to employees and their families during the emergency. Finally, they cover the development of Workforce Resilience Programs that include assistance for families of responders who may be deployed in the field and inaccessible for extended periods of time.

Recommendations for the Pandemic Period focus on delivery of psychosocial support services to response workers, on provision of occupational health information to healthcare providers, and on implementation of Workforce Resilience Programs.

BOX 1. ISSUES FOR STATE AND LOCAL PARTNERS THAT WILL REQUIRE REAL-TIME GUIDANCE DURING A PANDEMIC

- What are the case definitions for suspected and confirmed cases of pandemic influenza? What types of epidemiologic data should be collected? (The answers may change over time, depending on the characteristics of the pandemic virus and the geographical spread of the pandemic.)
- What are the drug susceptibilities of the pandemic virus?
- What amounts of antiviral drugs are available to your state from public and private stocks?
- What amounts of pandemic influenza vaccine are available to your state from public stocks?
- Which groups of people are at greatest occupational and medical risk (i.e., what are the age-specific and occupational attack rates)? What modifications should be made to the national recommendations for distribution and use of antiviral drugs and vaccines to reflect this information?
- Which laboratory tests may be used locally for laboratory confirmation of pandemic-influenza cases? Which isolates should be sent to CDC for subtyping?
- How fast is the pandemic spreading in your area? What does local surveillance data on the number of hospitalizations and deaths suggest in regard to:
  - Distribution of hospital supplies and hospital beds on a regional or statewide basis
  - How fast local and regional hospital resources are being depleted
  - Implementation of school closings and other community containment measures
  - Situating and opening alternative care sites and quarantine facilities
  - Absentee rates at hospitals and at businesses that provide essential services
  - Impact of the outbreak on the public health and medical workforce
- Is anything unusual or unexpected? If so, should any modifications be made in infection control practices or in the detection or management?
- Is there evidence from statistical modeling that predicts where and how fast the pandemic will spread?

BOX 2. ESTABLISHING A PANDEMIC INFLUENZA COORDINATING COMMITTEE FOR STATE-LEVEL PLANNING

Coordinating Committee members may include:

- Representatives from the Governor's Office (supplemented by representatives of the mayor's office for large metropolitan areas)
- Representatives from local, county, or district health departments
- Representatives from territorial and tribal health departments
  - State Epidemiologist
  - State Laboratory Director
- Public Health Information Officer
- Public Affairs/Communications Officer
- Immunization Project Director
- State Strategic National Stockpile (SNS) Coordinator
- Representatives from:
  - State and Local Offices of Emergency Preparedness
  - State Mental Health Office
  - State Transportation Office
  - Office of the General Counsel at the state health department
- Representatives from HRSA and CDC

Membership of the Pandemic Influenza Coordinating Committee may overlap with state or local bioterrorism preparedness coordinating committees.

Stakeholders who provide input to the Coordinating Committee may include:

- Infectious disease physicians
- Public health and private clinical laboratories
- Immunization program personnel
- State public health associations or state associations of county and city health officials
- State primary care associations representing health centers in the state
- Hospitals and other healthcare facilities, including VA Hospitals, DoD Hospitals, and Indian Health Service facilities
- Medical societies and nursing organizations
- Pharmacists
- Community immunizers
- Emergency medical services and emergency departments within hospitals
- Local media officials

Additional participants may include

- Volunteer organizations involved in response and recovery to various disasters
- Social service agencies
- Law enforcement agencies
- Infectious disease experts from universities
- Funeral directors
- Local military installations
- Large industries or employers in the area
- State aviation authorities
- Representatives of public utilities
- Education administrators

BOX 3. INFLUENZA: INFORMATION AND DEFINITIONS

Influenza

- Influenza is an acute viral disease of the respiratory tract characterized by fever, headache, myalgia, prostration, coryza, sore throat, and cough. Otitis media, nausea, and vomiting are also commonly reported among children.
- For surveillance purposes, influenza-like illness (ILI) is defined as respiratory illness with temperature greater than 38°C plus either sore throat or cough.

Seasonal or Interpandemic Influenza

- Seasonal influenza occurs each winter, primarily causing self-limiting disease for 2 to 7 days in most infected individuals. Influenza complications—especially viral and bacterial pneumonias—can cause severe illness or death in infants, the elderly, the immunocompromised, and those with certain chronic medical conditions.
- As seasonal influenza viruses replicate and evolve, they develop small changes in their surface antigens that allow them to evade existing immunity to influenza in the human population. Influenza vaccines must therefore be reformulated each year to provide protection against currently circulating strains of influenza A and B.

Pandemic Influenza

- Pandemic influenza is an uncommon type of influenza A that causes greater morbidity and mortality than seasonal influenza. An influenza pandemic occurs when a new influenza A virus (a "pandemic influenza virus") emerges in the human population, causes serious illness, and then spreads easily from person to person worldwide. Influenza pandemics occurred three times during the twentieth century—in 1918, 1957, and 1968.

Novel Strains of Influenza

- Novel strains of influenza are newly identified influenza viruses that require close monitoring to determine whether they (or their genetic offshoots) are capable of pandemic spread. They may include avian or animal influenza strains that can infect humans (like avian influenza A [H5N1]), or new, or re-emergent, human viruses that cause cases or clusters of human disease.

APPENDIX 1. CHECKLIST OF LEGAL CONSIDERATIONS FOR PANDEMIC INFLUENZA

The following checklist is a planning tool highlighting the relevant partners, resources, planning considerations, due process considerations, and issues of legal liability and immunity that may arise in the context of pandemic influenza. Next to each consideration are listed the legal partners (e.g., public health, hospitals, public safety, emergency management, judiciary) who may be called upon to address these considerations as part of the affected community's response. The challenge of the public health response is to protect the health of many, while safeguarding the rights of the individual. An integrated and coordinated response by attorneys at all levels in the community is essential to achieving this goal.

The checklist format is not intended to set forth mandatory requirements or establish a national standard for legal preparedness. Each state and local jurisdiction should determine for itself whether it is adequately prepared for disease outbreaks in accordance with its own laws and procedures. Relevant federal law also should be reviewed and statutes harmonized, as feasible.

Planning Considerations

- ❑ Ensure that public health personnel have a basic understanding of the intersection among federal, state, local, and tribal laws regarding quarantine and isolation as they relate to international airports and interstate border crossings. [public health/public safety/emergency management]
- ❑ Where applicable, draft or update legal orders, motions, and templates requiring medical evaluation of non-compliant persons who meet the pandemic influenza case definition and have symptoms of pandemic influenza. [public health/hospitals]
- ❑ Ensure that legal counsel has reviewed the feasibility of requiring persons to self-monitor for medical conditions (e.g., temperature checks) and (where applicable) drafted legal orders or agreements. [public health]
- ❑ Ensure that legal counsel has reviewed the feasibility of issuing "exclusion" orders (i.e., excluding contacts from using public transportation, attending public meetings) and, where applicable, drafted templates and legal orders. [public health/public safety/emergency management]
- ❑ Ensure the existence of a statute, regulation, or other administrative mechanism authorizing isolation/quarantine for pandemic influenza. [public health/public safety/judiciary]
- ❑ Draft legal orders, motions, and templates for isolation/quarantine in homes, hospitals, or other designated facilities. [public health/hospitals/emergency management/public safety]
- ❑ Ensure that legal counsel has reviewed the feasibility of using electronic methods to monitor suspected non-compliant individuals in home isolation and/or quarantine. [public health/public safety]
- ❑ Ensure that legal counsel has reviewed draft legal orders, motions, and templates to quarantine facilities and to credential ingress and egress into such facilities. [public health/public safety/emergency management]
- ❑ Ensure that legal counsel has reviewed the feasibility of using faith-based organizations to assist or provide services to persons in isolation and quarantine. [public health]
- ❑ Ensure that public health officials have reviewed the availability of workers' compensation and/or other forms of financial support for persons unable to return to work because of an isolation/quarantine order. [public health]
- ❑ Ensure that legal counsel has considered whether the health department should issue documents designed to assist with reintegration of persons subject to isolation/quarantine order (e.g., letter to employer or school explaining that patient is no longer infectious). [public health]
- ❑ Ensure that legal counsel has reviewed agreements relating to overtime and/or flexibility of hours for staff. [public health/hospitals/public safety/emergency management]
- ❑ Ensure that legal counsel has a clear understanding of legal authorities relevant to environmental remediation of buildings. [public health/hospitals/emergency management]

Partnerships/Outreach

- ❑ Assemble a legal preparedness task force with representation from public health, public safety, hospitals, emergency management, judiciary, and other relevant individuals and/or organizations at various levels of authority (federal, state, tribal, local, cross-border). [public health/public safety/hospitals/emergency management/judiciary]
- ❑ Establish procedures for enforcement of isolation/quarantine orders. [public health/public safety]
- ❑ Provide public safety personnel with educational materials relating to pandemic influenza and have a clear understanding for how to enforce an isolation/quarantine order. [public health/public safety]
- ❑ Ensure that procedures or protocols exist between hospitals and public health to manage a possible or known pandemic influenza case-patient who attempts to leave the hospital against medical advice. [public health/hospitals/public safety]
- ❑ Where applicable, draft memoranda of agreement (MOA) or understanding (MOU) to allow for the loaning of facilities or other services necessary to implement a quarantine and/or isolation order for persons who cannot be isolated at home (e.g., travelers, homeless populations). [public health/hospitals/emergency management]
- ❑ Ensure that judges and attorneys in the area, through local bar organizations or other entities, have received educational materials, training, or information related to SARS and the potential use of isolation/quarantine to interrupt disease transmission. [public health/judiciary]
- ❑ Ensure that legal counsel has reviewed and/or drafted data sharing/data use/confidentiality agreements related to sharing of confidential patient medical information between public health and other partners. [public health/hospitals/public safety/emergency management]

Due Process Considerations

- ❑ Draft legal orders and templates using terms such as "quarantine," "isolation," and "detention" consistently. [public health/judiciary)
- ❑ Ensure that legal counsel has reviewed all draft isolation/quarantine orders and forms, as well as applicable administrative hearing procedures, to ensure concurrence with basic elements of due process (e.g., adequate notice, opportunity to contest, administrative determination). [public health/judiciary]
- ❑ Ensure that procedures or protocols exist to ensure that persons subject to an isolation/quarantine order have access to legal counsel, if desired (e.g., list of attorneys willing to provide services at little or no cost). [public health/judiciary]
- ❑ Ensure that legal counsel has analyzed procedures needed to satisfy due process in different isolation/quarantine scenarios (e.g., "voluntary" home isolation, isolation in a guarded facility, exclusion from certain public activities). [public health/judiciary]
- ❑ Where applicable, ensure that public health officials have worked with the local court system to develop a 24 hours a day, 7 days a week "on call" list of judges or hearing officers to review emergency requests for isolation/quarantine. [public health/judiciary]
- ❑ Ensure that public health officials have worked with the local court system to develop a plan for hearing cases and/or appeals for persons subject to isolation/quarantine orders (e.g., participation via telephone, video conference). [public health/judiciary]

Legal Resources and Statutes

- ❑ Ensure that legal counsel has reviewed and has a clear understanding of the legal resources and tools relevant to a community's public health response. [public health/judiciary/emergency management]

  Such resources and tools include:

  - Draft Model State Emergency Health Powers Act
    www.publichealthlaw.net/MSEHPA/MSEHPA2.pdf

- Emergency Management Assistance Compact (model agreement)
  http://www.emacweb.org/?13
- Emergency Management Assistance Compact (as implemented in a state or jurisdiction)
- Memorandum of Understanding for Establishment of Local Public Health Mutual Aid and Assistance System:
  www.publichealthlaw.net/Resources/ResourcesPDFs/MOU.pdf
- American Bar Association Draft Checklist for State and Local Government
  Attorneys to Prepare for Possible Disasters
  http://www.publichealthlaw.net/Resources/BTlaw.htm
- Legal Authorities for Isolation and Quarantine
  http://www.cdc.gov/ncidod/sars/legal.htm
- Quarantine and Isolation: Lessons Learned from SARS
  http://www.louisville.edu/medschool/ibhpl/images/pdf/SARS%20REPORT.pdf
- Checklists on Legal Preparedness for Bioterrorism and other Public Health Emergencies
  http://www.publichealthlaw.net/Resources/BTlaw.htm
- Legal Materials Related to Public Health Legal Preparedness
  http://www2a.cdc.gov/phlp/sub_menu.asp

Additional materials and resources may be posted at http://www.cdc.gov/phlp/index.htm

❑ Distribute draft letters or fact sheets to hospitals and other healthcare providers describing permissible uses and disclosures of health information for public health purposes under the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) (www.hhs.gov/ocr/hipaa/). [public health/hospitals]

❑ Where applicable, ensure that legal counsel understands procedures for declaring a public health emergency (at various levels of government) and consequences of such a declaration. [public health/public safety/emergency management]

❑ Ensure that legal counsel is familiar with the requirements of the Emergency Medical Treatment and Active Labor Act (EMTALA) (www.aaem.org/emtala/index.shtml) and has determined if such requirements have been incorporated into public health and hospital planning for pandemic influenza. [public health/hospitals]

❑ Ensure that legal counsel has reviewed hospital screening and admission procedures for potential pandemic influenza patients (e.g., establishment of evaluation clinics for persons with influenza-like symptoms) for compliance with EMTALA. [public health/hospitals]

❑ Ensure that legal counsel has reviewed potential EMTALA implications of a community-wide EMS protocol for transport of pandemic influenza patients (e.g., protocol requiring transport of pandemic influenza patients to a hospital or facility other than the hospital that owns the ambulance). [public health/hospitals/emergency management]

Legal Liability and Immunity

❑ Ensure that legal counsel has reviewed the potential legal liability of implementing "working" quarantine for essential service personnel. [public health/hospitals]

❑ Ensure that legal counsel has reviewed the potential legal liability of housing pandemic influenza patients in home isolation with non-exposed residents subject to infection control precautions. [public health]

❑ Ensure that legal counsel has reviewed liability/immunity for volunteers providing assistance or services to persons in isolation/quarantine. [public health/emergency management]

❑ Ensure that legal counsel has reviewed hospital employment policies on emergency licensure and/or employment of retired or non-medical personnel or personnel from other medical departments or hospitals. [public health/hospitals]

APPENDIX 2. FACT SHEET: PRACTICAL STEPS FOR LEGAL PREPAREDNESS

Step 1: Know your legislation

State and local public health officers need to be familiar with the legal requirements in their jurisdictions regarding isolation of infectious persons and quarantine of exposed persons. Although most states have laws to compel isolation and/or quarantine, procedures may vary widely from jurisdiction to jurisdiction. Key persons, such as legal counsel, judges, and policymakers, should be identified and made part of your jurisdiction's planning for pandemic influenza.

HHS has statutory authority, which has been delegated to CDC, to quarantine or isolate individuals who have been exposed to or infected with pandemic influenza. President Bush added pandemic influenza to the list of quarantineable diseases by Executive Order 13375 on April 1, 2005.

Step 2: Plan "due process"

Procedural due process is implicated when the government seeks to deprive an individual of "liberty" interests within the meaning of the Due Process Clause of the Fifth or Fourteenth Amendment to the U.S. Constitution. Many states, through statute or regulation, have established specific administrative and judicial schemes for affording due process to a person subject to a quarantine and/or isolation order. Schemes in other jurisdictions may not directly address this issue.

Although due process is a flexible concept and calls for procedural protections as the particular situation demands, the basic elements of due process include: adequate notice (typically through written order) of the action the agency seeks to compel; right to be heard (typically through the right to present evidence and witnesses and to contest the government's evidence and witnesses); access to legal counsel; and a final administrative decision that is subject to review in a court of law. These due process protections should not impede the immediate isolation or quarantine of an individual for valid public health reasons in an emergency situation.

Step 3: Draft key documents in advance

State and local public health officers should consider drafting key documents in advance of an emergency. These template documents can be critical time savers in an emergency. Documents that jurisdictions should consider preparing in advance include: draft quarantine and/or isolation orders; supporting declarations and/or affidavits by public health and/or medical personnel; and an explanation of the jurisdiction's due process procedures for persons subject to an isolation/quarantine order. Examples of documents created by other jurisdictions are found at: http://www.cdc.gov/phlp/index.htm

Step 4: Contact other jurisdictions

It is possible for federal, state, tribal, and local health authorities simultaneously to have separate but concurrent legal quarantine power in a particular situation (e.g., an arriving aircraft at a large city airport). Furthermore, public health officials at the federal, state, tribal, and local level may occasionally seek the assistance of their respective counterparts, e.g., law enforcement, to assist in the enforcement of a public health order. State and local public health officers should therefore be familiar with the roles and responsibilities of other jurisdictions: vertically (local, state, tribal, federal), horizontally (public health, law enforcement, emergency management, and health care), and in geographical clusters (overlapping state/local neighbors).

Step 5: Engage the courts in advance

Some jurisdictions may rely on older public health statutes that have not been amended in over half a century, while other jurisdictions may have recently revised their legal authorities to respond to bioterrorism or other public health emergencies. Judges who may be called upon to review a public health order may not be familiar with the state or local health authority's

broad public health powers. During the 2003 SARS outbreak in Toronto, Canada, for example, many judges were unaware of the health officer's broad ex parte authority to compel isolation/quarantine under rarely used laws.

Step 6: Anticipate practical problems

State and local public health officers need to be prepared for the practical problems that may arise in affording adequate due process protections to persons subject to isolation and/or quarantine orders. Such problems may include how to arrange for the appearance and representation of persons in quarantine (e.g., video conference or other remote means); how to serve an isolation/quarantine order (likely through law enforcement) and other procedures to advise persons of their legal rights; and isolation arrangements for transient or homeless populations.

Step 7: Communication

Communication planning is vital not only for an effective public health response but also for an effective legal response to a public health emergency. Public health agency counsel should be aware of media training available to other public health officers. During the SARS and monkeypox outbreaks, CDC, through the Public Health Law Program (http://www.cdc.gov/phlp/index.htm), established telephone conferences for public health legal counsel to share experiences and engage in peer-to-peer consultations. Efforts are now underway to develop materials to assist state and local public health departments in conducting further outreach on emergency public health issues to the legal community through local bar associations.

supplement 1
pandemic influenza surveillance

TABLE OF CONTENTS

SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES IN PANDEMIC INFLUENZA SURVEILLANCE

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

State and local responsibilities:

- Continue to employ state influenza surveillance coordinators to oversee improvements in influenza surveillance (e.g., virologic, outpatient, hospitalization, and mortality surveillance).
- Conduct influenza surveillance year round, where possible.
- Implement enhanced surveillance for detection of the first U.S. cases of novel virus infection.

State and large local public health laboratory responsibilities:

- Isolate and subtype influenza viruses year round.
- Improve capacity for rapid identification of unusual influenza strains (see also **Supplement 2**).

HHS responsibilities:

- Coordinate and maintain all components of the National Influenza Surveillance System (Table 1).
- Help identify and characterize influenza strains collected by the U.S. WHO Collaborating Laboratory Network.
- Assist USDA, as requested, in monitoring new influenza strains in poultry and swine.
- Work with state and local partners to:
  - Implement enhancements to the National Influenza Surveillance System.
  - Explore options for additional enhancements to improve pandemic surveillance.

PANDEMIC PERIOD

If an influenza pandemic begins in the United States or another country:

State and local responsibilities:

- Implement enhanced surveillance for detection of the first cases.
- Enhance all influenza surveillance components (virologic, outpatient, hospitalization, and mortality).
- Communicate to all partners the heightened need for timely and complete surveillance data.

HHS responsibilities:

- Provide technical support, as requested, to ministries of health and WHO to track the pandemic virus and gather epidemiologic data on risk factors for infection or severe illness.
- Issue updated case definitions and guidance for laboratory testing and enhanced surveillance.
- Assist state and local health departments, as requested.
- Analyze influenza surveillance data on a regular and timely basis.

S1-I. RATIONALE

Pandemic influenza surveillance includes surveillance for influenza viruses (virologic surveillance) and surveillance for influenza-associated illness and deaths (disease surveillance).

The goals of virologic surveillance are to:

- Rapidly detect the introduction and early cases of a pandemic influenza virus in the United States.
- Track the virus' introduction into local areas.
- Monitor changes in the pandemic virus, including development of antiviral resistance.

The goals of disease surveillance are to:

- Serve as an early warning system to detect increases in influenza-like illness (ILI) in the community.
- Monitor the pandemic's impact on health (e.g., by tracking outpatient visits, hospitalizations, and deaths).
- Track trends in influenza disease activity and identify populations that are severely affected.

Virologic and disease surveillance data—supplemented by data from outbreak investigations and special studies—can help decision-makers identify effective control strategies and re-evaluate recommended priority groups for vaccination and antiviral therapy. They can also facilitate efforts to mathematically model disease spread during a pandemic. The national influenza surveillance system, which monitors seasonal influenza, will provide the virologic and disease surveillance data needed to guide response efforts during a pandemic (www.cdc.gov/flu/weekly/fluactivity.htm; Table 1). When a pandemic begins, some enhancements might be instituted to improve geographic and demographic coverage and increase the amount of detail captured by particular components of the national influenza surveillance system.

S1-II. OVERVIEW

Supplement 1 provides recommendations to state and local partners on surveillance for influenza viruses and on disease surveillance to monitor the health impact of influenza. The recommendations for the Interpandemic and Pandemic Alert Periods focus on disease surveillance during interpandemic influenza seasons, as well as on surveillance for human cases of infection with avian influenza A (H5N1) or other novel strains of influenza. They also address preparedness planning for enhanced disease surveillance during a pandemic. The recommendations for the Pandemic Period focus on surveillance activities that will be undertaken if a pandemic virus is reported outside the United States or if a pandemic virus emerges in or enters the United States.

Outbreak investigations and special studies (e.g., to address questions about viral transmission or the clinical course of disease) are described in Part 1. Efforts to monitor the effectiveness and safety of vaccines and antiviral drugs are addressed in **Supplement 6** and **Supplement 7**.

The U.S. Department of Agriculture (USDA), through its Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS) program, works with the states and the agricultural industry to conduct influenza surveillance in domestic animals. USDA also monitors wild avian populations for highly pathogenic avian influenza (HPAI) and other diseases of concern through the APHIS Wildlife Services program. Active and passive surveillance for influenza A viruses in poultry in the United States have increased substantially since the outbreak of HPAI in Pennsylvania and surrounding states in 1983 and 1984.

S1-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

CDC maintains and coordinates a national influenza surveillance system that identifies circulating influenza viruses and monitors disease activity during interpandemic influenza seasons. The seven components of the national influenza surveillance system—whose participants include healthcare providers, vital statistics offices, and local and state health departments and

public health laboratories—are listed in Table 1 and described in detail in Appendix 1. Components address virologic surveillance to determine when, where, and which influenza viruses are circulating, details of the various types of disease surveillance, and an overall state-level assessment of influenza activity.

A. Virologic surveillance during interpandemic influenza seasons

Public health goals for routine surveillance of influenza viruses are to identify and characterize circulating strains to inform annual vaccine formulation and to identify and characterize strains with pandemic potential. State and local public health laboratories, Department of Defense (DOD) laboratories, and clinical laboratories (including hospital and private commercial laboratories) should continue to participate in surveillance for influenza viruses through the U.S.-based collaborating laboratories of the World Health Organization (WHO) Global Influenza Surveillance Network and the National Respiratory and Enteric Virus Surveillance System (NREVSS) (see **Supplement 2)**. The aim of the network of WHO and NREVSS laboratories is to monitor influenza trends and compare seasonal differences, rather than to record all influenza tests performed in the United States. Network enhancements that might be useful during the Pandemic Period are discussed below (see S1-III.E).

B. Disease surveillance during interpandemic influenza seasons

1. National influenza surveillance system

The public health goals of influenza disease surveillance are to serve as an early warning system and to detect increases in ILI at the local level, to monitor the impact of influenza on health (e.g., by tracking outpatient visits, hospitalizations, and deaths), and to track trends in influenza disease activity and identify populations that are severely affected. During the Interpandemic Period, these goals are accomplished through the components of the national influenza surveillance system (Table 1). Public health and healthcare partners should continue to participate in these components of the national influenza surveillance system, which address the following types of disease surveillance.

a) Outpatient surveillance

- Sentinel Provider Network (SPN). Approximately 2,300 healthcare providers nationwide report the number of weekly outpatient visits for ILI and submit specimens from a small subset of patients to state public health laboratories for influenza virus testing.

b) Hospital surveillance

- Emerging Infections Program (EIP) influenza project. Laboratory-confirmed influenza-associated hospitalizations of children aged <18 years are monitored in 11 communities and reported to CDC on a bi-weekly basis.
- New Vaccine Surveillance Network (NVSN). Laboratory-confirmed influenza-associated hospitalizations of children aged <5 years are monitored in three communities and reported to CDC on a bi-weekly basis.

c) Mortality surveillance

- 122 Cities Mortality Reporting System. Vital statistics offices in 122 U.S. cities report pneumonia and influenza (P&I)-related deaths on a weekly basis.
- National Notifiable Disease Surveillance System (NNDSS) pediatric deaths. State health departments report influenza-associated pediatric deaths to CDC.

d) State-level assessments

- State and territorial epidemiologists' reports. Health departments provide weekly reports on the overall level of influenza activity in their states/territories.

It is not possible to provide an absolute case count for influenza or to determine population-based rates of infection or illness on a national level because many infected persons are asymptomatic or experience only mild illness and do not seek medical care. Also, laboratory testing is rare in less severe cases, and testing late in the course of illness (e.g., in cases with severe complications) can yield false-negative results because the patient is no longer shedding virus. Nevertheless, weekly data on outpatient visits for ILI, hospitalizations, and deaths allow CDC to monitor regional disease trends and to compare the timing and intensity of the current season to that of previous seasons.

Influenza surveillance has traditionally been conducted from October through May. In recent years, however, increasing numbers of healthcare providers, laboratories, and health departments have conducted influenza surveillance year-round. This enhancement is an important part of surveillance for novel strains of influenza.

2. Influenza surveillance coordinators

Currently, health departments in all 50 states—as well as in Chicago, New York City, and Washington, DC—have dedicated influenza surveillance coordinators who work at least part-time on influenza surveillance. The roles of the coordinators are to:

- Maintain the current influenza Sentinel Provider Network
- Oversee the surveillance enhancements described below
- Promote year-round influenza surveillance
- Remain in close contact with the CDC Influenza Branch
- Maintain working relationships with the state public health laboratory

C. Surveillance for novel strains of influenza during the Pandemic Alert Period

1. Monitoring for novel strains of influenza

During the Pandemic Alert Period, CDC will issue recommendations for enhanced surveillance to identify patients at increased risk for infection with a novel virus. Novel influenza strains might include avian influenza viruses that can infect humans, other animal influenza viruses (such as swine influenza viruses) that can infect humans, or new or re-emergent human influenza strains that cause cases or clusters of human disease.

The specific recommendations will depend on the epidemiology of the virus and the clinical characteristics of the human cases as they are known at the time, and will most likely focus on severely ill, hospitalized, or ambulatory patients who meet certain epidemiologic and clinical criteria. For example, since February 2004, CDC has recommended enhanced surveillance to identify patients potentially infected with avian influenza A (H5N1). The current recommendations are summarized in Appendix 2.

State and local health departments will be notified of current recommendations via the Health Alert Network (HAN) and Epi-X. Health departments should distribute the recommendations to healthcare providers and will be responsible for receiving initial reports of potential cases in their jurisdictions.

Once a novel strain detected abroad exhibits sustained human-to-human transmission (WHO Phase 6), recommendations for further intensified virologic and disease surveillance will be issued and might include recommendations for stepped-up disease surveillance at U.S. ports of entry (see **Supplement 8**).

2. Reporting novel strains of influenza

- Clinicians should immediately contact the health department when they suspect a human case of infection with an avian or animal strain of influenza or with any other novel human influenza strain. Clinical algorithms for managing patients with possible novel influenza infection are provided in **Supplement 5.**

- State and local health departments should in turn immediately report to CDC any influenza cases that:
  - Test positive for a novel influenza subtype, *or*
  - Meet the enhanced surveillance case definition in effect at that time, *and*
  - Cannot be subtyped in the state public health laboratory because appropriate reagents or biocontainment equipment is not available (see **Supplement 2**).

Reference testing guidelines for potential pandemic strains of influenza are provided in **Supplement 2**.

- Health departments should call the CDC Emergency Response Hotline (770-488-7100) to report a suspected case of infection with avian influenza A (H5N1) or any other novel influenza virus. This number is available 24 hours a day, 7 days a week. Hotline staff will notify a member of the Influenza Branch who will contact the health department to answer questions and provide guidance.
- Following the initial telephone report, health department officials should complete a CDC case screening and report form (obtained from the Hotline or from Epi-X) that includes the CDC case ID number provided during the phone consultation. CDC staff will assist local and state health departments, as needed, in completing the form, which should be faxed to CDC at 888-232-1322 with a cover sheet that says: "ATTN: Influenza case reporting." The case screening and report form used to report suspected cases of human infection with influenza A (H5N1) is provided in Appendix 3.
- If infection with a novel influenza virus is confirmed, states may request CDC assistance with a case investigation to identify the source of infection and determine the course of illness. CDC will assist the state health department in monitoring the close contacts of the ill person.

D. Veterinary surveillance

In the United States, surveillance for avian influenza is conducted by states, the poultry industry, and the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS) (Appendix 4). Diagnostic testing is performed by state and industry laboratories, with confirmatory testing by USDA/APHIS Veterinary Services at the National Veterinary Services Laboratories in Ames, Iowa.

CDC and state health departments will continue to assist USDA and state veterinary diagnostic laboratories, as requested, in monitoring influenza strains among poultry and swine. Recent instances of human infection with avian influenza viruses are described in **Supplement 2**, Box 2.

E. Preparedness planning for virologic and disease surveillance during a pandemic

Surveillance enhancements that will be needed during a pandemic should be developed during the Interpandemic and Pandemic Alert Periods so that baseline data for interpreting information gathered during the pandemic will be available and staff will have experience and familiarity with new methodologies.

1. Virologic surveillance

During an influenza pandemic, the volume of requests for laboratory testing is expected to increase dramatically. To meet these demands, laboratories should become proficient in methods that allow efficient testing of large numbers of specimens at a lower biosafety level than BSL 3 with enhancements—which is required for viral culture of avian influenza A (H5N1) viruses. To ensure adequate virologic surveillance during a pandemic, state public health laboratories should:

- Be equipped and trained to use RT-PCR for routine influenza testing and to detect novel influenza viruses by RT-PCR or by viral culture, using proper safety precautions
- Maintain reagents and supplies to allow influenza virus testing year-round

- Develop surge capacity to handle increased testing and reporting during a pandemic
- Assist CDC, if requested, in developing an electronic mechanism for reporting influenza testing and results

CDC is currently working with state and local partners to evaluate the utility and feasibility of reporting patient-level data (including zip code and/or county of residence) through an electronic mechanism other than the Public Health Laboratory Information System (PHLIS). Such a system would allow daily (rather than weekly) reporting during a pandemic and analysis of virus spread at the county or health district level. During a pandemic—as the burden of disease increases and state and local health departments face multiple, competing demands—it might be necessary to adjust surveillance strategies and reassess the need for frequent (or daily) reporting.

2. Outpatient surveillance

Surveillance for outpatient visits for ILI is conducted via the SPN, a collaborative effort among state health departments, healthcare providers, and CDC. State health departments recruit and maintain a local network of healthcare providers who report weekly the total number of patient visits and number of patients with ILI. SPN members may also send specimens from a subset of patients with ILI to the state public health laboratory for diagnostic testing at no cost. CDC develops and maintains reporting materials and systems, serves as a data repository, and provides feedback to the states. Each state should have at least one sentinel provider per 250,000 persons (or a minimum of 10 providers in states with smaller populations) that reports year-round.

CDC is exploring options for enhancing or supplementing ILI outpatient surveillance at the national, regional, and state levels, given that healthcare providers might not be able to report ILI in a timely manner when overwhelmed with patients during an emergency. Existing electronic data sources that might increase the geographic completeness, frequency of reporting, and sustainability of ILI data include:

- BioSense system, which includes ICD-9-coded outpatient visits at DOD ambulatory-care centers and Department of Veterans Affairs outpatient clinics. Studies are underway to determine if BioSense data can be combined with SPN data in a useful way and if they can be reported and analyzed daily.
- Existing emergency department "chief complaint" monitoring systems used by several states. Studies are underway to determine if these data can be added to SPN data and if they can be reported and analyzed daily.

CDC is also working with state and local partners to evaluate the need for and utility and feasibility of expanding SPN to allow analysis of ILI data at the county or health-district level and to provide data that are updated daily rather than weekly. Options for improving the analysis of ILI data include the use of:

- Outbreak detection algorithms that might identify aberrant increases in ILI activity at the individual provider/site level
- Daily analyses of SPN data for use by CDC and state health departments. CDC does not plan to ask sentinel providers to report more than once a week.

Some states are considering the use of systematic phone surveys to supplement SPN data during a pandemic by providing estimates of local cases and affected households. CDC will explore the utility and feasibility of conducting this type of survey on a national level.

3. Hospitalization surveillance

During a pandemic, hospitalization data will be needed on a frequent basis in all parts of the country to monitor disease severity and determine the most severely affected age groups. At present, however, surveillance for hospitalizations associated with influenza is limited to the collection of data on pediatric hospitalizations in 12 large metropolitan areas (see Table 1). In January 2006, the EIP influenza project will be expanded to include laboratory-confirmed influenza-associated hospitalizations of adults as well as children.

CDC is exploring options for expanding hospitalization surveillance to obtain data from all age groups in all parts of the country and obtaining more detailed information from a small number of sites. Some options under review include:

- Continuing to work with the Council of State and Territorial Epidemiologists (CSTE) to make laboratory-confirmed influenza-associated hospitalizations nationally notifiable. A position statement to add influenza infection requiring hospitalization to the list of nationally notifiable diseases was rejected by CSTE members in June 2005 but will be resubmitted in June 2006.
- Obtaining timely hospital discharge data to estimate the number of influenza-associated hospitalizations across the country
- Adding a hospitalization surveillance component to the national BioSense system
- Developing protocols for active population-based hospitalization surveillance, including specimen collection and virologic testing from a subset of hospitalized patients in all age groups in a limited number of sites
- Developing protocols for reporting the number of influenza-associated hospitalizations

4. Mortality surveillance

The collection of mortality data can also help health departments monitor the severity of a pandemic and determine which age groups and areas are most affected. Although pediatric deaths due to laboratory-confirmed influenza are nationally notifiable (as of October 2004), timely data on influenza deaths in other age groups are limited to information provided by the 122 Cities Mortality Reporting System, which provides weekly reports of the total number of death certificates that list P&I as a cause of death and the total number of death certificates filed (Table 1). Although the National Center for Health Statistics (NCHS) also collects mortality data, these data are not available until 2-3 years after each influenza season.

During a pandemic, state and local policy-makers and public health officials will likely ask health departments to provide mortality data to guide decision-making on control and response measures. In addition, CDC will request mortality data from each state to help guide national response measures. To help ensure uniform data collection across jurisdictions, CDC will provide case definitions and reporting procedures via HAN and Epi-X.

CDC is also investigating the feasibility of obtaining mortality data through the Electronic Death Registration (EDR) Project (http://www.naphsis.org/projects/index.asp?bid=374) and the validity of estimating national mortality based on data from the 122 Cities Mortality Reporting System. State-specific mortality cannot be estimated from data provided by the 122 Cities system.

5. State influenza activity assessments

During the Interpandemic Period, state health departments provide weekly assessments of the overall level of influenza activity (i.e., none, sporadic, local, regional, widespread) in the state. These assessments are used to compare the extent of influenza activity from state to state, and are the only state-level influenza surveillance data that CDC makes publicly available during interpandemic influenza seasons. The state influenza activity assessments are used to generate the influenza activity map, which is the most frequently referenced component of national influenza surveillance (see www.cdc.gov/flu/weekly/usmap.htm). During a pandemic, CDC will recommend that these assessments be made year-round, rather than only October through May.

S1-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

During a pandemic, more detailed information on age-specific, population-based rates of severe disease and patient outcomes will be needed than can be provided through routine national surveillance. This information will be obtained through enhanced national surveillance and carefully designed studies in a limited number of sites. These data will provide information to guide response and policy development during a pandemic. Outbreak investigations and special studies are described in Part 1.

A. Enhanced surveillance

During an influenza pandemic, CDC will use data from the U.S. collaborating laboratories of the WHO Global Influenza Surveillance Network and the NREVSS to detect the introduction and early cases of a pandemic influenza virus in the United States, track the virus' introduction into local areas, and monitor changes in the pandemic virus, including development of antiviral resistance. States should conduct the following activities:

- Distribute to healthcare providers the current CDC recommendations for enhanced surveillance for the detection of the first cases of the pandemic virus in their jurisdictions.
- Facilitate the collection and testing of appropriate specimens as recommended for early detection of pandemic virus at the local level.
- Increase testing and the frequency of reporting of virologic data. The most intense testing will be necessary during the early stages of a pandemic, when detecting the introduction of the virus into a state or community is the primary goal.
- Once the virus has been identified throughout the state, the level of testing can be decreased to a level more like that of a non-pandemic influenza season. State health officials can determine the level of testing for their jurisdictions.
- As part of the effort to monitor antigenic and genetic changes and changes in antiviral resistance patterns in the pandemic virus, state public health laboratories should forward a subset of virus isolates to CDC. CDC will advise states on the number of and clinical criteria for these isolates. **Supplement 2** contains additional information on monitoring for antiviral resistance.

During an influenza pandemic, CDC will use data from SPN, hospitalization surveillance, state and territorial epidemiologists' assessments, the 122 Cities Mortality Reporting System, NNDSS, and other data systems to:

- Monitor the pandemic's impact on health
- Track trends in influenza disease activity and identify populations that are severely affected
- Serve as an early warning system to detect increases in ILI in the community

State health departments should:

- Communicate to all partners the heightened need for timely and complete surveillance data.
- Ensure that all sentinel provider surveillance sites are reporting weekly, regardless of the time of year.
- Ensure that EIP and NVSN hospitalization surveillance is active.
- Report state influenza activity level in a timely manner.
- Facilitate timely reporting of 122 Cities Mortality Reports and pediatric deaths.
- Implement state and local collection of influenza-associated mortality data and reporting of statewide mortality data to CDC, following CDC guidelines for uniform data collection and reporting.

B. Scaled-back surveillance

Enhanced surveillance will be conducted during the introduction, initial spread, and first waves of a pandemic. Over time, as more persons are exposed, the pandemic strain is likely to become a routinely circulating influenza A subtype. When that happens, the activities of the national influenza surveillance system will revert to the frequency and intensity typically seen during interpandemic influenza seasons. The return to interpandemic surveillance will occur as soon as feasible, and the change will be communicated to all surveillance partners.

TABLE 1. COMPONENTS OF THE NATIONAL INFLUENZA SURVEILLANCE SYSTEM

Activity	Surveillance type	Description
U.S. collaborating laboratories of the: • WHO Global Influenza Surveillance Network • National Respiratory and Enteric Virus Surveillance System (NREVSS)	Virologic surveillance	Collaborating laboratories report weekly to CDC the number of influenza tests performed and the number of positive results by type, and in some cases, subtype and age group. If non-subtypable viruses or unusual subtypes are detected, the specimens are sent to the state public health laboratory or to CDC for further testing.
Sentinel Provider Network (SPN)	Outpatient surveillance	Approximately 2,300 healthcare providers monitor outpatient visits for ILI (fever >100°F or 37.8°C AND sore throat and/or cough in the absence of a known cause other than influenza). Specimens from a small subset of patients are submitted to state public health laboratories for influenza virus testing.
Emerging Infections Program (EIP) influenza project	Hospital surveillance	Eleven EIP sites report to CDC cases of laboratory-confirmed influenza-related hospitalizations in children aged <18 years on a bi-weekly basis.
New Vaccine Surveillance Network (NVSN) pediatric hospitalizations	Hospital surveillance	NVSN enrolls a subset of patients aged <5 years who are hospitalized with fever or respiratory symptoms. Nose and throat swabs are obtained and tested for influenza by viral culture and RT-PCR. The rate of laboratory-confirmed influenza-related hospitalizations is reported to CDC on a bi-weekly basis.
122 Cities Mortality Reporting System	Mortality surveillance	Municipal vital records offices transmit weekly data to CDC on the total number of death certificates filed and the number with pneumonia and/or influenza listed as a cause of death.
National Notifiable Disease Surveillance System (NNDSS) influenza-associated pediatric mortality	Mortality surveillance	Participating state health departments report to CDC all laboratory-confirmed influenza-related deaths among children <18 years.
State and territorial epidemiologists' reports	State-level assessments	Health departments report on a weekly basis the overall level of influenza activity as none, sporadic, local, regional, or widespread.

APPENDIX 1. TYPES OF INFLUENZA SURVEILLANCE

A. Virologic surveillance

- A network of ~75 WHO collaborating laboratories and ~90 NREVSS collaborating laboratories report the total number of respiratory specimens tested and the number positive for influenza by type, subtype, and age group to CDC each week. (Because ~40 of the NREVSS laboratories are also WHO laboratories, the total number in the WHO/NREVSS network is ~125.) Data from the two networks are combined and analyzed together.
- WHO collaborating laboratory network
  - All 50 state health department laboratories, 4 large county public health laboratories, a DOD reference laboratory, and ~25 tertiary-care hospital and academic center laboratories participate.
  - State and county public health laboratories subtype (i.e., A/H1 vs. A/H3) ~80% of their influenza A isolates.
  - Laboratories report the number of tests performed and results by age group to CDC's Influenza Branch.
  - Approximately 30% of laboratories report specimen-level data electronically using PHLIS, ~40% report aggregate weekly data via the Internet, and ~30% report aggregate weekly data via fax.
- NREVSS collaborating laboratory network
  - Primarily hospital laboratories
  - Most do not subtype influenza viruses, and none report age-group data
  - Laboratories report aggregate weekly numbers of tests performed and results to CDC's Respiratory and Enteric Viruses Branch (REVB) by phone or Internet.
- Laboratories test for influenza viruses by viral culture, PCR, or antigen detection.
- Most laboratories maintain the ability to test for influenza year-round.
- Data are available to state health department influenza surveillance coordinators on a password-protected website that is updated once a week during October through May and periodically throughout the summer. National and regional data are made available to all states, and state-specific data (including a laboratory-specific line list) are available to the states from which the data were reported.

B. Outpatient ILI surveillance (Sentinel Provider Network)

- Network of ~2,300 primary-care providers in all 50 states record the number of outpatients seen for any reason and the number with ILI by age group and report directly to CDC each week.
- ILI is defined as fever (>100°F or 37.8°C) AND sore throat and/or cough in the absence of a known cause other than influenza.
- All providers report from October through May, and approximately one third of the regular reporters report year-round.
- The network is a collaborative effort between CDC and state health departments.
  - State health department influenza surveillance coordinators recruit and maintain a network of providers and arrange for testing, free of charge, for a subset of specimens from providers.
  - CDC develops and maintains reporting materials and systems, serves as a data repository, and provides data feedback to the states.
- Providers collect two or three specimens from patients with ILI at the beginning, middle, and end of the season and from any unusual clinical cases, severe cases, outbreak-related cases, and patients with ILI during the summer.
- Providers report to CDC via a password-protected Internet site (75%), fax (13%), or phone (12%).

- Data are available to state health department influenza surveillance coordinators on a password-protected website. Data reported by providers on the Internet are available in real time, and data reported to CDC by fax are updated once each weekday. Regional data are available to all states, whereas state-specific data are available to the states from which the data were reported.

C. Hospitalization surveillance

- Hospitalizations associated with laboratory-confirmed influenza in children are monitored in 12 metropolitan areas through two surveillance networks that report patient-level data to CDC every 2 weeks.
  - Emerging Infections Program (EIP) influenza project. Children aged <18 years are monitored in 11 metropolitan areas from October 1 through April 30; laboratory testing is part of routine patient care. The EIP influenza project will expand to include all age groups in January 2006.
  - New Vaccine Surveillance Network (NVSN). A sample of children aged <5 years is monitored in three metropolitan areas (two are EIP influenza project sites) from October 1 through March/April; all sampled children with fever and respiratory symptoms are tested on admission.

D. Mortality surveillance

- Vital statistics offices in 122 cities covering between one-fourth and one-third of the U.S. population report weekly throughout the year the total number of death certificates filed and the number with pneumonia and/or influenza listed anywhere on the death certificate, by age group. No additional information (e.g., underlying medical condition, demographics) is available. On average, there is a 15-day lag from death to report to CDC.
- Weekly mortality data from the 122 cities are compared to a seasonal baseline calculated using a robust regression procedure run on the previous 5 years of data. If the proportion of P&I deaths for a given week exceeds the baseline value for that week by a statistically significant amount, P&I deaths are said to be above the epidemic threshold, and the proportion of deaths above threshold are considered attributable to influenza.
  - Data from all 122 cities are combined, and the percentage of all P&I deaths are calculated and compared to the expected percentage for that week.
  - Data can be analyzed by age group and geographic region, but interpretation of the data requires the development of a separate baseline for each data subset. It is not valid to compare data from a particular city or region to the national baseline.
- Detailed data (e.g., person-level data including multiple causes of death, underlying medical conditions, demographics) on ~99% of deaths in the United States are available from NCHS, but these data have a time lag of ~2-3 years.
- Pediatric deaths associated with laboratory-confirmed influenza were made nationally notifiable in October 2004. During the 2004-2005 season, the condition was reportable in 13 states; many others instituted voluntary reporting until the legal requirement was passed. CDC receives electronic, patient-level data on these deaths. The timeliness of these data cannot yet be assessed.

E. State-level influenza activity assessments

State health departments report a weekly assessment of the overall level of influenza activity (none, sporadic, local, regional, or widespread) in the state (see box below). These assessments are used to compare the extent of influenza activity from state to state and represent the only state-level influenza surveillance data that CDC makes publicly available during the interpandemic influenza season.

TABLE 2. COMPONENTS OF THE NATIONAL INFLUENZA SURVEILLANCE SYSTEM

Activity level	ILI activity*/outbreaks		Laboratory data
No activity	Low	**and**	No lab-confirmed cases†
Sporadic	Not increased	**and**	Isolated lab-confirmed cases
	or		Lab-confirmed outbreak in one institution‡
Local	Not increased		Recent (within the past 3 weeks) lab evidence of influenza in region with increased ILI
Regional (doesn't apply to states with ≤4 regions)	Increased ILI in 1 region**; ILI activity in other regions is not increased	**and**	Recent (within the past 3 weeks) lab evidence of influenza in region with the outbreaks; virus activity is no greater than sporadic in other regions
	or		
	2 or more institutional outbreaks (ILI or lab confirmed) in 1 region; ILI activity in other regions is not increased		Recent (within the past 3 weeks) lab-confirmed influenza in the affected regions
Widespread	Increased ILI in ≥2 but less than half of the regions	**and**	Recent (within the past 3 weeks) lab-confirmed influenza in the affected regions
	or		
	Institutional outbreaks (ILI or lab confirmed) in ≥2 and less than half of the regions	**and**	Recent (within the past 3 weeks) lab-confirmed influenza in the state.
	Increased ILI and/or institutional outbreaks (ILI or lab confirmed) in at least half of the regions		

* ILI activity can be assessed using a variety of data sources, including Sentinel providers, school/workplace absenteeism, and other syndromic surveillance systems that monitor influenza-like illness.

† Lab-confirmed case = case confirmed by rapid diagnostic test, antigen detection, culture, or PCR. Care should be given when relying on results of point-of-care rapid diagnostic test kits during times when influenza is not circulating widely. The sensitivity and specificity of these tests vary, and the predicative value positive may be low outside of peak influenza activity. Therefore, a state may wish to obtain laboratory confirmation of influenza by testing methods other than point-of-care rapid tests for reporting the first laboratory-confirmed case of influenza of the season.

‡ Institution = nursing home, hospital, prison, school, etc.

** Region = population under surveillance in a defined geographical subdivision of a state. A region could be comprised of one or more counties and would be based on each state's specific circumstances. Depending on the size of the state, the number of regions could range from 2 to approximately 12. The definition of regions would be left to the state, but existing state health districts could be used in many states. Allowing states to define regions would avoid somewhat arbitrary county lines and allow states to establish divisions that make sense based on geographic population clusters. Focusing on regions larger than counties would also improve the likelihood that data needed for estimating activity would be available.

APPENDIX 2. INTERIM RECOMMENDATIONS: ENHANCED U.S. SURVEILLANCE AND DIAGNOSTIC EVALUATION TO IDENTIFY CASES OF HUMAN INFECTION WITH AVIAN INFLUENZA A (H5N1)

NOTE: This guidance pertains to the avian influenza A (H5N1) circulating as of October 2005 CDC will provide updated guidance for avian influenza A (H5N1) or for new situations, as needed, through the Health Alert Network.

Enhanced surveillance efforts by state and local health departments, hospitals, and clinicians are needed to identify patients at increased risk for influenza A (H5N1). Interim recommendations are as follows:

- Testing for avian influenza A (H5N1) is indicated for **hospitalized** patients with:
  - Radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established, **and**
  - History of travel within 10 days of symptom onset to a country with documented avian influenza A (H5N1) infections in poultry and/or humans. (For a regularly updated listing of H5N1-affected countries, see the World Organization for Animal Health [OIE] website at http://www.oie.int/eng/en_index.htm and the WHO website at http://www.who.int/en/).

OR

- Testing for avian influenza A (H5N1) should be considered on a case-by-case basis in consultation with state and local health departments for **hospitalized or ambulatory** patients with:
  - Documented temperature of >100.4°F (>38°C); **and**
  - One or more of the following: cough, sore throat, or shortness of breath; **and**
  - History of contact with poultry (e.g., visited a poultry farm, a household raising poultry, or a bird market) or a known or suspected human case of influenza A (H5N1) in an H5N1-affected country within 10 days prior to onset of symptoms.

APPENDIX 3. CDC HUMAN INFLUENZA A(H5) CASE SCREENING AND REPORT FORM

Human Influenza A (H5)

Human Influenza A (H5) Domestic Case Screening Form

CDC Case ID:

1. Reported By

Date reported to state or local health department: __ __ / __ __ / __ __ __ __ (m m d d y y y y)	State/ local Assigned Case ID:
Last Name:	First Name:
State:	Affiliation:	Email:
Phone 1:	Phone 2:	Fax:

2. Patient Information

City of Residence: County: State:

Age at onset: _____ ☐ Year(s) ☐ Month(s)

Race: *(Choose One)*
☐ American Indian/Alaska Native ☐ White
☐ Asian ☐ Unknown
☐ Black
☐ Native Hawaiian/Other Pacific Islander

Sex: ☐ Male ☐ Female

Ethnicity: ☐ Non Hispanic ☐ Hispanic

3. Optional Patient Information

Last Name: First Name:

4. Signs and Symptoms

A. Date of symptom onset: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

B. What symptoms and signs did the patient have during the course of illness? (check all that apply)

☐ Fever > 38° C (100.4° F) ☐ Feverish (temperature not taken) ☐ Conjunctivitis

☐ Cough ☐ Headache ☐ Shortness of breath

☐ Sore throat ☐ Other (specify): _____

C. Was a chest X-ray or chest CAT scan performed? ☐ Yes* ☐ No ☐ Unknown

If yes*, did the patient have radiographic evidence of pneumonia or respiratory distress syndrome (RDS)? ☐ Yes* ☐ No ☐ Unknown

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
SAFER • HEALTHIER • PEOPLE™

Epidemiologic Risk Factors

CDC Case ID:

5. Travel/Exposures

A. In the 10 days prior to illness onset, did the patient travel to any of the countries listed in the table below? If yes*, please fill in arrival and departure dates for all countries that apply. ☐ Yes* ☐ No** ☐ Unknown

****If patient did not travel outside U.S., skip to question 6.**

Country	Arrival Date	Departure Date	Country	Arrival Date	Departure Date
☐ Afghanistan			☐ Myanmar (Burma)		
☐ Bangladesh			☐ Nepal		
☐ Brunei			☐ North Korea		
☐ Cambodia			☐ Oman		
☐ China			☐ Pakistan		
☐ Hong Kong			☐ Papua New Guinea		
☐ India			☐ Philippines		
☐ Indonesia			☐ Saudi Arabia		
☐ Iran			☐ Singapore		
☐ Iraq			☐ South Korea		
☐ Israel			☐ Syria		
☐ Japan			☐ Taiwan		
☐ Jordan			☐ Thailand		
☐ Laos			☐ Turkey		
☐ Lebanon			☐ Viet Nam		
☐ Macao			☐ Yemen		
☐ Malaysia					

For the questions 5B to 5E,
In the 10 days prior to illness onset, <u>while in the countries</u> listed above . . . .

B. Did the patient come within 1 meter (3 feet) of any live poultry or domesticated birds (e.g. visited a poultry farm, a household raising poultry, or a bird market)? ☐ Yes* ☐ No ☐ Unknown

If Yes*

C. Did patient touch any recently butchered poultry? ☐ Yes ☐ No ☐ Unknown

D. Did the patient visit or stay in the same household with anyone with pneumonia or severe flu-like illness? ☐ Yes ☐ No ☐ Unknown

E. Did the patient visit or stay in the same household with a suspected human influenza A(H5) case?* ☐ Yes ☐ No ☐ Unknown

F. Did the patient visit or stay in the same household with a known human influenza A(H5) case?* ☐ Yes ☐ No ☐ Unknown

** SEE Influenza A (H5): Interim U.S. Case Definitions*

(continued from previous page)

CDC ID:

6. Exposure for Non Travelers	
For patients whom did not travel outside the U.S., **in the 10 days prior to illness onset**, did the patient visit or stay in the same household with a traveler returning from one of the countries listed above who developed pneumonia or severe flu-like illness?	☐ Yes* ☐ No ☐ Unknown
If yes*, was the contact a confirmed or suspected H5 case patient?	☐ Yes* ☐ No ☐ Unknown
If yes*: CDC ID: _____ STATE ID: _____	

Laboratory Evaluation

7. State and local level influenza test results	
Specimen 1	
☐ NP swab ☐ Broncheoalveolar lavage specimen (BAL) ☐ NP aspirate ☐ OP swab ☐ Other _____	Date Collected: __ __ / __ __ / __ __ __ __ m m d d y y y y
Test Type: ☐ RT-PCR ☐ Direct fluorescent antibody (DFA) ☐ Viral Culture ☐ Rapid Antigen Test* *Name of Rapid Test:	Result: ☐ Influenza A ☐ Influenza B ☐ Influenza (type unk) ☐ Negative ☐ Pending
Specimen 2	
☐ NP swab ☐ Broncheoalveolar lavage specimen (BAL) ☐ NP aspirate ☐ OP swab ☐ Other _____	Date Collected: __ __ / __ __ / __ __ __ __ m m d d y y y y
Test Type: ☐ RT-PCR ☐ Direct fluorescent antibody (DFA) ☐ Viral Culture ☐ Rapid Antigen Test* *Name of Rapid Test:	Result: ☐ Influenza A ☐ Influenza B ☐ Influenza (type unk) ☐ Negative ☐ Pending
Specimen 3	
☐ NP swab ☐ Broncheoalveolar lavage specimen (BAL) ☐ NP aspirate ☐ OP swab ☐ Other _____	Date Collected: __ __ / __ __ / __ __ __ __ m m d d y y y y
Test Type: ☐ RT-PCR ☐ Direct fluorescent antibody (DFA) ☐ Viral Culture ☐ Rapid Antigen Test* *Name of Rapid Test:	Result: ☐ Influenza A ☐ Influenza B ☐ Influenza (type unk) ☐ Negative ☐ Pending

(continued from previous page)

CDC ID:

8. List specimens sent to the CDC

Select a SOURCE* from the following list for each specimen: Serum (acute), serum (convalescent), NP swab, NP aspirate, broncheoalveolar lavage specimen (BAL), OP swab, tracheal aspirate, or tissue

Specimen 1: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 2: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 3: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 4: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Specimen 5: ☐ Clinical Material ☐ Extracted RNA ☐ Virus Isolate	Source*: ----------	Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y) Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Carrier:	Tracking #:	

9. Case Notes:

(continued from previous page)

CDC ID:

CDC Contact Information (FOR CDC USE ONLY)	
Case status and date status applied: ☐ Clinical Case (lab results pending) __ __ / __ __ / __ __ __ __ (m m d d y y y y) ☐ Influenza A pos. Case (subtype pending) __ __ / __ __ / __ __ __ __ (m m d d y y y y) ☐ Confirmed Case __ __ / __ __ / __ __ __ __ (m m d d y y y y)	☐ Ruled Out/Non-Case: __ __ / __ __ / __ __ __ __ (m m d d y y y y) Reason: ☐ Influenza A neg. (by PCR, viral culture, or influenza A serology) ☐ Non-H5 Influenza Strain ☐ Other etiology* ☐ Did not meet case definition
Date Entered by CDC: __ __ / __ __ / __ __ __ __ (m m d d y y y y)	Contact Date: __ __ / __ __ / __ __ __ __ (m m d d y y y y)
Name of CDC Contact:	

*Alternative Diagnosis			
A. Was an alternative non-influenza respiratory pathogen detected? If yes* specify:	☐ Yes*	☐ No	☐ Unknown
B. Was there a diagnosis other than respiratory infection? If yes* specify:	☐ Yes*	☐ No	☐ Unknown

supplement 2
laboratory diagnostics
TABLE OF CONTENTS

SUMMARY OF ROLES AND RESPONSIBILITIES FOR PUBLIC HEALTH AND CLINICAL LABORATORIES IN LABORATORY DIAGNOSTICS

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

Clinical and hospital laboratories:

- Work with state and local health departments to address laboratory surge capacity issues and train personnel in management of respiratory specimens during an influenza pandemic.
- Send clearly labeled specimens from patients with suspected novel influenza to state or local health departments. Hospital labs should NOT attempt to isolate influenza viruses from patients with suspected novel influenza virus infection.
- Institute surveillance for influenza-like illnesses (ILI) among laboratory personnel working with novel influenza viruses.

State and local public health laboratories:

- Work with federal partners to enhance laboratory-based monitoring of seasonal influenza virus subtypes, as described in **Supplement 1**.
- Conduct testing for novel subtypes of influenza viruses only if BSL-3 biocontainment conditions with enhancements are available.
- Institute surveillance for ILI among laboratory personnel.
- Conduct preparedness planning to support the response to an influenza pandemic.

HHS responsibilities:

- Monitor preparedness and laboratory capacity for seasonal influenza and assess surge capacity.
- Provide technical support to the WHO Influenza Network and ministries of health and agriculture, as requested, in analyzing novel influenza virus subtypes—including avian isolates and human isolates with pandemic potential—in terms of antigenicity, RNA sequence, and drug sensitivities.
- Work with state and local public health laboratories to ensure that diagnostics for identifying "pandemic alert" strains are available and are used safely and effectively.
- Provide guidance on biosafety and safe handling of respiratory specimens from potential cases of pandemic influenza.

PANDEMIC PERIOD

Clinical and hospital laboratories:

- Scale up to manage increased numbers of requests for influenza testing.
- Send selected specimens from possible pandemic influenza patients to state or local health departments.

State and local public health laboratories:

- Scale up to manage increased numbers of requests for influenza testing.
- Work with federal partners to provide healthcare providers and clinical laboratories with guidelines on all aspects of specimen management and diagnostic testing.

- Work with federal partners to monitor the pandemic virus and conduct special studies related to vaccine development, or other aspects of the response.

HHS responsibilities:

- Work with U.S. and global partners to characterize new pandemic viruses in terms of antigenicity, RNA sequence, and drug sensitivities, and to monitor changes over time.
- Work with state and local public health laboratories to ensure the availability and the safe and effective use of diagnostic tests and reagents.
- Conduct reference testing of positive samples, and perform viral isolation, especially at the beginning of a pandemic.
- Provide laboratory support for the selection of seed strains to be used in a vaccine against the pandemic virus.

S2-I. RATIONALE

The goals of diagnostic testing during a pandemic are to:

- Identify the earliest U.S. cases of pandemic influenza (whether the pandemic begins in the United States or elsewhere).
- Support disease surveillance to monitor the pandemic's geographic spread and impact of interventions.
- Facilitate clinical treatment by distinguishing patients with influenza from those with other respiratory illnesses.
- Monitor circulating viruses for antiviral resistance.

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 (see Box 1 and Appendix 1).

During the earliest stages of a pandemic, public health, hospital, and clinical laboratories might receive a large and potentially overwhelming volume of clinical specimens. Pre-pandemic planning is therefore essential to ensure the timeliness of diagnostic testing and the availability of diagnostic supplies and reagents, address staffing issues, and disseminate protocols for safe handling and shipping of specimens. Once a pandemic is underway, the need for laboratory confirmation of clinical diagnoses may decrease as the virus becomes widespread.

S2-II. OVERVIEW

Supplement 2 provides recommendations to state and local public health partners and other laboratories on the use of diagnostic tests to detect, characterize, and monitor novel subtypes of influenza, including avian influenza A (H5N1) and other viruses with pandemic potential. The recommendations for the Interpandemic and Pandemic Alert Periods focus on laboratory testing in support of seasonal influenza surveillance, laboratory-based detection of novel influenza subtypes, and preparedness planning to support the laboratory component of the response to a pandemic (e.g., detection and characterization of viruses, case reporting, specimen management, surge capacity). The recommendations for the Pandemic Period focus on the provision of laboratory support for disease surveillance and to assist clinicians and hospitals. The recommendations also cover occupational health issues for laboratory workers.

S2-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Laboratory support for seasonal influenza surveillance

State and local public health laboratories and clinical laboratories (including hospital and private commercial laboratories) should continue to participate in laboratory-based surveillance for new subtypes of influenza through the U.S.-based laboratories in the World Health Organization (WHO) Global Influenza Surveillance Network and the National Respiratory and Enteric Virus Surveillance System (NREVSS). Additional information on seasonal influenza surveillance (including surveillance for influenza mortality and pediatric hospitalizations) is provided in **Supplement 1**. Information on the WHO Global Influenza Surveillance Network and NREVSS is provided in Box 2.

B. Laboratory testing for novel influenza subtypes

During the Pandemic Alert Period, state and local health departments, hospitals, and clinicians should enhance surveillance to identify patients who may present with possible cases of novel influenza (see Appendix 2). Health Alert Network (HAN) messages will be issued, as needed, to provide updates and guidance as new situations arise.

State and local public health laboratories should be prepared to process and, in some instances, test—if they have the capability (see below)—specimens from suspected cases of infection with:

- Avian influenza A (H5N1) and other avian influenza viruses
- Other animal influenza viruses (e.g., swine influenza viruses)
- New or re-emergent human influenza viruses (e.g., H2) with pandemic potential

Clinicians should contact their state or local health departments if they suspect a human case of infection with any novel influenza A virus. State and local health departments, in turn, should contact CDC via the CDC Emergency Response Hotline: 770-488-7100.

Guidelines on when to send specimens or isolates of suspected novel avian or human strains to CDC for reference testing are provided in Appendix 3.

1. Testing for human cases of avian influenza

Currently, avian influenza strains implicated in human disease (in addition to influenza A [H5N1]) include the highly pathogenic avian influenza (HPAI) strain H7N7 and the low pathogenic avian influenza (LPAI) strains H9N2, H7N2, and H7N3 (see Box 3). As of October 2005, no laboratory-confirmed cases of human infection with influenza A (H5N1) had been reported in the United States. However, CDC has confirmed two non-fatal cases of avian A (H7N2) influenza in Virginia and New York (Box 3). As new U.S. cases of human infection with avian influenza viruses are reported, they will be posted at: www.aphis.usda.gov/vs/birdbiosecurity/hpai.html and at: www.cdc.gov/flu.

Recommendations on laboratory testing for human cases of avian influenza are as follows:

- State public health laboratories may conduct testing to identify suspected subtypes of avian influenza, including H5 and H7, if appropriate laboratory capacity and biocontainment equipment are available. Because of the danger that HPAI strains present to the U.S. agricultural industry, U.S. Department of Agriculture (USDA) regulations require that HPAI strains such as H5N1 (which are classified as select agents) must be cultured using BSL-3 biocontainment conditions with enhancements (see Appendix 4).

- Public health laboratories that lack BSL-3 facilities may use RT-PCR with BSL-2 containment to test clinical specimens from suspected human cases of avian influenza to identify and subtype influenza A viruses (e.g., H1, H3, H5, and H7; see S2-III.C). Or, they may send specimens to CDC, using the collection, handling, and shipping procedures described in Appendix 5.

During the Pandemic Alert Period, specimens from suspected cases of human infection with novel influenza viruses should be sent for testing to public health laboratories with proper biocontainment facilities:

- RT-PCR – BSL-2
- Virus isolation – BSL-3 with enhancements

The American Society for Microbiology maintains a list of emergency contacts in state public health laboratories, which is available at: www.asm.org/ASM/files/0000000527/labemergencycontacts[1].pdf.

If an avian influenza strain—or a human virus variant that evolves from it—causes an influenza pandemic, it might become necessary to re-evaluate biocontainment requirements and select agent registration requirements for laboratory testing. CDC and the Laboratory Response Network (LRN) will assist USDA, as requested, in making such a decision.

2. Testing for human influenza strains with pandemic potential

During the Pandemic Alert Period, diagnostic laboratories should be on the alert for new human subtypes of influenza that might have pandemic potential. Recommendations are as follows:

- State and local public health laboratories that can detect human and avian influenza subtypes by RT-PCR should report all unusual subtypes to CDC via the Emergency Response Hotline (770-488-7100).
- Public health laboratories that can detect human (but not avian) influenza subtypes by IFA staining or RT-PCR should send influenza A isolates that cannot be subtyped to CDC. (If an avian strain is suspected, virus isolation and IFA should be performed under BSL-3 conditions with enhancements.)
- Public health laboratories should send specimens to CDC if a patient meets the clinical and epidemiologic criteria for infection with a novel influenza virus and:
  - Tests positive for influenza A by RT-PCR or by rapid diagnostic testing, *or*
  - Tests negative for influenza A by rapid diagnostic testing and/or RT-PCR testing for influenza is not available
- Clinical laboratories that receive diagnostic specimens from patients with suspected novel influenza (based on clinical and epidemiologic data) should contact their state or local health departments.
- If new or re-emergent human influenza strains with pandemic potential are suspected, laboratories should conduct RT-PCR only under BSL-2 containment conditions and viral culture only under BSL-3 conditions with enhancements (see Appendix 4).

C. Laboratory planning to support the response to an influenza pandemic

Advance planning is essential to anticipate adequate laboratory capacity to support medical and public health partners during an influenza pandemic. Some aspects of this planning, such as surge capacity planning, can be coordinated with bioterrorism preparedness planning.

1. Detection and characterization of novel influenza strains

- As of October 2005, about 48 state and large local public health laboratories have received training in RT-PCR protocols for molecular detection of H1, H3, H5, and H7 subtypes. These laboratories should incorporate RT-PCR testing into their standard influenza laboratory activities. Real-time RT-PCR protocols are available through the website of the Association of Public Health Laboratories (APHL) and will be updated as required to monitor the appearance and evolution of novel influenza viruses. A positive RT-PCR test result for a novel influenza strain should be considered presumptive, pending testing by a second reference laboratory.
- State and local public health laboratories should provide hospitals and healthcare providers with information on how to contact the laboratory when a novel influenza subtype is suspected and how to handle, label, and ship clinical specimens for diagnostic evaluation.
- State and local public health laboratories should contact laboratories in their jurisdictions that conduct RT-PCR influenza testing or that have BSL-3 containment facilities to remind them to notify the state health department if they receive specimens from suspected cases of novel influenza.

2. Laboratory reporting

State and local health departments that report laboratory-confirmed seasonal influenza cases to CDC use a variety of reporting mechanisms, including faxes, the Public Health Information System (PHLIS), and a web-based NREVSS data-entry system. Cases of novel influenza should be reported to CDC by the same mechanisms.

3. Distribution of diagnostics reagents and test information

CDC is working with USDA and the Food and Drug Administration (FDA) to address any regulatory barriers to emergency distribution and use of diagnostic tests and reagents during a pandemic. CDC will provide updated preparedness information regarding diagnostic tests and reagents to state and local public health partners via the LRN and HAN.

4. Laboratory surge capacity planning

Health departments should assess projected statewide needs for scaled-up diagnostic activity during the early stages of a pandemic, in terms of laboratory staffing, training, reporting, and supplies, and should develop strategies to address them.

a) Staffing and training

Laboratories should plan for increased staffing needs. Some strategies include:

- Cross-training personnel during the regular influenza season in the use of rapid diagnostic tests and RT-PCR protocols and in reporting results through existing surveillance systems
- Arranging to recruit and train temporary staff for employment during a pandemic

b) Supplies and equipment

Laboratories are likely to require additional diagnostic supplies and equipment to process large numbers of samples during the initial stages of a pandemic. Some preparedness strategies include:

- Establishing the current level of diagnostic supplies, including personal protective equipment for laboratorians (e.g., gloves, masks)
- Assessing anticipated equipment and supply needs, and determining a trigger point for ordering extra resources. Laboratories should also consider the need for back-up sources of supplies if most laboratories in a state or large city rely on the same manufacturer for particular supplies or equipment.
- Determining how consumption of supplies will be tracked during a pandemic

c) Specimen management

State and local health departments should inform and educate public health staff (including laboratorians), local physicians, and hospital workers on safe and effective methods for specimen collection and management, making use of the guidelines in Appendix 5, Guidelines for Collecting and Shipping Specimens for Influenza Diagnostics. Safety issues related to specimen handling are also addressed in **Supplement 4**.

Procedures for specimen collection, handling, and shipping during a pandemic will be the same as those used for seasonal disease surveillance. However, laboratory staff should anticipate shipping a much larger number of specimens in a very short time, especially during the early stages of a pandemic. Once the pandemic is underway and healthcare providers rely on clinical criteria and rapid test kits, more diagnostic activities may be conducted locally and fewer shipments may be needed.

5. Partnerships with healthcare providers and clinical laboratories

Good working relationships between healthcare providers and public health laboratories will facilitate diagnostic activities during a pandemic.

- Public health laboratories should continue to build partnerships with healthcare providers in their jurisdictions, including physicians who participate in the Sentinel Provider Network (SPN) during the regular influenza season (see **Supplement 1**).
- Public health laboratories should build partnerships with clinical laboratories and provide them with updated information and (if feasible) training in influenza diagnostics.

S2-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

A. Laboratory support for disease surveillance

- Public health, hospital, and clinical laboratories will support surveillance for pandemic influenza through the same mechanisms that support laboratory-based surveillance for seasonal influenza. CDC and the LRN will work with state and local health departments to make diagnostic testing for the pandemic virus readily available, both at CDC and at state and local public health laboratories that have implemented RT-PCR protocols.
- As soon as a pandemic strain has been identified, CDC's Influenza Laboratory will develop, produce, and disseminate RT-PCR and IFA reagents, as needed. As necessary, CDC and APHL will also update the RT-PCR protocol currently available to public health laboratories through the APHL website.
- As the pandemic continues, CDC will advise states on when confirmatory testing (i.e., subtyping) is required. Although confirmatory testing will be required when the pandemic begins, the level of testing will decrease as the virus becomes widespread.
- CDC will advise states on the percentage of isolates per week or month that they should send to CDC as part of efforts to monitor changes in the antigenicity and antiviral susceptibility of the pandemic virus. Throughout the pandemic, CDC will provide updated instructions on the collection of clinical and epidemiologic data that should accompany isolates. CDC could ask some state public health laboratories to perform virus isolation or RT-PCR subtyping before sending specimens to CDC.
- CDC may work with the U.S.-based WHO collaborating laboratories, NREVSS laboratories, and/or Emerging Infectious Program sites (www.cdc.gov/ncidod/osr/site/eip/index.htm) to conduct special studies or establish additional laboratory-based surveillance systems to answer critical questions related to vaccine development or other aspects of the public health response. For example, CDC and state and local partners could conduct serosurveys to determine the number of persons who develop antibodies to the pandemic virus over time.

B. Laboratory support for clinicians

- When a pandemic begins, public health and clinical laboratories will scale up to manage increased numbers of requests for influenza testing. As part of this effort, CDC will work with state and local public health laboratories and the LRN to provide clinical laboratories with guidelines for safe handling, processing, and rapid diagnostic testing of clinical specimens from patients who meet the case definition for pandemic influenza.

If private laboratories perform RT-PCR testing during the early phase of an influenza pandemic, the results should be confirmed in consultation with the state public health laboratory.

- State and local health laboratories should provide local healthcare providers with:
  - Specimen submission forms that specify the clinical and epidemiologic data that should accompany clinical specimens sent to state public health laboratories. (During the early stages of a pandemic, clinicians should include information on patients' symptoms and risk factors, if known.)
  - Rapid communication of test results and reminders that a negative test result (especially by rapid diagnostic testing) might not rule out influenza and should not affect patient management or infection control decisions.
  - Guidance on the use of commercially available rapid diagnostic tests for the detection of influenza A. These tests may be used by physicians to supplement clinical diagnoses of pandemic influenza. Because the sensitivity of rapid diagnostic kits might not be optimal, physicians should take their positive and negative predictive values into consideration when interpreting test results (Appendix 6).
  - Guidance on which specimens to send to state public health laboratories as the pandemic continues.

C. Biocontainment procedures

During an influenza pandemic, laboratory procedures should be conducted under appropriate biosafety conditions:

- Commercial antigen detection testing for influenza should be conducted using BSL-2 work practices.
- Public health laboratories may conduct RT-PCR testing using BSL-2 work practices and virus isolation using BSL-3 practices with enhancements.

Additional information on laboratory biocontainment is provided in Appendix 4.

D. Occupational health issues for laboratory workers

To protect the health of laboratory workers during a pandemic, public health, clinical, and hospital laboratories should maintain the safety practices used during the Interpandemic and Pandemic Alert Periods. These include:

- Conducting laboratory procedures under appropriate biocontainment conditions
- Encouraging routine vaccination of all eligible laboratory personnel who are exposed to specimens from patients with respiratory infections

Guidelines for medical surveillance of laboratory personnel are provided in Appendix 7.

BOX 1. USE OF DIAGNOSTIC ASSAYS DURING AN INFLUENZA PANDEMIC

Public health and clinical laboratories will use different types of diagnostic tests for influenza at different stages of a pandemic. Each of the tests discussed below is described in detail in Appendix 1.

Virus Isolation

Virus isolation—growing the viral strain in cell culture—is the "gold standard" for influenza diagnostics because it confirms that the virus is infectious. During a pandemic, virus isolation followed by antigenic and genetic (sequencing) analysis will be used to characterize the earliest pandemic isolates, as well as to monitor their evolution during the pandemic. Laboratories that participate in the WHO Global Influenza Surveillance Network typically use virus isolation followed by hemagglutination inhibition (HAI), IFA staining, or RT-PCR to monitor circulating seasonal strains of influenza. If clinical and epidemiologic data suggest that a human case of influenza might be due to infection with avian influenza A (H5N1) or another highly pathogenic avian influenza strain (see Box 3), the virus should not be cultured except under BSL-3 conditions with enhancements. Laboratories that lack BSL-3 enhanced facilities may either perform RT-PCR subtyping using BSL-2 containment procedures or send the specimen to CDC for isolation and characterization.

Immunofluorescence Antibody Staining

IFA staining following virus isolation can be used to identify influenza types (A, B) and influenza A HA subtypes using a panel of specific antisera. In some cases, IFA can be used for direct testing of cells pelleted from original clinical samples. CDC's Influenza Branch produces and distributes a reagent kit to WHO collaborating laboratories that includes monoclonal antibodies for typing and subtyping currently circulating influenza viruses by IFA. Many laboratories use commercially available reagents to type influenza viruses by direct immunofluorescence tests (DFA).

RT-PCR Subtyping

Influenza specimens may also be typed and subtyped using RT-PCR, which does not require *in vitro* growth or isolation of virus. As of October 2005, CDC has trained scientists from 48 states to use RT-PCR subtyping to identify human and avian HA subtypes of public health concern. APHL members can access protocols and sequences of primers and probes that can be used for typing and subtyping on the APHL website.

Serologic Tests

Tests based on detection of antibodies in patient sera—e.g., enzyme-linked immunosorbent assay (ELISA), HAI, and microneutralization assay—can be used to retrospectively confirm influenza infection. Although microneutralization assay is the most comprehensive test for detection in humans of antibodies to avian influenza viruses, it is available in only a few state public health laboratories.

Rapid Diagnostic Tests

Several rapid diagnostic test kits based on antigen detection are commercially available for influenza. Laboratories in outpatient settings and hospitals can use these tests to detect influenza viruses within 30 minutes. Some tests can detect influenza A viruses (including avian strains); others can detect influenza A and B viruses without distinguishing between them, and some can distinguish between influenza A and B viruses. The type of specimens used in these tests (i.e., nasal wash/aspirate, nasopharyngeal swabs, or nasal swab or throat swab) may also vary. Like RT-PCR, rapid diagnostic tests do not require *in vitro* growth or isolation of virus. During a pandemic, rapid diagnostic tests will be widely used to distinguish influenza A from other respiratory illnesses. See Appendix 6 for additional information.

BOX 2. LABORATORY SUPPORT FOR SEASONAL INFLUENZA SURVEILLANCE

U.S. Collaborating Laboratories of the WHO Global Influenza Surveillance Network

All state and several large local public health laboratories, as well as about 25 tertiary-care hospital and academic center laboratories, participate as U.S. collaborating laboratories in the WHO Global Influenza Surveillance Network, which collects worldwide data on circulating strains of influenza viruses. These data are used to develop recommendations for the formulation of each year's influenza vaccines, as well as to detect new human influenza viruses that might have pandemic potential. CDC's Influenza Laboratory serves as the WHO Collaborating Center for Surveillance, Epidemiology, and Control of Influenza, along with the WHO Collaborating Centers for Reference and Research on Influenza in Australia, Japan, and the United Kingdom.

The U.S.-based WHO collaborating laboratories provide CDC with weekly reports of laboratory-confirmed cases of influenza A and B viruses, by age group. These laboratories typically use virus isolation followed by antigenic testing with IFA staining or HAI—or by molecular testing with RT-PCR—to identify known subtypes of human influenza viruses. If unusual subtypes are detected, or if the specimens cannot be subtyped using available techniques, the specimens are sent to CDC for further testing.

NREVSS Collaborating Laboratories

The National Respiratory and Enteric Virus Surveillance System (NREVSS; http://www.cdc.gov/ncidod/dvrd/revb/nrevss/) includes more than 90 laboratories throughout the country, including many hospital laboratories, some state public health laboratories, and a few private commercial laboratories. About 40 of the NERVSS laboratories are also WHO collaborating laboratories.

Like the WHO collaborating laboratories, NREVSS laboratories provide CDC with weekly reports of laboratory-confirmed cases of influenza A and B viruses. These laboratories typically test respiratory specimens with commercially available rapid diagnostic tests. Several NREVSS laboratories also perform virus isolation followed by rapid diagnostic tests or antigenic typing by IFA. If untypable viruses or unusual subtypes are detected, the specimens are sent to the state public health laboratory or to CDC for further testing.

BOX 3. AVIAN INFLUENZA STRAINS WITH HIGH AND LOW PATHOGENICITY

The U.S. Department of Agriculture (USDA) classifies avian influenza viruses as low pathogenic avian influenza (LPAI) viruses or highly pathogenic avian influenza (HPAI) viruses, based on characteristics of a virus' hemagglutinin cleavage site or its virulence in birds, as determined by laboratory testing. LPAI strains are endemic in wild birds worldwide and are responsible for most avian influenza outbreaks in poultry. LPAI strains with H5 and H7 subtypes sometimes evolve into highly pathogenic forms. HPAI strains are extremely contagious and cause severe illness and high mortality rates in poultry.

LPAI strains include:

- H5N2, the cause of poultry outbreaks in New York, Maine, and California in 2002
- H7N2, the cause of poultry outbreaks in Delaware, Maryland, and New Jersey in 2004

HPAI strains include:

- H5N1, the cause of major poultry outbreaks in Southeast Asia
- H7N7, the cause of a 2003 outbreak in the Netherlands
- H7N3, the cause of a 2004 outbreak in British Columbia
- H5N2, the cause of a 2004 outbreak in poultry in Texas

The 2004 outbreak in Texas was the first HPAI outbreak in the United States since a previous outbreak of H5N2 in 1983-84 in the northeastern United States. The 1983-84 disease control effort involved the destruction of approximately 17 million birds and cost more than $70 million.

Although avian influenza A viruses do not usually infect humans, several instances of human infections of avian influenza have been reported since 1997. Cases of avian influenza infection in humans are apparently caused by contact with infected poultry or with surfaces contaminated with avian influenza viruses.

LPAI strains associated with human infection include:

- H9N2, which caused three cases of influenza-like illness in Hong Kong between 1999 and 2003, and other cases in China in 1998 and 1999
- H7N2, which was detected by serology in one person involved in the culling of sick chickens during the response to a poultry outbreak in Virginia in 2002, and was isolated from a New York resident in 2003 (unknown source of the infection)

HPAI viruses associated with human infection include:

- H5N1, which caused 51 deaths in Southeast Asia between January 2004 and April 2005
- H7N7, which caused the death of a veterinarian as well as 83 cases of mild human disease (including conjunctivitis) during the 2003 poultry outbreak in the Netherlands.
- H7N3, which caused 2 cases of very mild human disease (conjunctivitis, headache) in persons culling sick poultry in British Columbia in 2004

APPENDIX 1. INFLUENZA DIAGNOSTIC ASSAYS

Among the several types of assays used to detect influenza, rapid antigen tests, reverse-transcription polymerase chain reaction (RT-PCR), viral isolation, immunofluorescence assays (IFA), and serology are the most commonly used. The sensitivity and specificity of any test for influenza will vary by the laboratory that performs the test, the type of test used, and the type of specimen tested. A chart that lists influenza diagnostic procedures and commercially available rapid diagnostic tests follows more detailed descriptions provided below.

Virus Isolation

Biocontainment level: Interpandemic and Pandemic Alert Periods – BSL-3 with enhancements; Pandemic Period – BSL-2

Virus isolation is a highly sensitive and very useful technique when the clinical specimens are of good quality and have been collected in a timely manner (optimally within 3 days of the start of illness). Isolation of a virus in cell culture along with the subsequent identification of the virus by immunologic or genetic techniques are standard methods for virus diagnosis. Virus isolation amplifies the amount of virus from the original specimen, making a sufficient quantity of virus available for further antigenic and genetic characterization and for drug-susceptibility testing if required. Virus isolation is considered the "gold standard" for diagnosis of influenza virus infections.

> Highly pathogenic avian influenza (HPAI) viruses are BSL-3 agents. During the Interpandemic and Pandemic Alert Periods, laboratories should attempt to culture HPAI viruses—as well as other influenza viruses with pandemic potential—only under BSL-3 conditions with enhancements in order to optimally reduce the risk of a novel influenza virus subtype spreading to persons or animals. During the Pandemic Period, biocontainment of BSL-2 is appropriate to prevent laboratory-acquired infection and the virus will already be widespread.

In recent years, the use of cell lines has surpassed the use of embryonated eggs for culturing of influenza viruses, although only viruses grown in embryonated eggs are used as seed viruses for vaccine production. Because standard isolation procedures require several days to yield results, they should be used in combination with the spin-amplification shell-vial method. The results of these assays can be obtained in 24–72 hours, compared to an average of 4.5 days using standard culture techniques. Spin-amplification should not be performed using 24-well plates because of increased risk of cross-contamination. The most effective combination of cell lines recommended for public health laboratories is primary rhesus monkey for standard culture, along with Madin Darby Canine Kidney (MDCK) in shell vial.[1] The use of these two cell lines in combination has demonstrated maximum sensitivity over time for recovery of evolving influenza strains. Some clinical laboratories have recently reported good isolation rates using commercially available cell-line mixed-cell combinations; however, data are lacking on the performance of these mixed cells with new subtypes of Influenza A viruses.

Appropriate clinical specimens for virus isolation include nasal washes, nasopharyngeal aspirates, nasopharyngeal and throat swabs, tracheal aspirates, and bronchoalveolar lavage. Ideally, specimens should be collected within 72 hours of the onset of illness.

Viral culture isolates are used to provide specific information regarding circulating influenza subtypes and strains. This information is needed to compare current circulating influenza strains with vaccine strains, to guide decisions on influenza treatment and chemoprophylaxis, and to select vaccine strains for the coming year. Virus isolates also are needed to monitor

[1] The shell-vial technique is described in: *Manual of Clinical Virology,* 3rd edition. Steven Specter, Richard Hodinka, and Stephen Young, eds. ASM Press, 2000.

the emergence of antiviral resistance and of novel influenza A subtypes that might pose a pandemic threat. During outbreaks of influenza-like illness, viral culture may help identify other causes of illness when influenza is not the etiology (except when using MDCK cells or the MDCK shell-vial technique).

Immunofluorescence Assays

Biocontainment level: BSL-2 when performed directly on clinical specimens; if used on cultures for earlier detection of virus, biocontainment recommendations for viral culture apply

Direct (DFA) or indirect (IFA) immunofluorescence antibody staining of virus-infected cells is a rapid and sensitive method for diagnosis of influenza and other viral infections. DFA and IFA can also be used to type and subtype influenza viruses using commercially available monoclonal antibodies specific for the influenza virus HA. The sensitivity of these methods is greatly influenced by the quality of the isolate, the specificity of the reagents used, and the experience of the person(s) performing, reading, and interpreting the test.

Although IFA can be used to stain smears of clinical specimens directly, when rapid diagnosis is needed it is preferable to first increase the amount of virus through growth in cell culture. For HPAI isolates, attempts to culture the virus should be made only under BSL-3 conditions with enhancements.

Reverse-Transcription Polymerase Chain Reaction (RT-PCR)

Biocontainment level: BSL-2

PCR can be used for rapid detection and subtyping of influenza viruses in respiratory specimens. Because the influenza genome consists of single-stranded RNA, a complementary DNA (cDNA) copy of the viral RNA must be synthesized using the reverse-transcriptase (RT) enzyme prior to the PCR reaction.

Laboratories can obtain CDC protocols and sequences of primers and probes for rapid RT-PCR detection of human and avian HA subtypes of current concern at the APHL website (available for members only). These protocols use real-time RT-PCR methods with fluorescent-labeled primers that allow automatic, semi-quantitative estimation of the input template. The RT-PCR results are analyzed and archived electronically, without the need for gel electrophoresis and photographic recording. A large number of samples may be analyzed at the same time, reducing the risk of carry-over contamination.

As with all PCR assays, interpretation of real-time RT-PCR tests must account for the possibility of false-negative and false-positive results. False-negative results can arise from poor sample collection or degradation of the viral RNA during shipping or storage. Application of appropriate assay controls that identify poor-quality samples (e.g., an extraction control and, if possible, an inhibition control) can help avoid most false-negative results. [2]

The most common cause of false-positive results is contamination with previously amplified DNA. The use of real-time RT-PCR helps mitigate this problem by operating as a contained system. A more difficult problem is the cross-contamination that can occur between specimens during collection, shipping, and aliquoting in the laboratory. Use of multiple negative control samples in each assay and a well-designed plan for confirmatory testing can help ensure that laboratory contamination is detected and that negative specimens are not inappropriately identified as influenza-positive.

Specimens that test positive for a novel subtype of influenza virus should be forwarded to CDC for confirmatory testing. (Due to the possibility of contamination, it is important to provide original clinical material.) All laboratory results should be interpreted in the context of the clinical and epidemiologic information available on the patient.

[2] CDC is working with the private sector to provide inactivated RNA virus for use as RT-PCR controls for influenza A (H5) testing in LRN laboratories. CDC is working with USDA to resolve any permit issues that might affect the ability of LRN members to use these controls.

Rapid Diagnostic Tests

Biocontainment level: BSL-2

Commercial rapid diagnostic tests can be used in outpatient settings to detect influenza viruses within 30 minutes. These rapid tests differ in the types of influenza viruses they can detect and in their ability to distinguish among influenza types. Different tests can 1) detect influenza A viruses only (including avian strains); 2) detect both influenza A and B viruses, without distinguishing between them; or 3) detect both influenza A and B viruses and distinguish between them.

The types of specimens acceptable for use (i.e., nasal wash/aspirate, nasopharyngeal swab, or nasal swab and throat swab) also vary by test. The specificity and, in particular, the sensitivity of rapid tests are lower than for viral culture and vary by test and specimen tested. The majority of rapid tests are >70% sensitive and >90% specific. Thus, as many as 30% of samples that would be positive for influenza by viral culture may give a negative rapid test result with these assays.

When interpreting results of a rapid influenza test, physicians should consider the level of influenza activity in the community. When influenza prevalence is low, positive rapid test results should be independently confirmed by culture or RT-PCR. When influenza is known to be circulating, clinicians should consider confirming negative tests with viral culture or other means because of the lower sensitivity of the rapid tests. Package inserts and the laboratory performing the test should be consulted for more details regarding use of rapid diagnostic tests. Additional information on diagnostic testing is provided at: http://www.cdc.gov/flu/professionals/labdiagnosis.htm. Detailed information on the use of rapid diagnostics tests is provided in Appendix 6.

Serologic Tests[3]

Hemagglutination Inhibition (HAI)

Biocontainment level: BSL-2

Serologic testing can be used to identify recent infections with influenza viruses. It can be used when the direct identification of influenza viruses is not feasible or possible (e.g., because clinical specimens for virus isolation cannot be obtained, cases are identified after shedding of virus has stopped, or the laboratory does not have the resources or staff to perform virus isolation).

Since most human sera contain antibodies to influenza viruses, serologic diagnosis requires demonstration of a four-fold or greater rise in antibody titer using paired acute and convalescent serum samples. HAI is the preferred diagnostic test for determining antibody rises. In general, acute-phase sera should be collected within one week of illness onset, and convalescent sera should be collected 2–3 weeks later.

There are two exceptions in which the collection of single serum samples can be helpful in the diagnosis of influenza. In investigations of outbreaks due to novel viruses, testing of single serum samples has been used to identify antibody to the novel virus. In other outbreak investigations, antibody test results from single specimens collected from persons in the convalescent phase of illness have been compared with results either from age-matched persons in the acute phase of illness or from non-ill controls. In such situations, the geometric mean titers between the two groups to a single influenza virus type or subtype can be compared. In general, these approaches are not optimal, and paired sera should be collected whenever possible.

Because HAI titers of antibodies in humans infected with avian influenza viruses are usually very low or even undetectable, more sensitive serologic tests, such as microneutralization, may be needed.

[3] Enzyme-linked immunoassay (EIA) is not included on this list because of non-specificity issues. Complement fixation is not included because it is currently out of use.

Microneutralization Assay

Biocontainment level: Interpandemic and Pandemic Alert Periods – BSL-3 with enhancements; Pandemic Period – BSL-2

The virus neutralization test is a highly sensitive and specific assay for detecting virus-specific antibody in animals and humans. The neutralization test is performed in two steps: 1) a virus-antibody reaction step, in which the virus is mixed with antibody reagents, and 2) an inoculation step, in which the mixture is inoculated into a host system (e.g. cell cultures, embryonated eggs, or animals). The absence of infectivity constitutes a positive neutralization reaction and indicates the presence of virus-specific antibodies in human or animal sera.

The virus neutralization test gives the most precise answer to the question of whether or not a person has antibodies that can neutralize the infectivity of a given virus strain. The neutralization test has several additional advantages for detecting antibody to influenza virus. First, the assay primarily detects antibodies to the influenza virus HA and thus can identify functional, strain-specific antibodies in animal and human serum. Second, since infectious virus is used, the assay can be developed quickly upon recognition of a novel virus and before suitable purified viral proteins become available for use in other assays.

The microneutralization test is a sensitive and specific assay for detecting virus-specific antibody to avian influenza A (H5N1) in human serum and potentially for detecting antibody to other avian subtypes. Microneutralization can detect H5-specific antibody in human serum at titers that cannot be detected by HAI. Because antibody to avian influenza subtypes is presumably low or absent in most human populations, single serum samples can be used to screen for the prevalence of antibody to avian viruses. However, if infection of humans with avian viruses is suspected, the testing of paired acute and convalescent sera in the microneutralization test would provide a more definitive answer regarding the occurrence of infection. Conventional neutralization tests for influenza viruses based on the inhibition of cytopathogenic effect (CPE)-formation in MDCK cell cultures are laborious and rather slow, but in combination with rapid culture assay principles the neutralization test can yield results within 2 days. For HPAI viruses, neutralization tests should be performed at BSL-3 enhanced conditions.

QUICK REFERENCE CHART OF INFLUENZA DIAGNOSTIC TESTS[1]

(From: *Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP).* MMWR 2004;53(RR-6):1-40.

Procedure	Influenza Types Detected	Acceptable Specimens	Time for Results	Rapid result available
Viral culture	A and B	nasal wash/aspirate, NP swab,2 nasal aspirate, nasal swab and throat swab, sputum	5–10 days[3]	No
Immunofluorescence Antibody Staining	A and B	nasal wash/aspirate, NP swab,2 nasal aspirate, nasal swab and throat swab, sputum	2–4 hours	No
RT-PCR[5]	A and B	nasal wash/aspirate, NP swab,2 nasal aspirate, throat swab, bronchial wash, nasal aspirate, sputum	Hours	No
Serology	A and B	paired acute/convalescent serum samples6	>2 weeks	No
Rapid Diagnostic Tests				
Directigen Flu A[7] (Becton-Dickinson)	A	NP swab,2 throat swab, nasal wash, nasal aspirate	See insert	Yes
Directigen Flu A+B[7, 9] (Becton-Dickinson)	A and B	NP swab,2 throat swab, nasal wash, nasal aspirate	See insert	Yes
FLU OIA[7] (Thermo Electron)	A and B[4]	NP swab,2 throat swab, nasal aspirate, sputum	See insert	Yes
FLU OIA A/B[7, 9] (Thermo Electron)	A and B	NP swab,2 throat swab, nasal aspirate, sputum	See insert	Yes
XPECT Flu A/B[7, 9] (Remel)	A and B	Nasal wash, NP swab,2 throat swab	See insert	Yes
NOW Flu A Test[7, 9] NOW Flu B Test[7, 9] (Binax)	A B	Nasal wash, NP swab2 Nasal wash, NP swab2	See insert	Yes Yes
QuickVue Influenza Test[8] (Quidel)	A and B[4]	NP swab,2 nasal wash, nasal aspirate	See insert	Yes
QuickVue Influenza A+B Test[8] (Quidel)	A and B[9] A	NP swab,2 nasal wash, nasal aspirate	See insert	Yes
SAS Influenza A[7, 9] SAS Influenza B[7, 9]	B	NP wash,2 NP aspirate2 NP wash,2 NP aspirate2	See insert	Yes Yes
ZstatFlu[8] (ZymeTx)	A and B[4]	throat swab	See insert	Yes

[1] The list might not include all FDA-approved test kits.
[2] NP = nasopharyngeal
[3] Shell-vial culture, if available, may reduce time for results to 2 days.
[4] Does not distinguish between influenza A and B virus infections.
[5] RT-PCR = reverse-transcription polymerase chain reaction
[6] A fourfold or greater rise in antibody titer from the acute- (collected within the first week of illness) to the convalescent-phase sample (collected 2–4 weeks after the acute sample) indicates recent infection.
[7] Moderately complex test that requires specific laboratory certification
[8] CLIA-waived test. Can be used in any office setting. Requires a certificate of waiver or higher laboratory certification
[9] Distinguishes between influenza A and B virus infections.

Disclaimer: Use of trade names or commercial sources is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention or the Department of Health and Human Services.

APPENDIX 2. INTERIM RECOMMENDATIONS: ENHANCED U.S. SURVEILLANCE AND DIAGNOSTIC EVALUATION TO IDENTIFY CASES OF HUMAN INFECTION WITH AVIAN INFLUENZA A (H5N1)

NOTE: This guidance pertains to the avian influenza A (H5N1) situation in October 2005. CDC will provide updated guidance for avian influenza A (H5N1) and for new situations, as needed, through the Health Alert Network (HAN).

Enhanced surveillance efforts by state and local health departments, hospitals, and clinicians are needed to identify patients at increased risk for influenza A (H5N1). Interim recommendations include the following:

Testing for avian influenza A (H5N1) is indicated for **hospitalized** patients with:

- Radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established, *and*
- History of travel within 10 days of symptom onset to a country with documented avian influenza A (H5N1) infections in poultry and/or humans. (For a regularly updated listing of H5N1-affected countries, see the OIE website at http://www.oie.int/eng/en_index.htm and the WHO website at http://www.who.int/en/).

or

Testing for avian influenza A (H5N1) should be considered on a case-by-case basis in consultation with state and local health departments for **hospitalized or ambulatory** patients with:

- Documented temperature of >100.4°F (>38°C), *and*
- One or more of the following: cough, sore throat, or shortness of breath, *and*
- History of close contact either with poultry (e.g., visited a poultry farm, a household raising poultry, or a bird market) in an H5N1-affected country, or with a known or suspected human case of influenza A (H5N1) within 10 days prior to onset of symptoms.

APPENDIX 3. REFERENCE TESTING GUIDELINES FOR POTENTIAL PANDEMIC STRAINS OF INFLUENZA

State and local laboratories may conduct initial testing on patient specimens for influenza A or potential highly pathogenic strains, if laboratory capacity is available. Due to the spread of avian influenza A (H5N1) in poultry in Asia, laboratories should be on the alert for avian and human H5 viruses. Procedures for diagnosis of human cases of influenza A (H5N1) are provided in Appendix 2. Influenza A viruses other than currently circulating H1 and H3 subtypes should also be considered as potentially pandemic if detected in humans.

- State/local laboratories should send specimens to CDC if:
  - A sample tested by the state or local laboratory is positive for H5 or another novel subtype;

    Note: *A laboratory should test for influenza A (H5) only if it is able to do so by PCR or has a BSL-3-enhanced facility for influenza A(H5) viral culture.*

  or

  - A sample from a patient who meets the clinical and epidemiologic criteria for possible infection with a potentially pandemic virus is positive for influenza A by RT-PCR or rapid antigen detection,* is negative for influenza A(H1) and A(H3), and the referring jurisdiction is not equipped to test for specific strains;

  or

  - The referring jurisdiction is not equipped to test samples for novel influenza viruses by RT-PCR and is requesting testing at CDC.

Shipping procedures for potential pandemic strains of influenza are provided in Appendix 5.

**Because the sensitivity of commercially available rapid diagnostic tests for influenza may not always be optimal, CDC will also accept specimens taken from persons who meet the clinical and epidemiological criteria even if they test negative by influenza rapid diagnostic testing—if PCR assays are not available at the state laboratory.*

APPENDIX 4. LABORATORY BIOSAFETY GUIDELINES FOR HANDLING AND PROCESSING SPECIMENS OR ISOLATES OF NOVEL INFLUENZA STRAINS

Key Messages

- Commercial antigen detection testing for influenza may be conducted under BSL-2 containment conditions if a Class II biological safety cabinet is used.
- Clinical specimens from suspected novel influenza cases may be tested by RT-PCR using standard BSL-2 work practices in a Class II biological safety cabinet for initial processing of patient specimens.
- If a specimen is confirmed positive for influenza A (H5N1) by RT-PCR, additional testing should be performed only under BSL-3 conditions with enhancements. CDC's Influenza Branch should be informed immediately by contacting the CDC Director's Emergency Operations Center (DEOC) at 770-488-7100.
- A detailed description of recommended facilities, practices, and protective equipment for the various laboratory biosafety levels can be found in the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) manual at www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm
- BSL-3 with enhancements and Animal Biosafety Level 3 include: all BSL-3 practices, procedures, and facilities, plus the use of negative-pressure, HEPA-filtered respirators or positive air-purifying respirators, and clothing change and personal showering protocols. Additional practices and/or restrictions may be added as conditions of USDA-APHIS permits. Registration of personnel and facilities with the Select Agent Program is required for work with highly pathogenic avian influenza (HPAI) viruses, which are classified as agricultural select agents.

- State and local public health laboratories may test clinical specimens from suspected novel influenza cases by RT-PCR using standard BSL-2 work practices in a Class II biological safety cabinet. Commercial rapid antigen detection testing may also be conducted under BSL-2 biocontainment conditions.
- Highly pathogenic avian influenza A (H5) and A (H7) viruses are classified as select agents. USDA regulations require that these viruses (as well as exotic low pathogenic avian influenza viruses) be handled under BSL-3 laboratory containment conditions, with enhancements (i.e., controlled-access double-door entry with change room and shower, use of respirators, decontamination of all wastes, and showering of all personnel). Laboratories that work with these viruses must be certified by USDA.
- Laboratories should not perform virus isolation on respiratory specimens from patients who may be infected with an avian influenza virus unless stringent BSL-3 enhanced containment conditions can be met and diagnostic work can be kept separate from studies with other human influenza A viruses (i.e., H1 or H3). Therefore, respiratory virus cultures should not be performed in most clinical laboratories. Cultures for patients suspected of having influenza A (H5N1) infection should be sent only to state laboratories with appropriate BSL-3 with enhancement containment facilities or to CDC.

APPENDIX 5. GUIDELINES FOR COLLECTING AND SHIPPING SPECIMENS FOR INFLUENZA DIAGNOSTICS

Key Messages

- Appropriate specimens for influenza testing vary by type of test.
- Before collecting specimens, review the infection control precautions are described in Supplement 3.

I. RESPIRATORY SPECIMENS[4]

Eight types of respiratory specimens may be collected for viral and/or bacterial diagnostics:

1) nasopharyngeal wash/aspirates, 2) nasopharyngeal swabs, 3) oropharyngeal swabs, 4) broncheoalveolar lavage, 5) tracheal aspirate, 6) pleural fluid tap, 7) sputum, and 8) autopsy specimens. Nasopharyngeal wash/aspirates are the specimen of choice for detection of most respiratory viruses and are the preferred specimen type for children aged <2 years.

Respiratory specimens for detection of most respiratory pathogens, and influenza in particular, are optimally collected within the first 3 days of the onset of illness. Before collecting specimens, review the infection control precautions in **Supplement 4**.

A. Collecting specimens from the upper respiratory tract

1. Nasopharyngeal wash/aspirate

- Have the patient sit with head tilted slightly backward.
- Instill 1 ml–1.5 ml of nonbacteriostatic saline (pH 7.0) into one nostril. Flush a plastic catheter or tubing with 2 ml–3 ml of saline. Insert the tubing into the nostril parallel to the palate. Aspirate nasopharyngeal secretions. Repeat this procedure for the other nostril.
- Collect the specimens in sterile vials. Label each specimen container with the patient's ID number and the date collected.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, pack in dry ice (see shipping instructions below).

2. Nasopharyngeal or oropharyngeal swabs

- Use only sterile dacron or rayon swabs with plastic shafts. Do **not** use calcium alginate swabs or swabs with wooden sticks, as they may contain substances that inactivate some viruses and inhibit PCR testing.
- To obtain a **nasopharyngeal swab**, insert a swab into the nostril parallel to the palate. Leave the swab in place for a few seconds to absorb secretions. Swab both nostrils.
- To obtain an **oropharyngeal swab**, swab the posterior pharynx and tonsillar areas, avoiding the tongue.
- Place the swabs immediately into sterile vials containing 2 ml of viral transport media. Break the applicator sticks off near the tip to permit tightening of the cap. Label each specimen container with the patient's ID number and the date the sample was collected.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, pack in dry ice (see shipping instructions below).

[4] All types of respiratory specimens may used in RT-PCR tests. Fresh-frozen unfixed tissue specimens may also be submitted for RT-PCR.

B. Collecting specimens from the lower respiratory tract

1. Broncheoalveolar lavage, tracheal aspirate, or pleural fluid tap

- During bronchoalveolar lavage or tracheal aspirate, use a double-tube system to maximum shielding from oropharyngeal secretions.
- Centrifuge half of the specimen, and fix the cell pellet in formalin. Place the remaining unspun fluid in sterile vials with external caps and internal O-ring seals. If there is no internal O-ring seal, then seal tightly with the available cap and secure with Parafilm®. Label each specimen container with the patient's ID number and the date the sample was collected.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, ship fixed cells at room temperature and unfixed cells frozen (see shipping instructions below).

2. Sputum

- Educate the patient about the difference between sputum and oral secretions.
- Have the patient rinse the mouth with water and then expectorate deep cough sputum directly into a sterile screw-cap sputum collection cup or sterile dry container.
- If shipping domestically, use cold packs to keep the sample at 4°C. If shipping internationally, pack in dry ice (see shipping instructions below).

II. BLOOD COMPONENTS

Both acute and convalescent serum specimens should be collected for antibody testing. Collect convalescent serum specimens 2–4 weeks after the onset of illness. To collect serum for antibody testing:

- Collect 5 ml–10 ml of whole blood in a serum separator tube. Allow the blood to clot, centrifuge briefly, and collect all resulting sera in vials with external caps and internal O-ring seals. If there is no internal O-ring seal, then seal tightly with the available cap and secure with Parafilm®.
- The minimum amount of serum preferred for each test is 200 microliters, which can easily be obtained from 5 ml of whole blood. A minimum of 1 cc of whole blood is needed for testing of pediatric patients. If possible, collect 1 cc in an EDTA tube and in a clotting tube. If only 1cc can be obtained, use a clotting tube.
- Label each specimen container with the patient's ID number and the date the specimen was collected.
- If unfrozen and transported domestically, ship with cold packs to keep the sample at 4°C. If frozen or transported internationally, ship on dry ice.

III. AUTOPSY SPECIMENS

CDC can perform immunohistochemical (IHC) staining for influenza A (H5) viruses on autopsy specimens. Viral antigens may be focal and sparsely distributed in patients with influenza, and are most frequently detected in respiratory epithelium of large airways. Larger airways (particularly primary and segmental bronchi) have the highest yield for detection of influenza viruses by IHC staining. Collection of the appropriate tissues ensures the best chance of detecting the virus by (IHC) stains.

- If influenza is suspected, a minimum total of 8 blocks or fixed-tissue specimens representing samples from each of the following sites should be obtained and submitted for evaluation:
  - Central (hilar) lung with segmental bronchi
  - Right and left primary bronchi
  - Trachea (proximal and distal)
  - Representative pulmonary parenchyma from right and left lung

In addition, representative tissues from major organs should be submitted for evaluation. In particular, for patients with suspected myocarditis or encephalitis, specimens should include myocardium (right and left ventricle) and CNS (cerebral cortex, basal ganglia, pons, medulla, and cerebellum). Specimens should be included from any other organ showing significant gross or microscopic pathology.

- Specimens may be submitted as:
  - Fixed, unprocessed tissue in 10% neutral buffered formalin, or
  - Tissue blocks containing formalin-fixed, paraffin-embedded specimens, or
  - Unstained sections cut at 3 microns placed on charged glass slides (10 slides per specimen)
- Specimens should be sent at room temperature (**NOT FROZEN**).
- Fresh-frozen unfixed tissue specimens may be submitted for RT-PCR.
- Include a copy of the autopsy report (preliminary, or final if available), and a cover letter outlining a brief clinical history and the submitter's full name, title, complete mailing address, phone, and fax numbers, in the event that CDC pathologists require further information. Referring pathologists may direct specific questions to CDC pathologists. The contact number for the Infectious Disease Pathology Activity is 404-639-3133, or the pathologists can be contacted 24 hours a day, 7 days a week through the CDC Emergency Response Hotline at 770-488-7100.

IV. SHIPPING INSTRUCTIONS

- State and local health departments should call the CDC Emergency Response Hotline (770-488-7100) before sending specimens for influenza A reference testing. This number is available 24 hours a day, 7 days a week. Hotline staff will notify a member of the Influenza Branch who will contact the health department to answer questions and provide guidance. In some cases, the state health department may arrange for a clinical laboratory to send samples directly to CDC.
- Specimens should be sent by Priority Overnight Shipping for receipt within 24 hours. Samples (such as fresh-frozen autopsy samples for RT-PCR or other clinical materials) may be frozen at –70 if the package cannot be shipped within a specified time (e.g., if the specimen is collected on a Friday but cannot be shipped until Monday).
- When sending clinical specimens, include the specimen inventory sheet (see below), include the assigned CDC case ID number, and note "Influenza surveillance" on all materials and specimens sent.

Include the CDC case ID number on all materials forwarded to CDC. Protocols for standard interstate shipment of etiologic agents should be followed, and are available at http://www.cdc.gov/od/ohs/biosfty/shipregs.htm. All shipments must comply with current DOT/IATA shipping regulations.

V. INFLUENZA SPECIMEN INVENTORY SHEET

CDC CASE ID:

List specimens sent to the CDC

Select a SOURCE* from the following list for each specimen: Serum (acute), serum (convalescent), NP swab, NP aspirate/wash, broncheoalveolar lavage specimen (BAL), OP swab, tracheal aspirate, or tissue.

Specimen Type #1:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #2:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #3:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #4:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Specimen Type #5:

❑ Clinical Material
❑ Extracted RNA
❑ Virus Isolate

Source*:_____

Collected : __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Date Sent: __ __ / __ __ / __ __ __ __ (m m d d y y y y)

Carrier: _____ Tracking _____

APPENDIX 6. RAPID DIAGNOSTIC TESTING FOR INFLUENZA

The following information in this appendix is designed to assist clinicians and clinical laboratory directors in the use of rapid diagnostic tests during interpandemic influenza seasons. During an influenza pandemic, one or more of these tests may be sensitive and specific enough to be used by clinicians to supplement clinical diagnoses of pandemic influenza. However, clinicians should be reminded that a negative test result might not rule out pandemic influenza and should not affect patient management or infection control decisions.

I. INFORMATION FOR CLINICIANS

A. Background

Rapid diagnostic tests for influenza can help in the diagnosis and management of patients who present with signs and symptoms compatible with influenza. They also are useful for helping to determine whether institutional outbreaks of respiratory disease might be due to influenza. In general, rapid diagnostic testing for influenza should be done when the results will affect a clinical decision.

Rapid diagnostic testing can provide results within 30 minutes.

B. Reliability and interpretation of rapid test results

The reliability of rapid diagnostic tests depends largely on the conditions under which they are used. Understanding some basic considerations can minimize being misled by false-positive or false-negative results.

Median sensitivities of rapid diagnostic tests are generally ~70%–75% when compared with viral culture, but median specificities of rapid diagnostic tests for influenza are approximately 90%–95%. False-positive (and true negative) results are more likely to occur when disease prevalence in the community is low, which is generally at the beginning and end of the influenza season. False-negative (and true positive) results are more likely to occur when disease prevalence is high in the community, which is typically at the height of the influenza season.

C. Minimizing the occurrence of false results

- Use rapid diagnostic tests that have high sensitivity and specificity.
- Collect specimens as early in the illness as possible (within 4–5 days of symptom onset).
- Follow the manufacturer's instructions, including those for handling of specimens.
- Consider sending specimens for viral culture when:
  - Community prevalence of influenza is low and the rapid diagnostic test result is positive, *or*
  - Disease prevalence is high but the rapid diagnostic test result is negative.

  (Contact your local or state health department for information about influenza activity.)

D. For further information

- Information about influenza is available at the CDC influenza website (www.cdc.gov/flu) or from the CDC Flu Information Line (800-CDC-INFO [English and Spanish]; 800-243-7889 [TTY]).
- For more information about influenza diagnostics, contact your state laboratory or state health department (http://www.cdc.gov/other.htm#states).
- Additional resources:
  - Association of Public Health Laboratories: http://www.aphl.org/Public_Health_Labs/index.cfm

- Weekly U.S. influenza activity reports: http://www.cdc.gov/flu/weekly/fluactivity.htm
- CDC Clinician Outreach and Communication Activity: http://www.bt.cdc.gov/coca/index.asp
- CDC website: http://www.cdc.gov/flu/professionals/labdiagnosis.htm

II. INFORMATION FOR CLINICAL LABORATORY DIRECTORS

A. Background

Rapid diagnostic tests for influenza are screening tests for influenza virus infection; they can provide results within 30 minutes. The use of commercial influenza rapid diagnostic tests by laboratories and clinics has increased substantially in recent years. At least ten rapid influenza tests have been approved by the U.S. Food and Drug Administration (FDA) (see Appendix 1).

Rapid tests differ in some important respects. Some can identify influenza A and B viruses and distinguish between them; some can identify influenza A and B viruses but cannot distinguish between them. Some tests are waived from requirements under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). Most tests can be used with a variety of specimen types, but sensitivity and specificity can vary with specimen type. FDA approval is based upon specific specimen types.

Rapid tests vary in terms of sensitivity and specificity when compared with viral culture. Product insert information and research publications indicate that median sensitivities are approximately 70%–75% and median specificities are approximately 90%–95%.

Specimens to be used with rapid tests generally should be collected as close as possible to the start of symptoms and usually no more than 4–5 days later in adults. In very young children, influenza viruses can be shed for longer periods; therefore, in some instances, testing for a few days after this period may still be useful. Test sensitivity will be greatest in children, who generally have higher viral titers, if the specimen is obtained during the first 2 days of illness, and if the clinician or laboratory has more experience performing the test. The quality of the specimen tested also is critical for test sensitivity.

B. Accuracy depends on disease prevalence

The positive and negative predictive values of rapid tests vary considerably depending on the prevalence of influenza in the community. False-positive (and true negative) influenza test results are more likely to occur when disease prevalence is low, which is generally at the beginning and end of the influenza season. False-negative (and true positive) influenza test results are more likely to occur when disease prevalence is high, which is typically at the height of the influenza season.

1. Clinical considerations when influenza prevalence is low

When disease prevalence is low, the positive-predictive value (PPV) is low and false-positive test results are more likely. By contrast, the negative-predictive value (NPV) is high when disease prevalence is low, and negative results are more likely to be truly negative (see Graphs 1 and 2).

If flu prevalence is...	**and specificity is...**	**then PPV is...**	**false-positive rate is...**
VERY LOW (2.5%)	POOR (80%)	V POOR (6%–12%)	V. HIGH (88%–94%)
VERY LOW (2.5%)	GOOD (98%)	POOR (39%–56%)	HIGH (44%–61%)
MODERATE (20%)	POOR (80%)	POOR (38%–56%)	HIGH (44%–62%)
MODERATE (20%)	GOOD (98%)	GOOD (86%–93%)	LOW (7%–14%)

Interpretation of positive results should take into account the clinical characteristics of the case-patient. If an important clinical decision is affected by the test result, the rapid test result should be confirmed by another test, such as viral culture or PCR.

2. Clinical considerations when influenza prevalence is high

When disease prevalence is relatively high, the NPV is low and false-negative test results are more likely. By contrast, when disease prevalence is high, the PPV is high and positive results are more likely to be true (see Graph 2).

If flu prevalence is...	and sensitivity is...	then NPV is...	false-negative rate is...
MODERATE (20%)	POOR (50%)	MODERATE (86%–89%)	MODERATE (11%–14%)
MODERATE (20%)	HIGH (90%)	V. GOOD (97%–99%)	V. LOW (2%–3%)
HIGH (40%)	POOR (50%)	MODERATE (70%–75%)	MODERATE (25%–30%)
HIGH (40%)	HIGH (90%)	V. GOOD (93%–94%)	LOW (6%–7%)

Interpretation of negative results should take into account the clinical characteristics of the case-patient. If an important clinical decision is affected by the test result, the rapid test result should be confirmed by another test, such as viral culture or PCR.

C. Selecting tests

Selection of a test should take into consideration several factors, such as the types of specimens that are considered optimal for that test. Also, tests with high sensitivity and specificity will provide better positive and negative predictive values. Information about test characteristics is provided in product inserts and scientific articles and by the manufacturer.

D. Changes in recommended procedures can affect test results

Modification by the user can affect test performances and increase false-positive and/or false-negative rates. Such modifications include using specimens for which the test is not optimized or using swabs that did not come with the rapid test kit (unless recommended).

E. When are rapid diagnostic tests beneficial?

Use of rapid diagnostic tests are beneficial in these situations:

- To test cases during an outbreak of acute respiratory disease to determine if influenza is the cause, *or*
- To test selected patients during the influenza season, *or*
- In the fall or winter, to test selected patients presenting with respiratory illnesses compatible with influenza to help establish whether influenza is present in a specific population and to guide healthcare providers in diagnosing and treating respiratory illnesses.

In general, the exclusive use of rapid tests does not address the public health need for obtaining viral isolates so that influenza virus strain subtyping and characterization can be conducted to monitor antigenic and genetic changes.

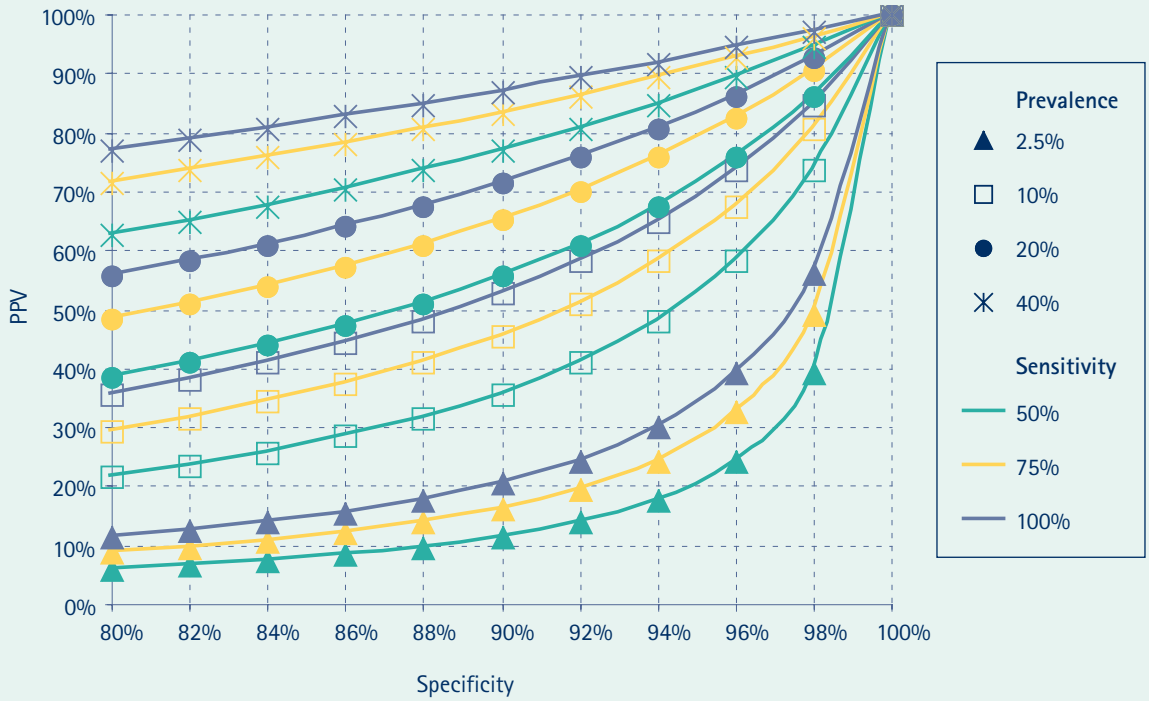
During an influenza pandemic, some rapid diagnostic tests may be able to detect the pandemic strain with adequate sensitivity and specificity. Rapid tests can be used by physicians to supplement clinical diagnoses of pandemic influenza.

> Physicians should be reminded that a negative test result might not rule out influenza and should not affect patient management or infection control decisions.

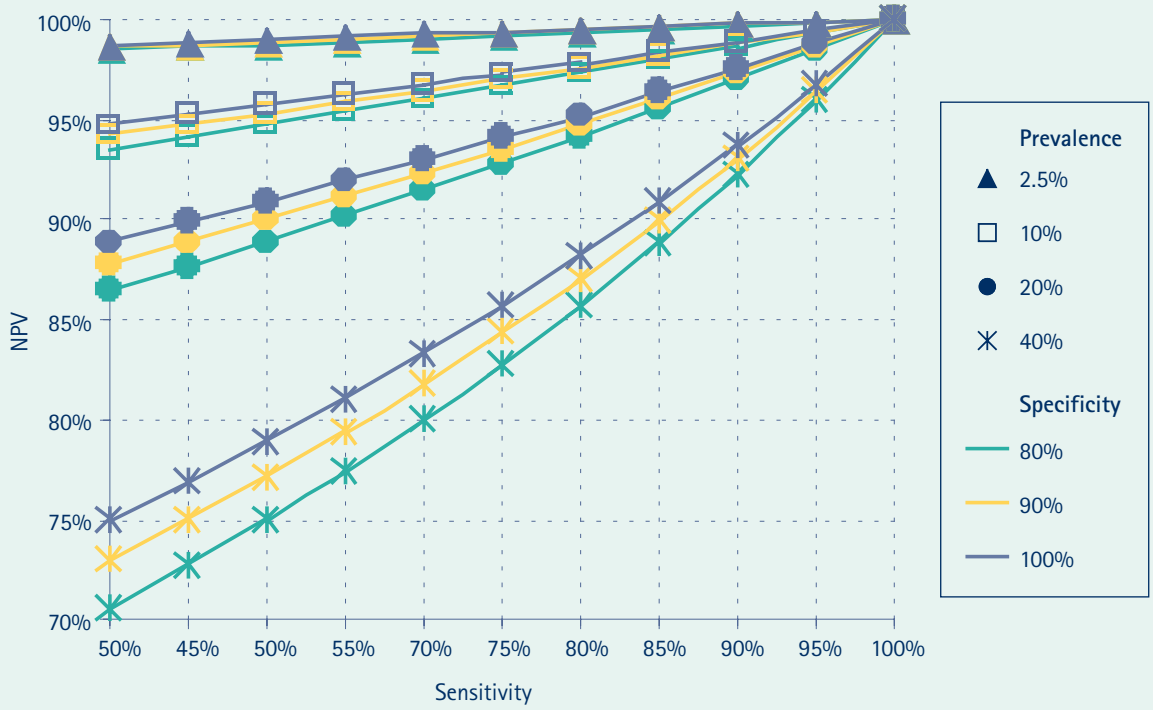
F. For further information

Information on influenza diagnostics is provided on the CDC website at: http://www.cdc.gov/flu/professionals/labdiagnosis.htm.

GRAPH 1: IMPACT OF PREVALENCE, SENSITIVITY AND SPECIFICITY ON POSITIVE PREDICTIVE VALUE



GRAPH 2: IMPACT OF PREVALENCE, SENSITIVITY AND SPECIFICITY ON NEGATIVE PREDICTIVE VALUE



APPENDIX 7. GUIDELINES FOR MEDICAL SURVEILLANCE OF LABORATORY RESEARCH PERSONNEL WORKING WITH NOVEL STRAINS OF INFLUENZA, INCLUDING AVIAN STRAINS AND OTHER STRAINS WITH PANDEMIC POTENTIAL

Key Messages

- Laboratory workers should receive training on the appropriate biosafety level for the type of work being performed.
- Before working with avian influenza A viruses, including highly pathogenic strains, laboratory workers should have a baseline serum sample obtained and stored for future reference.
- Workers in laboratories that contain avian influenza A viruses should report any fever or lower respiratory symptoms to their supervisors. Workers should be evaluated for possible exposures, and the clinical features and course of the illness should be closely monitored.
- Laboratory workers who are believed to have had a laboratory exposure to an avian influenza A virus or other highly pathogenic strain should be evaluated, counseled about the risk of transmission to others, and monitored for fever or lower respiratory symptoms as well as for any of the following: sore throat, rhinorrhea, chills, rigors, myalgia, headache, diarrhea.
- Local and/or state public health departments should be notified promptly of laboratory exposures and illnesses in exposed laboratory workers.

Medical surveillance of laboratory personnel can help to ensure that workers who are at risk of occupational exposure to avian influenza viruses or other novel animal or human influenza strains and who develop symptoms of illness receive appropriate medical evaluation and treatment, both for the benefit of their health and to prevent further transmission.

I. PREREQUISITES FOR WORKING WITH NOVEL AVIAN OR HUMAN INFLUENZA VIRUSES

A. Baseline serum samples

Before working with novel avian or human influenza viruses, laboratory workers should have a baseline serum sample obtained and stored for future reference.

B. Influenza vaccine

Laboratories should offer the current inactivated influenza vaccine to laboratory personnel. Its use is especially encouraged for personnel working with avian viruses in BSL-3 enhanced laboratory conditions and for those who may be exposed to these viruses in the field. Immunization might reduce the chance of illness from exposure to human influenza viruses currently circulating in the community that could lead to confusion in monitoring for avian influenza A infection. Vaccines against novel influenza A viruses (e.g., H5N1) are undergoing clinical trials and might be available in the future.

C. Oseltamivir prophylaxis

- It is not necessary to require oseltamivir for laboratory research personnel working with highly pathogenic influenza strains, but encourage it for those doing animal experiments only for the time they are working with animals and especially while working with ferrets.

- When considering oseltamivir prophylaxis, be sure to evaluate appropriate candidates for contraindications, answer their questions, review adverse effects, and explain the benefits.
- Maintain a log of persons on oseltamivir, persons evaluated and not on oseltamivir, doses dispensed, and adverse effects.
- Periodically evaluate and update oseltamivir policies and procedures.

D. Post-exposure prophylaxis

Conditions for use of oseltamivir for post-exposure prophylaxis include a known or suspected laboratory exposure to live avian influenza virus, including highly pathogenic strains, for a person not on oseltamivir. Appropriate healthcare personnel should be available to evaluate immediately and dispense oseltamivir if the exposure occurs during working hours. If exposure occurs after working hours, an exposed laboratory person should present to the Emergency Department and, after evaluation, communicate with CDC for recommendations.

II. MANAGEMENT OF INFLUENZA-LIKE ILLNESS IN PERSONNEL WITH POSSIBLE EXPOSURE TO NOVEL AVIAN OR HUMAN INFLUENZA VIRUSES

A. General procedures

- Maintain a daily sign-in/out sheet to record name, date, time in/out, use of oseltamivir, and brief description of job tasks. This record will facilitate retrospective documentation if an illness occurs.
- Workers should report any influenza-like illness and any potential laboratory exposures to the supervisor (see also **Supplement 4**).

B. Evaluation and treatment

1. During regular working hours

- The affected employee should notify the supervisor. The supervisor should immediately contact the appropriate healthcare personnel and facility contacts (e.g., occupational health, infection control, or designee).
- Upon arrival at the designated clinic, the employee should be placed in a private room for isolation where a healthcare provider can provide consultation and evaluation.
- The healthcare provider should obtain a respiratory specimen (e.g. nasopharyngeal swab or aspirate) for viral culture. A rapid antigen test[5] with the ability to differentiate between influenza A and B should be used for initial diagnosis, followed by virus isolation.
- Based on: 1) the rapid test result (if influenza A positive), 2) the status of oseltamivir prophylaxis, and 3) the clinical evaluation, the healthcare provider should determine whether the patient will return to work, be sent home, or be sent to an infectious disease consultant.

2. During working hours when the employee calls from home

- The employee should notify the supervisor. The supervisor should discuss the situation with the appropriate healthcare personnel and determine where and by whom the employee will be evaluated and specimens for viral culture will be obtained.

[5] If laboratory capacity is available, RT-PCR should be used to rule out the suspected pathogen.

- The employee may come to an on-site clinic for evaluation or may elect to see a personal physician. If the employee chooses to see a personal physician, the on-site clinician should discuss with the personal physician the likelihood of a laboratory-acquired infection. The personal physician should be asked to collect specimens for antigen detection and viral culture.
- An employee who is not sick enough to be admitted to a hospital should remain at home under the care of a personal physician, pending results from the viral culture. If influenza A (H3N2) or A (H1N1) is identified, the employee should be advised and can resume normal activities as soon as symptoms subside.
- If avian influenza A (e.g., H5, H7, H9) is identified, the family and other contacts should be monitored for illness.[6]
- Local public health officials should be notified about any confirmed avian influenza infections.

3. After working hours

- The employee should notify the supervisor. The supervisor should inform other persons as the situation dictates.
- If the employee is acutely ill with symptoms consistent with influenza, the employee and/or supervisor should contact the appropriate healthcare provider for instructions. The healthcare provider should conduct the initial evaluation and patient management.
- The supervisor should immediately ask the healthcare provider to collect specimens for rapid testing and viral culture.
- The employee should follow the advice of the healthcare provider with regard to further evaluation/treatment.

[6] Persons living with the ill person should be managed as described in Supplement 4.