

Resource Manual for Seasonal and Pandemic Influenza Testing in Texas

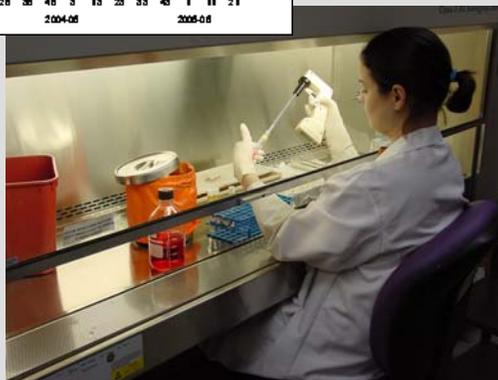
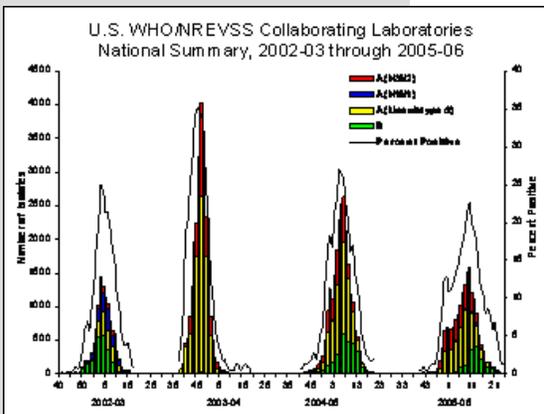
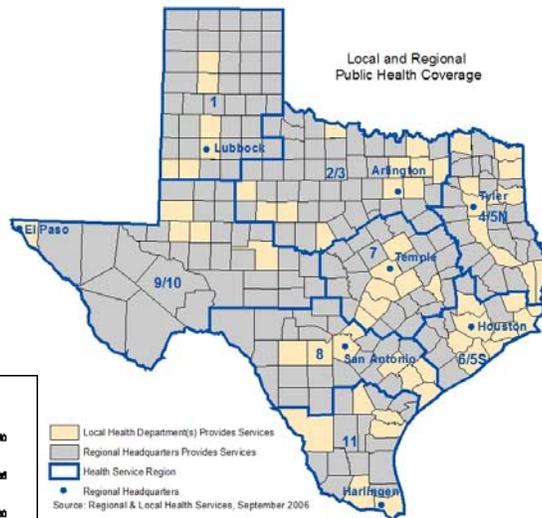
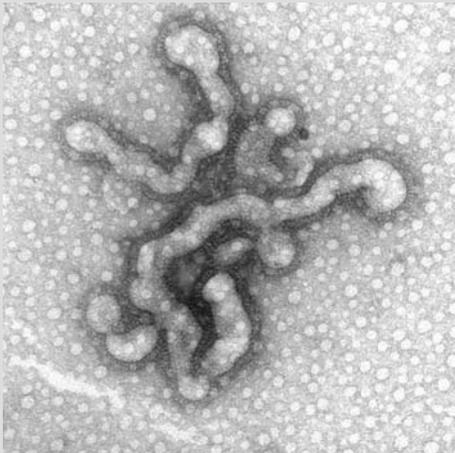


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Introduction:

Both seasonal and pandemic influenza pose a serious threat to the health of the public. Seasonal influenza accounts for over 36,000 deaths in the United States each year. The table below lists estimates for the number of Texans that would be affected by an influenza pandemic. Clinical laboratories typically receive the first specimens for testing during a public health emergency and therefore have an important role in preventing or limiting the impact of a pandemic. This manual is being provided as a resource document to improve understanding of influenza surveillance in Texas and the pandemic influenza testing capabilities of the Texas public health system. In addition, this manual will provide guidance for the over 300 clinical or hospital laboratories in Texas that are involved in influenza diagnosis and pandemic influenza planning efforts.

Estimated Number of Texans affected by an influenza pandemic

Characteristic	Number Texans affected
Illness	11.5 million
Outpatient medical	5.75 million
Hospitalization	1,265,000
ICU care	199,750
Mechanical ventilation	94,780
Deaths	247,250
Absent from work	Up to 50%

*Calculations based on Texas population of 23 million using CDC percentages

Key roles of the clinical laboratory before and during an influenza pandemic will include:

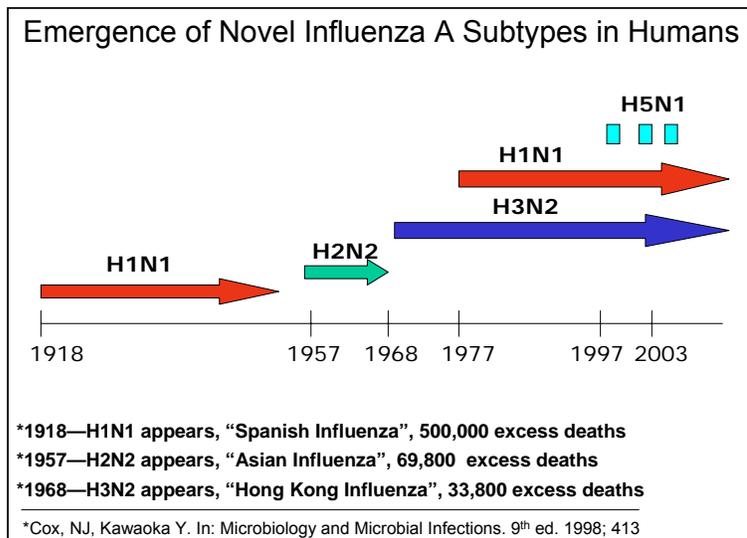
- Following specimen selection, collection, and transport guidance
- Expediting collection, processing, and transport of post-mortem samples if requested
- Submitting samples from cases of novel influenza or isolates to a public health laboratory
- Adjusting protocols to identify high-risk patients
- Maintaining other diagnostic service
- Adjusting algorithms for specimen and testing triage/prioritization
- Supporting state influenza surveillance activities

Influenza Background/Laboratory Diagnosis

Influenza viruses are single stranded RNA viruses that belong to the family Orthomyxoviridae. Influenza viruses are divided into types A, B, and C. Influenza types A and B cause epidemics of respiratory illness during the winter in temperate climates. Influenza type C causes a mild or subclinical illness and is not associated with epidemics.

Influenza type A viruses are further divided into subtypes. These subtypes are based on differences in the two surface proteins, hemagglutinin (H) and neuraminidase (N). There are 16 hemagglutinin subtypes and 9 neuraminidase subtypes that have been identified. Influenza A viruses are unique in the fact that they are able to cause infection in animal species as well as in humans. Influenza B and C infections are associated with humans only. All subtypes of influenza A have been isolated from avian species. Influenza A subtypes have also been found in pigs, horses, seals, whales, as well as many other animal species.

Influenza viruses undergo two different methods of antigenic change: antigenic drift and antigenic shift. Antigenic drift is the result of point mutations that occur during viral replication resulting in new virus strains. Antigenic drift is the reason why the influenza vaccine must be updated each year. Antigenic shift is a more dramatic change resulting in a novel subtype of influenza A. Each time an antigenic shift has occurred in the last century it has been associated with a dramatic increase in mortality.



Influenza illness in humans is characterized by fever, cough, sore throat, body aches, and malaise. Symptoms of influenza usually come on suddenly, one to four days after the virus enters the body. Among children, otitis media, nausea, and vomiting are also commonly reported with the influenza illness. Influenza is usually a limiting infection but in people with chronic medical conditions such as heart or lung disease, it can lead to pneumonia and other life-threatening illnesses. Older adults account for more than 90% of deaths attributed to pneumonia and influenza.

Laboratory Diagnosis

Appropriate treatment of patients with respiratory illness depends on accurate and timely diagnosis. Early diagnosis of influenza can reduce the inappropriate use of antibiotics and provide the option of using antiviral therapy. However, certain bacterial infections can produce symptoms similar to influenza; therefore, bacterial infections should be considered and appropriately treated, if suspected. In addition, bacterial infections can occur as a complication of influenza.

Influenza surveillance information and diagnostic testing can aid clinical judgment and help guide treatment decisions. The accuracy of clinical diagnosis of influenza on the basis of symptoms alone is limited because symptoms from illness caused by other pathogens can overlap considerably with influenza. Influenza surveillance by state and local health departments and CDC can provide information regarding the presence of influenza viruses in the community. Surveillance can also identify the predominant circulating types, influenza A subtypes, and strains of influenza.

Diagnostic tests available for influenza include viral culture, serology, rapid antigen testing, polymerase chain reaction (PCR), and immunofluorescence assays. Sensitivity and specificity of any test for influenza might vary by the laboratory that performs the test, the type of test used, and the type of specimen tested. Among respiratory specimens for viral isolation or rapid detection, nasopharyngeal specimens are typically more effective than throat swab specimens. As with any diagnostic test, results should be evaluated in the context of other clinical and epidemiologic information available to health-care providers.

Commercial rapid diagnostic tests are available that can detect influenza viruses within 30 minutes. Some tests are approved for use in any outpatient setting, whereas others must be used in a moderately complex clinical laboratory. These rapid tests differ in the types of influenza viruses they can detect and whether they can distinguish between influenza types. Different tests can detect 1) only influenza A viruses; 2) both influenza A and B viruses, but not distinguish between the two types; or 3) both influenza A and B and distinguish between the two types.

None of the tests provide any information about influenza A subtypes. The types of specimens acceptable for use (i.e., throat, nasopharyngeal, or nasal aspirates, swabs, or washes) also vary by test. The specificity and, in particular, the sensitivity of rapid tests are lower than for viral culture and vary by test. Due to the lower sensitivity of the rapid tests, physicians should consider confirming negative tests with viral culture or other means because of possible false-negative rapid test results, especially during periods of peak community influenza activity. In contrast, false-positive rapid test results are less likely, but can occur during periods of low influenza activity. Therefore, when interpreting rapid influenza test results, physicians should consider the positive and negative predictive values of the test in the context of the level of influenza activity in their community.

Despite the availability of rapid diagnostic tests, collecting clinical specimens for viral culture is critical, because only culture isolates can provide specific information regarding circulating strains and subtypes of influenza viruses. This information is needed to compare current circulating influenza strains with vaccine strains, to guide decisions regarding influenza treatment and chemoprophylaxis, and to formulate vaccine for the coming year. Virus isolates also are needed to monitor the emergence of antiviral resistance and of novel influenza A subtypes that might pose a pandemic threat.

Laboratory Diagnosis information accessed at the Centers for Disease Control website: <http://www.cdc.gov/flu/professionals/diagnosis/labrole.htm>

Influenza Diagnosis Table			
	Type Detected	Specimen types	Turnaround Time for Results
Enzyme Immuno Assay	A, B and A + B (undifferentiated)	NP swab , throat swab, nasal wash, bronchial wash	< 1 hour
DFA	A and B	NP swab, nasal wash, bronchial wash, nasal aspirate, sputum	2-4 hours
RT-PCR	A and B	NP swab, throat swab, nasal wash, bronchial wash, nasal aspirate, sputum	6-8 hours
Serology	A and B	Acute and convalescent serum samples	> 2 weeks
Viral culture	A and B	NP swab, throat swab, nasal wash, bronchial wash, nasal aspirate, sputum	3-10 days

Rapid Influenza Tests

Rapid diagnostic tests for influenza can provide timely results that may be helpful with patient management. It is important to understand how the conditions under which these tests are used affect their reliability. To minimize false results:

- ❖ ***Use rapid diagnostic tests with high sensitivity and specificity***
- ❖ ***Collect specimens as early in the illness as possible (within 4-5 days)***
- ❖ ***Follow manufacturer's instructions, including handling of specimens***
- ❖ ***Consider sending specimens for viral culture to confirm results of rapid tests especially when community prevalence of influenza is low and the rapid diagnostic test result is positive and when the rapid diagnostic test result is negative but disease prevalence is high.***

Information accessed at Centers for Disease Control
www.cdc.gov/flu/professionals/diagnosis/rapidclin

Rapid Diagnostic Testing for Influenza: Information for Clinical Laboratory Directors

- The availability and use of commercial influenza rapid diagnostic tests by laboratories and clinics have substantially increased in recent years.
- Influenza rapid diagnostic tests are screening tests for influenza virus infection that can provide results within 30 minutes.
- More than 10 rapid influenza tests have been approved by the U.S. Food and Drug Administration (FDA).
- Rapid tests differ in some important respects:
 - Some tests identify influenza A and B viruses and distinguish between the two strains.
 - Some tests identify influenza A and B viruses but cannot distinguish between the two strains.
 - 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 the accuracy of the tests can vary based on the type of specimen collected (for example throat swab versus nasal swab).
- FDA approval is based upon specific specimen types.
- The 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%
 - Median specificities are approximately 90-95%
- When using rapid tests, the optimal specimen collection time in adults is as close as possible to the start of symptoms but usually no more than 4-5 days later. 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.

Accuracy Depends Upon Prevalence

The positive and negative predictive values vary considerably depending upon 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.

Clinical Considerations of Testing When Influenza Prevalence is Low

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

If Flu Prevalence is...	And Specificity is...	Then PPV is...	False Pos. 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%)

The interpretation of positive results should take into account the clinical characteristics of the case. 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 polymerase chain reaction (PCR).

Clinical Considerations of Testing When Influenza Prevalence Is High

When disease prevalence is relatively high, the NPV is low and false-negative test results are more likely. When disease prevalence is high, the PPV is high and positive results are more likely to be true.

If Flu Prevalence is...	And Sensitivity is...	Then NPV is...	False Neg. 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%)

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

Selecting Tests

Many factors should be considered when selecting a test, including the following:

- Sensitivity and specificity. Tests with higher sensitivity and specificity will provide better positive and negative predictive values.
- Types of specimens that provide the most accurate results.

Information about these characteristics can be found in product inserts and scientific articles, and by contacting the manufacturer.

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
- Using swabs that did not come with the rapid test kits [unless recommended].

When Is Use of Rapid Diagnostic Tests Beneficial?

- Testing during an outbreak of acute respiratory disease can determine if influenza is the cause.
- During influenza season, testing of selected patients presenting with respiratory illnesses compatible with influenza can help establish whether influenza is present in a specific patient population and help health-care providers determine how to use their clinical judgment for diagnosing and treating respiratory illness. (Testing need not be done for all patients.)

“Rapid Diagnostic Testing: Information for Clinical Laboratory Directors”

accessed at Centers for Disease Control:

<http://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm>

****Commercial rapid influenza antigen testing in the evaluation of suspected influenza H5N1 cases should be interpreted with caution. Clinicians should be aware that these tests have relatively low sensitivities, and a negative result would not exclude a diagnosis of influenza H5N1. In addition, a positive result does not distinguish between seasonal and avian A viruses.**

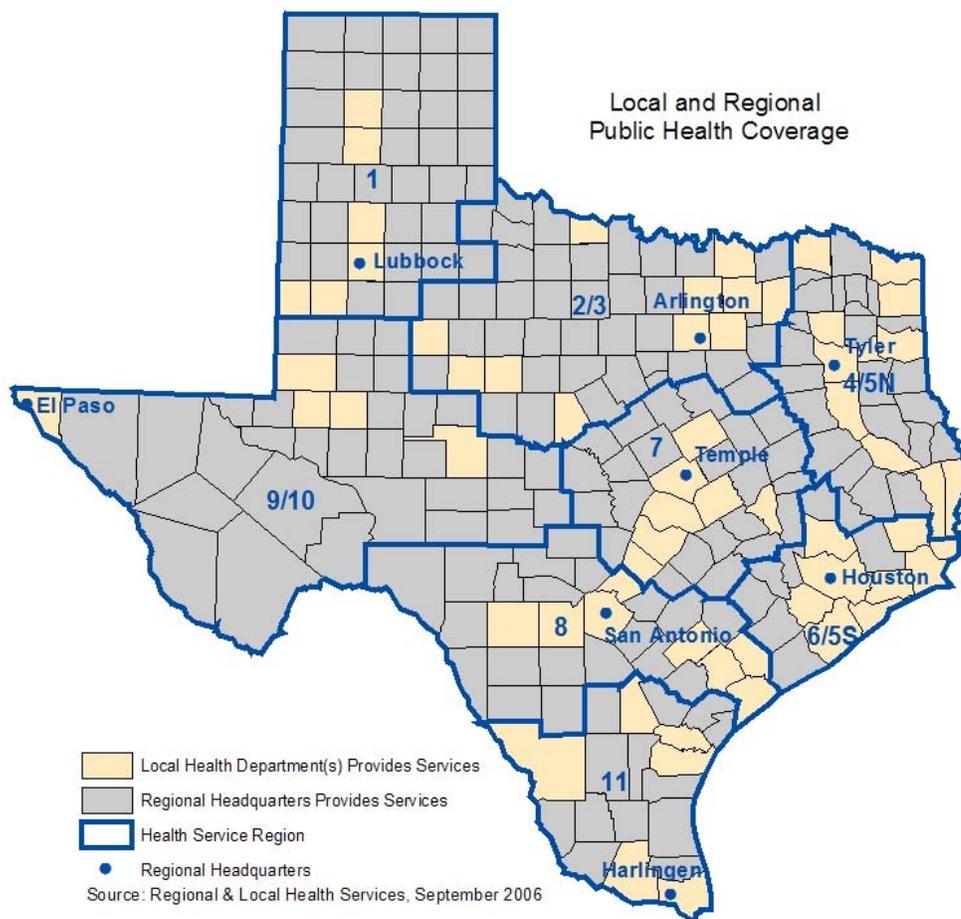
****Although at times beneficial, rapid tests do not address the public health need for cell cultures that provide a virus isolate. Influenza virus isolates are essential for determining the match between circulating influenza viruses and those viruses contained in the vaccine and for aiding in the selection of new vaccine strains.**

Influenza Surveillance

Influenza surveillance in Texas is conducted to determine: when influenza is circulating; the type and subtype of influenza; how well the circulating strains match the vaccine strains, and which communities and regions are experiencing flu activity and to some extent the degree of activity. Influenza is not a notifiable condition in Texas. Influenza surveillance in Texas consists of 3 major components: culture surveillance data from any source; influenza-like illness (ILI) information, and other laboratory information on positive rapid flu tests taken in clinics or point of care settings such as emergency rooms or walk-in clinics. Influenza-Like-Illness (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. The compiled data is analyzed, designated an activity level, and submitted to the Centers for Disease Control and Prevention (CDC) on a weekly basis. Influenza activity levels are reported as no activity, sporadic, local, regional, or widespread based on the CDC definitions below.

No Activity	Overall clinical activity remains low and there are no laboratory confirmed cases
Sporadic	Isolated cases of laboratory confirmed influenza in the state; Influenza-Like-Illness (ILI) activity is not increased. OR a laboratory confirmed outbreak in a single institution‡ in the state; ILI activity is not increased.
Local	Increased ILI within a single region AND recent (within the past 3 weeks) laboratory evidence of influenza in that region. ILI activity in other regions is not increased. OR Two or more institutional outbreaks (ILI or laboratory confirmed) within a single region AND recent (within the past 3 weeks) laboratory confirmed influenza in that region. Other regions do not have increased ILI and virus activity is no greater than sporadic in those regions.
Regional (This level of activity does not apply for small states with 4 or fewer regions.)	Increased ILI in ≥ 2 but less than half of the regions AND recent (within the past 3 weeks) laboratory confirmed influenza in the affected regions. OR Institutional outbreaks (ILI or laboratory confirmed) in ≥ 2 and less than half of the regions AND recent laboratory confirmed influenza in the affected regions.
Widespread	Increased ILI and/or institutional outbreaks (ILI or laboratory confirmed) in at least half of the regions AND recent (within the past 3 weeks) laboratory confirmed influenza in the state.

Texas is divided into 11 public health service regions. Volunteer health care providers collect and submit viral cultures to the Texas Department of State Health Services (DSHS) laboratory on a weekly basis during influenza season. Each year designated submitters from across the state are provided with transport medium, submission forms, and specific instructions for patient selection and specimen collection, storage, and transport. Influenza viruses that are identified through this program are subtyped to determine the strain(s) of influenza that are circulating in the community. This information, along with a select number of isolates, is provided to the Centers for Disease Control (CDC) and the World Health Organization (WHO) to be compiled with surveillance data from laboratories around the world. Other laboratories, regional and local health departments, facilities participating in influenza research, and private physicians around the state also participate in flu surveillance. The efforts of these health care providers and laboratories in Texas as well as other states aid the CDC in developing a national picture of influenza activity, a geographic distribution of influenza, and a clinical impact of the circulating viruses.



Texas Sentinel Provider Network:

Sentinel providers report the total number of patient visits for ILI by age group (0-4 years, 5-24 years, 25-64 years, >65 years) along with the total number of patient visits for any reason. These data are transmitted once a week via internet or fax to the CDC. Most providers report that the entire process takes less than 20 minutes a week. In addition, sentinel providers can submit specimens from a subset of patients for virus isolation at no cost to the provider.

Providers of any specialty (e.g., family practice, internal medicine, pediatrics, infectious diseases) in any type of practice (e.g., private practice, public health clinic, urgent care center, emergency room, university student health center) are eligible to be sentinel providers. Nurse Practitioners and Physician Assistants are also eligible.

Data from sentinel providers are critical for monitoring the impact of influenza and, in combination with other influenza surveillance data, can be used to guide prevention and control activities, vaccine strain selection, and patient care. Sentinel providers receive feedback on the data submitted, summaries of regional and national influenza data, and free subscriptions to CDC's Morbidity and Mortality Weekly Report and Emerging Infectious Diseases journal.

To participate in the Texas Sentinel Provider Network contact the coordinator, Irene Brown at 512-458-7676.

Overview of Influenza Surveillance in the United States:

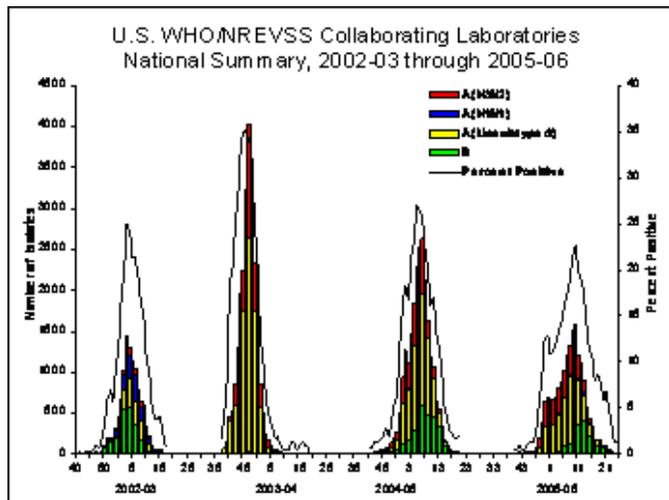
The Influenza Branch at CDC collects and reports information on influenza activity in the United States each week from October through May. The U.S. influenza surveillance system has seven different components, including four that operate year-round that allow CDC to:

- Find out when and where influenza activity is occurring
- Determine what type of influenza viruses are circulating
- Detect changes in the influenza viruses
- Track influenza-related illness
- Measure the impact influenza is having on deaths in the United States

The Seven Components of Influenza Surveillance:

1. World Health Organization(WHO) and National Respiratory and Enteric Virus Surveillance System (NREVSS) Collaborating Laboratories

About 80 WHO and 50 NREVSS collaborating laboratories located throughout the United States report the total number of respiratory specimens tested and the number positive for influenza types A and B each week. Most of the US WHO collaborating laboratories also report the influenza A subtype (H1N1 or H3N2) of the viruses they have isolated and the ages of the persons from whom the specimens were collected. Some of the influenza viruses collected by laboratories are sent to CDC for more testing.



2. U.S. Influenza Sentinel Providers Surveillance Network

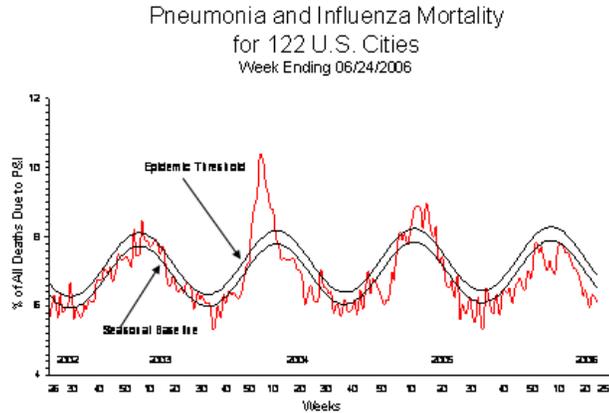
Each week, approximately 1,200 health-care providers around the country report the total number of patients seen and the number of those patients with influenza-like illness (ILI) by age group. For this system, ILI is defined as fever (temperature of $\geq 100^{\circ}\text{F}$ [37.8°C]) and a cough and/or a sore throat in the absence of a KNOWN cause other than influenza.

The percentage of patient visits to sentinel providers for ILI reported each week is weighted on the basis of state population. This percentage is compared each week with the national baseline of 2.1%. The baseline is the mean percentage of patient visits for ILI during non-influenza weeks for the previous three seasons plus two standard deviations. Non-influenza weeks are defined as weeks in which the percentage of specimens tested for influenza that are influenza

positive is less than 10%. Due to wide variability in regional level data, it is not appropriate to apply the national baseline to regional data. Region specific baselines are calculated using the same method as the national baseline.

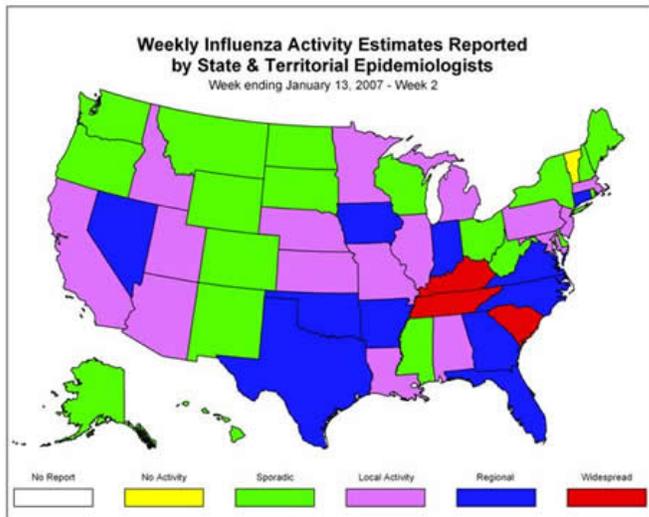
3. 122 Cities Mortality Reporting System

Each week, the vital statistics offices of 122 cities report the total number of death certificates received and the number of those for which pneumonia or influenza was listed as the underlying or as a contributing cause of death by age group. The percentage of all deaths due to pneumonia and influenza are compared with a seasonal baseline and epidemic threshold value calculated for each week.



4. State and Territorial Epidemiologists Reports

State health departments report the estimated level of influenza activity in their states each week. States report influenza activity as no activity, sporadic, local, regional, or widespread. These levels are defined as follows:



No Activity: No laboratory-confirmed cases of influenza and no reported increase in the number of cases of ILI.

Sporadic: Small numbers of laboratory-confirmed influenza cases or a single laboratory-confirmed influenza outbreak has been reported, but there is no increase in cases of ILI.

Local: Outbreaks of influenza or increases in ILI cases and recent laboratory-confirmed influenza in a single region of the state.

Regional: Outbreaks of influenza or increases in ILI and recent laboratory confirmed influenza in at least 2 but less than half the regions of the state.

Widespread: Outbreaks of influenza or increases in ILI cases and recent laboratory-confirmed influenza in at least half the regions of the state.

5. Influenza-associated pediatric mortality

Influenza-associated pediatric mortality is a newly added nationally notifiable condition. Laboratory-confirmed influenza-associated deaths in children less

than 18 years old are reported through the Nationally Notifiable Disease Surveillance System.

6. Emerging Infections Program (EIP)

The EIP Influenza Project conducts surveillance for laboratory-confirmed influenza related hospitalizations in persons less than 18 years of age in 60 counties covering 12 metropolitan areas of 10 states (San Francisco CA, Denver CO, New Haven CT, Atlanta GA, Baltimore MD, Minneapolis/St. Paul MN, Albuquerque NM, Las Cruces, NM, Albany NY, Rochester NY, Portland OR, and Nashville TN). Cases are identified by reviewing hospital laboratory and admission databases and infection control logs for children with a documented positive influenza test (viral culture, direct/indirect fluorescent antibody assay (DFA/IFA), reverse transcription-polymerase chain reaction (RT-PCR), or a commercial rapid antigen test) conducted as a part of routine patient care. EIP estimated hospitalization rates are reported every two weeks during the influenza season.

7. New Vaccine Surveillance Network (NVSN)

The New Vaccine Surveillance Network (NVSN) provides population-based estimates of laboratory-confirmed influenza hospitalization rates for children less than 5 years old residing in three counties: Hamilton County OH, Davidson County TN, and Monroe County NY. Children admitted to NVSN hospitals with fever or respiratory symptoms are prospectively enrolled and respiratory samples are collected and tested by viral culture and RT-PCR. NVSN estimated rates are reported every two weeks during the influenza season. Together, the seven influenza surveillance components are designed to provide a national picture of influenza activity. Pneumonia and influenza mortality is reported on a national level only. Sentinel provider and laboratory data are reported on a national level and by influenza surveillance region. The state and territorial epidemiologists' reports of influenza activity are the only state-level information reported. Both the EIP and NVSN data provide population-based, laboratory-confirmed estimates of influenza-related pediatric hospitalizations but are reported from limited geographic areas.

It is Important to Remember the Following about Influenza Surveillance in the United States:

- ❖ All influenza activity reporting by states and health-care providers is voluntary.
- ❖ The reported information answers the questions of where, when, and what influenza viruses are circulating. This information may also be used to determine if influenza activity is increasing or decreasing, but cannot be used to ascertain how many people have become ill with influenza during the influenza season.
- ❖ The system consists of seven complementary surveillance components. These components include reports from more than 120 laboratories, 2,000 sentinel health care providers, vital statistics offices in 122 cities, research and health-care personnel at the NVSN and EIP sites, and influenza surveillance coordinators and state epidemiologists from all 50 state health

departments, and the New York City and District of Columbia health departments.

- ❖ Influenza surveillance data collection is based on a reporting week that starts on Sunday and ends on Saturday of each week. Each surveillance participant is requested to summarize weekly data and submit it to CDC by Tuesday afternoon of the following week. Those data are then downloaded, compiled, and analyzed at CDC. The report is distributed and posted on the CDC Web site (<http://www.cdc.gov/flu/weekly/fluactivity.htm>) each Friday.

Information accessed at: Centers for Disease Control:
<http://www.cdc.gov/flu/weekly/pdf/flu-surveillance-overview.pdf>

Laboratory Response Network/State Public Health Laboratory

The Laboratory Response Network:

The Laboratory Response Network (LRN) was established in 1999 by the Department of Health and Human Services Centers for Disease Control and Prevention (CDC), in response to Presidential Decision Directive 39.



This network is comprised of state and local public health, federal, military, and international laboratories. The main function of the LRN is to ensure that these laboratories have the capacity to respond to biological and chemical threats as well as other public health emergencies.

The LRN laboratories are categorized as either national, reference or sentinel laboratories based on their respective testing capabilities. National laboratories, such as the CDC, perform definitive testing of specimens that cannot be tested or confirmed by a reference laboratory due to its Biosafety Level rating. Reference laboratories, which include state public health, veterinary, and international laboratories, provide confirmatory testing for many select agents. The sentinel laboratory category contains the largest number of LRN laboratories and is composed of hospital, clinical, and commercial diagnostic laboratories that perform routine diagnostic and rule-out testing in addition to referring specimens to reference laboratories.

Texas has eleven geographically distinct LRN reference laboratories capable of responding to biological threats, emerging infectious diseases, and other public health emergencies. These LRN laboratories maintain 24/7/365 testing capabilities for biological agents such as *B. anthracis*, *F. tularensis*, *Y. pestis*, and other organisms that pose a threat to public health. Nine of the eleven Texas LRN laboratories will support rapid testing of human specimens for avian influenza H5 (Asian lineage). The following



appendices will provide information on collection, packaging, and shipment of specimens for rapid H5 testing, a list of 24/7/365 contact information for each Texas LRN, and a listing of the service area for each LRN by county.

State Public Health Laboratory:

The Laboratory Services Section (LSS) of the Texas Department of State Health Services (DSHS) provides comprehensive laboratory services for human, animal and environmental specimens in addition to providing professional expertise and consultation. The LSS consists of the state public health laboratory in Austin, the Women's Health Laboratory in San Antonio, and the South Texas Laboratory in Harlingen. In addition to the DSHS laboratories, there are a number of other city and/or county public health laboratories throughout the state that maintain various testing capabilities required for their jurisdictions.

The state public health laboratory in Austin is heavily involved in influenza surveillance by performing viral culture of seasonal influenza. The goal of culture surveillance is to identify and track drift variants of currently circulating virus types and subtypes and to detect the emergence of novel influenza A subtypes. Viral culture surveillance also allows for monitoring of the match between vaccine strains and currently circulating viruses and selection of optimal vaccine components each year. The laboratory relies on specimen submissions from health care providers around the state to provide information on the circulating strains and when and where influenza activity is occurring in Texas. This information is distributed weekly to health officials around Texas and is reported to national surveillance systems. The state laboratory is a participating member of the World Health Organization Influenza Collaborating Network and the National Respiratory and Enteric Virus Surveillance System. In addition, as a member of the Laboratory Response Network, the state laboratory also provides PCR testing of patients meeting the avian influenza case definition.

The laboratory requests the following submissions:

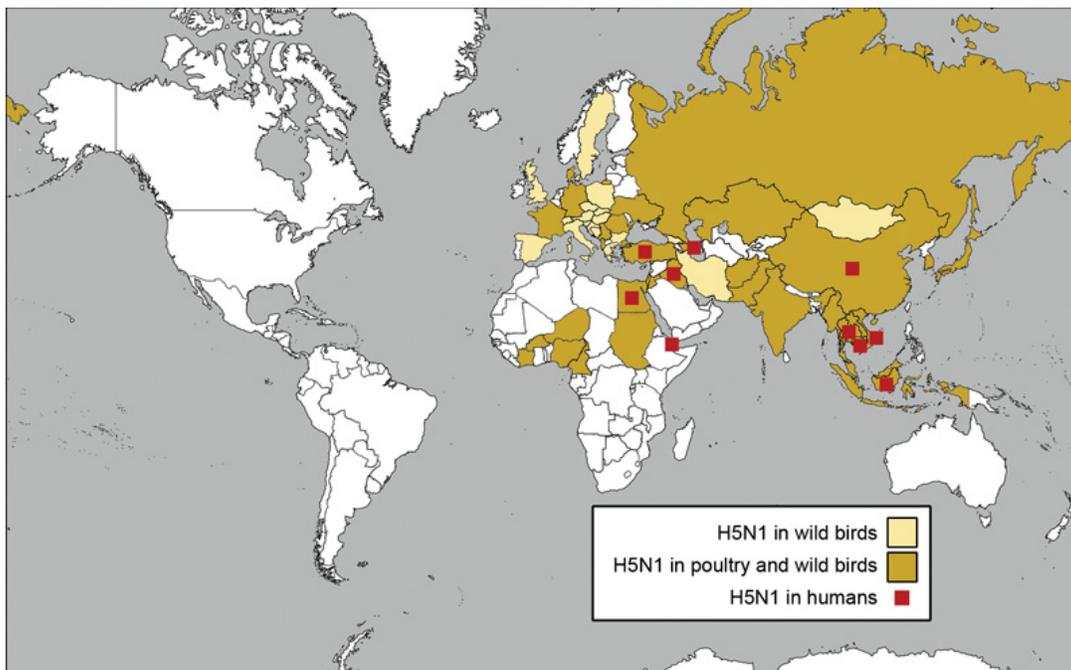
- Pre-season isolates and the first of the season isolates: These isolates can provide important information regarding circulation of strains as compared to the previous season, the match between vaccine and circulating strains, and information necessary for the vaccine formulation for the next year.
- Representative number of isolates collected during peak activity
- Late season isolates, after major outbreak activity is over
- Specimens obtained during outbreaks. Outbreaks may occur in immunized populations or in non-immunized populations where the attack rate is high.
- Isolates from persons receiving an antiviral agent or from their contacts that become ill. The increased use of antiviral agents for treatment and prophylaxis of influenza in some areas of the world has created the potential for the emergence and spread of antiviral resistant viruses, which must be monitored.
- Isolates from cases of suspected animal to human transmission of influenza viruses.

Appendix C provides specimen submission instructions to laboratories or health care providers interested in sending clinical specimens to the state public health laboratory for influenza surveillance.

Pandemic Influenza

- ❖ Pandemic influenza is a global outbreak of influenza by a new influenza virus to which few people have any immunity.
- ❖ It is not known when a pandemic will occur, how severe it will be or if it will be caused by avian flu (H5N1) or another influenza virus.
- ❖ In the last century, pandemic influenza outbreaks occurred in 1918, 1957, and 1968.
- ❖ Development of a perfect match vaccine cannot occur until a new influenza virus shifts to person-to-person transmission.
- ❖ Until a vaccine can be produced against this new strain, effective vaccine protection will not be possible.
- ❖ Antivirals are used to treat influenza viruses. Current manufacturing capacity for antivirals cannot produce enough to meet a worldwide demand.
- ❖ The ability to detect and control infectious diseases has improved greatly since the last pandemic. Future planning will focus on how to reduce the effects of a new and serious strain of emerging influenza.
- ❖ Due to the ease and frequency of international travel, a new viral strain could reach the United States in hours or days.
- ❖ A pandemic can occur simultaneously in hundreds or thousands of places. A pandemic can continue to spread illness in waves lasting for a year or more.
- ❖ A severe pandemic could change daily life for a long time, including limits on travel and public gatherings, work and school attendance.

Nations with Confirmed Cases H5N1 Avian Influenza (July 7, 2006)



Source: <http://www.pandemicflu.gov/map.html>

Pandemic Influenza planning:

Stages of a Pandemic

The World Health Organization (WHO) has developed a [global influenza preparedness plan](#), which defines the stages of a pandemic, outlines the role of WHO, and makes recommendations for national measures before and during a pandemic. The phases are:

Inter-pandemic phase	Low risk of human cases	1
New virus in animals, no human cases	Higher risk of human cases	2
Pandemic alert: New virus causes human cases	No or very limited human to human transmission	3
	Evidence of increased human to human transmission	4
	Evidence of significant human to human transmission	5
Pandemic	Efficient and sustained human to human transmission	6

Interpandemic period

Phase 1: No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low.

Phase 2: No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease.

Pandemic alert period

Phase 3: Human infection(s) with a new subtype but no human-to-human spread, or at most rare instances of spread to a close contact.

Phase 4: Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.

Phase 5: Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans but may not yet be fully transmissible (substantial pandemic risk).

Pandemic period

Phase 6: Pandemic: increased and sustained transmission in general population.

Notes: The distinction between **phases 1** and **2** is based on the risk of human infection or disease resulting from circulating strains in animals. The distinction is based on various factors and their relative importance according to current scientific knowledge. Factors may include pathogenicity in animals and humans, occurrence in domesticated animals and livestock or only in wildlife, whether the virus is enzootic or epizootic, geographically localized or widespread, and other scientific parameters. The distinction among **phases 3, 4, and 5** is based on an assessment of the risk of a pandemic. Various factors and their relative importance according to current scientific knowledge may be considered. Factors may include rate of transmission, geographical location and spread, severity of illness, presence of genes from human strains (if derived from an animal strain), and other scientific parameters.

Texas DSHS Laboratory's Role in an Influenza Pandemic:

- Provide laboratory specimen submission forms containing at least the following information fields: Demographics, Symptom onset date, Date of collection, Specimen source, Vaccination history
- Maintain reference capability and capacity to isolate influenza in cell culture and subtype using reagents provided by WHO
- Maintain Laboratory Response Network (LRN) protocols for identifying influenza subtypes
- Submit influenza isolates to CDC according to WHO guidelines: isolates that cannot be subtyped with kit reagents; pre-season, early-season, late-season isolates and a representative number of isolates during peak activity; isolates obtained during an outbreak; isolates from persons receiving antivirals or from their contacts who become ill; and isolates from cases of suspect animal-to-human transmission
- Identify additional staff required for surge capacity
- Identify and maintain a list of laboratories that, in addition to those in the Laboratory Response Network, may serve as resources for specimen analysis.
- The DSHS Laboratory Services Section will coordinate assistance for specimen transport to national labs as per protocol.
- Continue testing routine influenza specimens, referring isolates to CDC
- Test specimens suspected of being a novel subtype, using nonculture techniques as requested by DSHS epidemiologists
- Refer specimens that test positive for Influenza A to CDC as needed.
- Provide staff identified for surge capacity with Just In Time (JIT) training
- Determine need for increased transportation resources and additional shipping materials for viral specimens
- Ensure nonroutine laboratory submitters have current instructions for collecting appropriate samples for influenza specimens and how to package and ship those specimens to meet the laboratory requirements.
- Continue to separate specimens for routine surveillance from specimens for enhanced surveillance and testing specimens for enhanced surveillance using nonculture techniques.
- Develop and evaluate diagnostic tests for novel subtype.

- Ensure availability of diagnostic reagents to identify the novel subtype.
- Develop and evaluate diagnostic tests for novel subtype.
- Provide laboratory support to test clinical specimens for influenza and identify a novel subtype.
- Consider acquiring laboratory space that meets Bio Safety Level 3 with enhancements specifications.
- The DSHS laboratory will test clinical specimens for influenza and identify the novel subtype.
- IDCU or the Infectious Disease Surveillance and Epidemiology Branch will determine specimen selection.
- Maintain heightened surveillance activities.

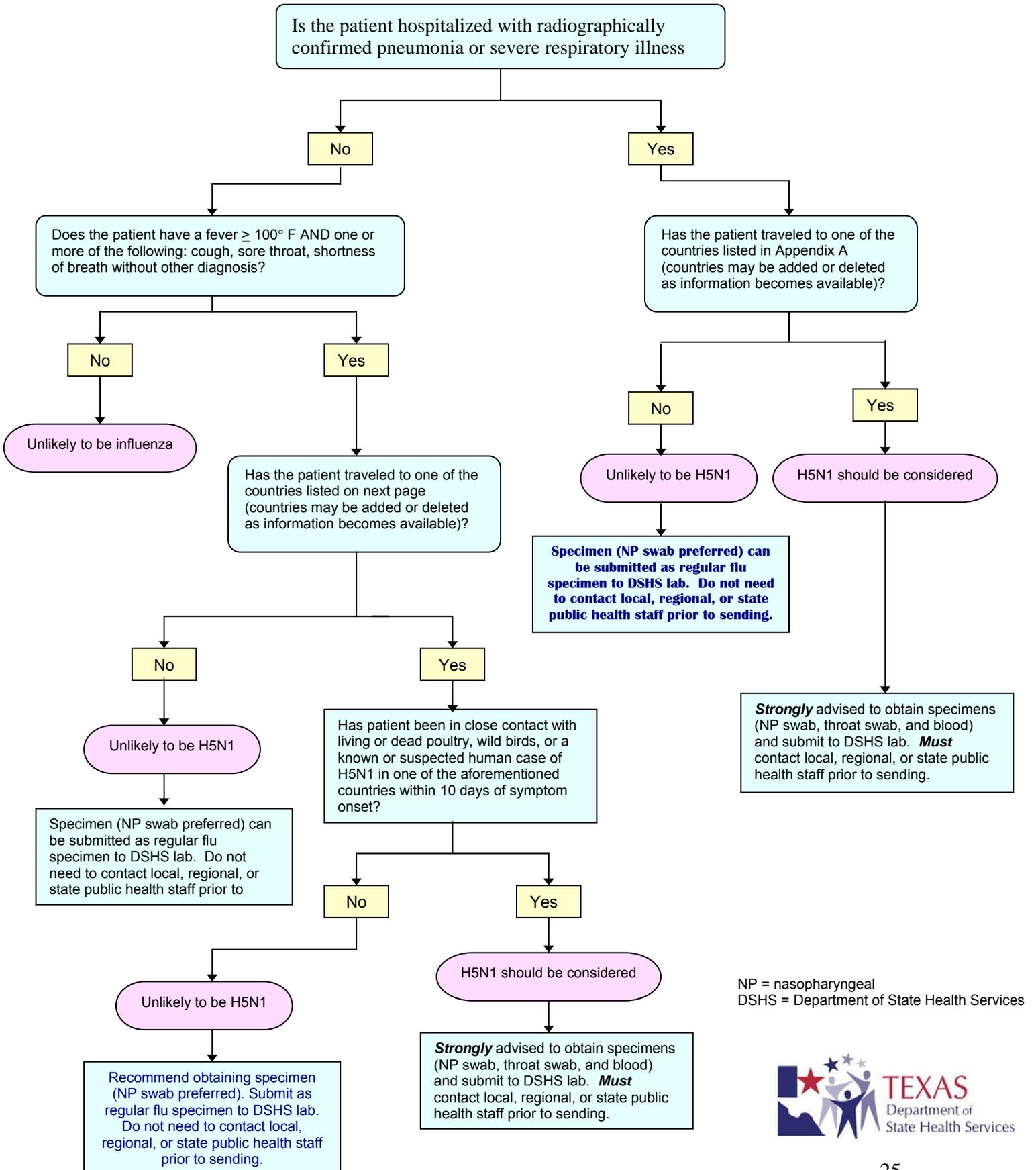
Pandemic Influenza Testing

Clinicians should contact their local, regional, or state health department as soon as possible to report any suspected human case of influenza H5N1 in the United States. Contact information for public health officials in Texas is provided in Appendix A. Quick action will allow public health officials to investigate, begin outbreak control measures, and assist in arranging for specimen testing, all with the goal of limiting the scope and severity of illness.

The following pages provide guidelines on the process of testing for pandemic influenza, including evaluating the risk of the patient to determine if testing is warranted, arranging for testing in the nearest available laboratory in Texas, and collecting specimens.

- ❖ **Algorithm for Determining Risk of Highly Pathogenic Avian Influenza (subtype H5N1) in Patients Presenting with Febrile Respiratory Illness**
- ❖ **How to arrange for testing**
- ❖ **Specimen collection and testing guidelines for Influenza A H5N1**
- ❖ **Appendix A: List of contact names and phone numbers of Department of State Health Services and Laboratory Response Network staff to coordinate testing.**

Algorithm for Determining Risk of Highly Pathogenic Avian Influenza (subtype H5N1) in Patients Presenting with Febrile Respiratory Illness



NP = nasopharyngeal
 DSHS = Department of State Health Services



List of Countries with Influenza A H5N1 activity (as of 12-24-2007)

Afghanistan	Jordan
Albania	Kazakhstan
Austria	Korea
Azerbaijan	Kuwait
Bangladesh	Laos
Benin	Malaysia (peninsular)
Bosnia and Herzegovina	Mongolia
Bulgaria	Myanmar
Burkina Faso	Niger
Cambodia	Nigeria
Cameroon	Palestinian Auton. Territories
Canada	Pakistan
China	Philippines
Côte d'Ivoire	Poland
Croatia	Romania
Czech Republic	Russia
Denmark	Saudi Arabia
Djibouti	Serbia and Montenegro
Egypt	Slovakia
France	Slovenia
Georgia	South Africa
Germany	Spain
Ghana	Sudan
Greece	Sweden
Hong Kong	Switzerland
Hungary	Taipei China
Kazakhstan	Thailand
India	Togo
Indonesia	Turkey
Iraq	Ukraine
Iran	United Kingdom
Israel	Vietnam
Italy	Zimbabwe
Japan	

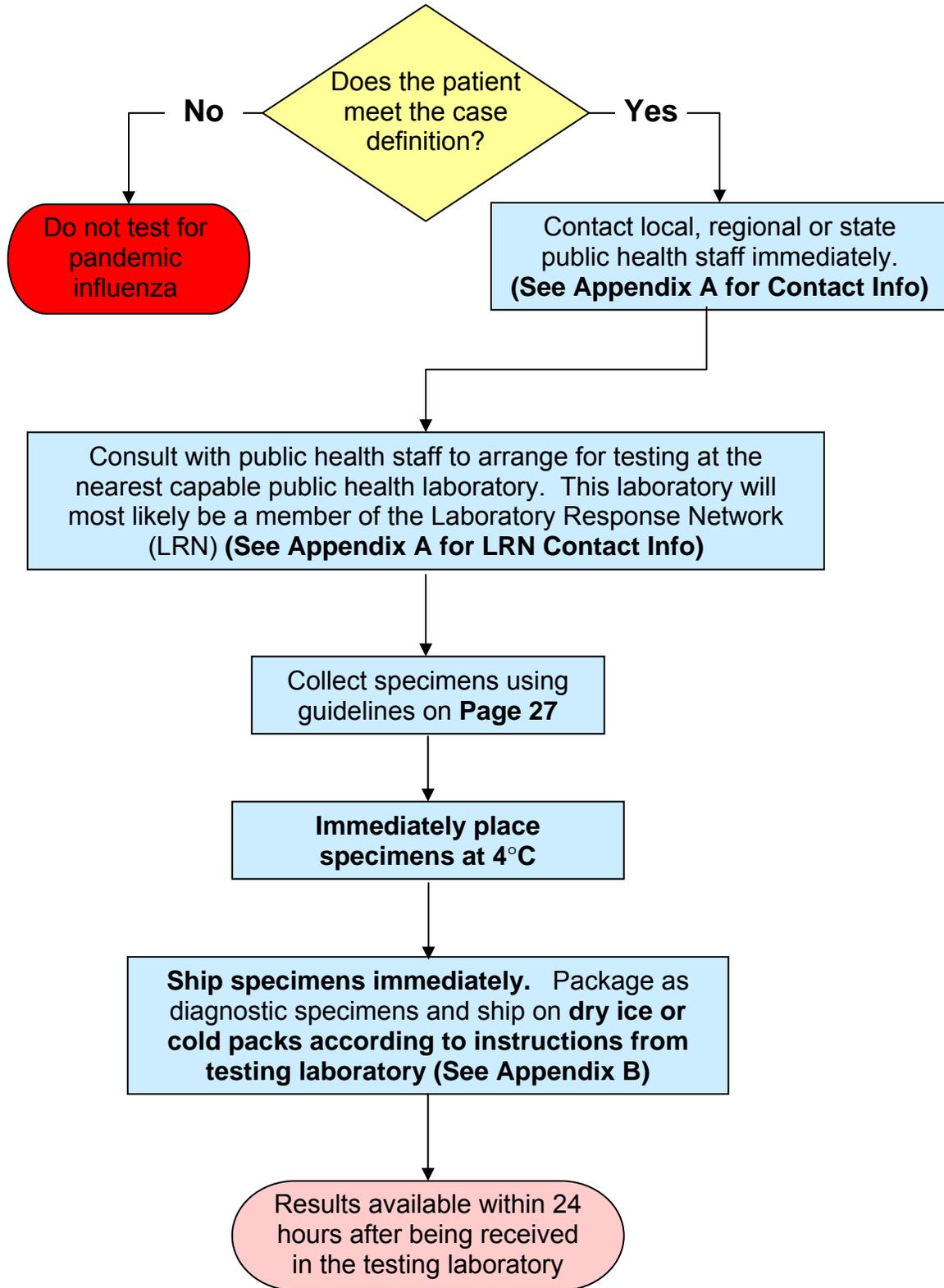
H5N1 affected countries list is updated at the following websites:

<http://www.cdc.gov/flu/avian/outbreaks/current.htm>

http://www.oie.int/eng/en_index.htm

http://www.who.int/csr/disease/avian_influenza/en/

How to Arrange for Avian Influenza Testing



Specimen Collection and Testing Guidelines for Influenza A H5N1

- ❖ Oropharyngeal swab specimens and lower respiratory tract specimens (e.g., bronchoalveolar lavage or tracheal aspirates) are preferred because they appear to contain the highest quantity of virus for influenza H5N1 detection, as determined on the basis of available data. Nasal or nasopharyngeal swab specimens are acceptable, but may contain fewer virus particles and therefore not optimal specimens for virus detection.
- ❖ Detection of influenza H5N1 is more likely from specimens collected within the first 3 days of illness onset. If possible, serial specimens should be obtained over several days from the same patient.
- ❖ Bronchoalveolar lavage is considered to be a high-risk aerosol-generating procedure. Therefore, infection control precautions should include the use of gloves, gown, goggles or face shield, and a fit-tested respirator with an N-95 or higher rated filter. A loose-fitting powered air-purifying respirator (PAPR) may be used if fit-testing is not possible (e.g., if the person has a beard). Detailed guidance on infection control precautions for health care workers caring for suspected influenza H5N1 patients is available.
- ❖ Swabs used for specimen collection should have a Dacron tip and an aluminum or plastic shaft. Swabs with calcium alginate or cotton tips and wooden shafts are not recommended. **Specimens should be put into an approved biohazard bag and placed at 4°C immediately after collection.**
- ❖ For reverse-transcriptase polymerase chain reaction (RT-PCR) analysis, nucleic acid extraction lysis buffer can be added to specimens (for virus inactivation and RNA stabilization), after which specimens can be stored and shipped at 4°C. Otherwise, specimens should be frozen at or below -70°C and shipped on dry ice. For viral isolation, specimens can be stored and shipped at 4°C. If specimens are not expected to be inoculated into culture within 2 days, they should be frozen at or below -70°C and shipped on dry ice. Avoid repeated freeze/thaw cycles.
- ❖ Influenza H5N1-specific reverse-transcriptase polymerase chain reaction (RT-PCR) testing conducted under Biosafety Level 2 (BSL-2) or higher conditions is the preferred method for diagnosis. All state public health laboratories, most LRN laboratories, and CDC are able to perform influenza H5N1 RT-PCR testing. LRN reference laboratories are the recommended sites for preliminary testing.
- ❖ **Viral culture should NOT be attempted on specimens from patients suspected to have influenza H5N1, unless conducted under BSL-3 conditions with enhancements.**
- ❖ Commercial rapid influenza antigen testing in the evaluation of suspected influenza H5N1 cases should be interpreted with caution. Clinicians should be aware that these tests have relatively low sensitivities. Thus, a negative result would not exclude a diagnosis of influenza H5N1. In addition, a positive result does not distinguish between seasonal and avian influenza A viruses.
- ❖ Serologic testing for measuring influenza H5N1-specific antibody, utilizing appropriately timed specimens, can be considered if other H5N1 diagnostic testing methods are unsuccessful (e.g., due to delays in respiratory specimen collection). Paired serum specimens from the same patient are required for influenza H5N1 diagnosis. One sample should be tested within the first week of illness and a

second sample should be tested 2-4 weeks later. A demonstrated rise in the H5N1-specific antibody level is required for a diagnosis of H5N1 infection. Currently, the microneutralization assay, which requires live virus, is the recommended test for measuring H5N1-specific antibody. Any work with live wild-type highly pathogenic influenza H5N1 viruses must be conducted in a USDA-approved BSL-3 with enhancements facility. For more information about procedures and facilities recommended for manipulating highly pathogenic avian influenza viruses, visit <http://www.cdc.gov/flu/h2n2bsl3.htm>.

- ❖ Laboratory testing results positive for influenza A (H5N1) in the United States should be confirmed at CDC, which has been designated as a WHO H5 Reference Laboratory.

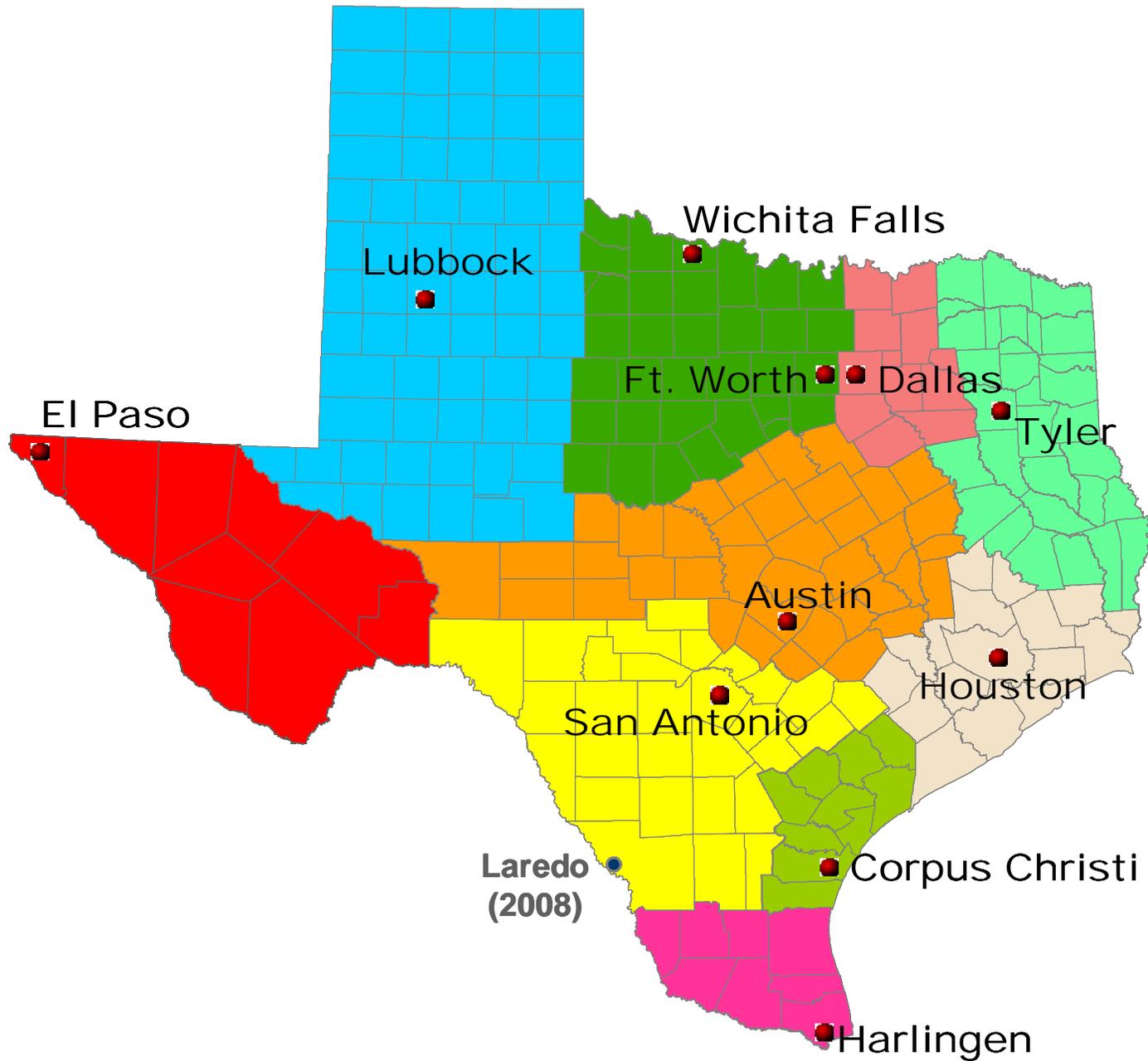
Information taken from: Updated Interim Guidance for Laboratory Testing of Persons with Suspected Infection with Avian Influenza A (H5N1) Virus in the United States, Distributed via Health Alert Network June 7, 2006

Appendix A: Contact Information

Texas DSHS Central Office (Austin):	Name	Phone Number	24/7 Phone Number
Epidemiologist-IDCU	Lesley Bullion	512-458-7111 x 6364	
Epidemiologist-IDCU	Neil Pascoe	512-458-7111 x 2358	
Physician-on-call		888-963-7111	888-963-7111
Laboratory: Virus Isolation Team		512-458-7594 512-458-7111 x 2452	
Laboratory: Medical Virology Group	Maryann Patterson	512-458-7515	
Laboratory: Microbiological Sciences	Elizabeth Delamater	512-458-7592	512-634-6734
Laboratory: Containers and Supplies		512-458-7661	
Texas HSR Influenza Surveillance Contacts: (HSR map on p 9)	Name	Phone Number	24/7 Phone Number
HSR 1	Janice Dennis	806-767-0406	
HSR 2/3	Thi Nguyen	817-264-4657 or Nextel 817-822-9747	
HSR 4/5	Vicki Harris	903-533-5262	
HSR 5S/6	Huai Lin	713-767-9032	
HSR 7	Sandi Henley	254-778-6744 x 2532	
HSR 8	Beth Hannemann	210-692-1457	
HSR 9/10	Kathy Wehmeyer	432-571-4138	
HSR 11	Vivienne Heines	361-888-7837 x 235	
Texas LRN contacts	Name	Phone Number	24/7 Phone Number
Austin	Rahsaan Drumgoole Grace Kubin	512-458-7185 512-458-7552	512-689-5537 512-634-6727
Corpus Christi	Donna Rosson	361-850-1323	361-533-3500
	Sandra Heatherley	361-851-7214	361-533-3499
Dallas County	Joey Stringer	972-692-2762	214-677-7415
	Edward Bannister	214-819-1952	214-677-7876
El Paso	Michael Villanueva	915-543-3255	915-252-0398
Fort Worth/Tarrant County	Rebecca McMath	817-321-4755	817-929-4720
Harlingen/South Texas	Kristina Zamora	956-364-8369	956-454-4387
Houston	Jane O'Brien	713-558-3490	713-376-0484
Lubbock	Kim Swacina	806-775-2908	806-252-3943
	Michael Lipton	806-775-3087	806-392-5125
San Antonio	Patricia Blevins	210-207-5883	210-669-2863
Tyler/PHLET	Irene Krumins	903-877-5071	903-528-2093
Wichita Falls	Jo Harp	940-761-7873	888-801-5792

Prepared: 12-28-2007

Texas Laboratory Response Network (LRN) Facilities



LRN/Full Service Local Health Departments and Districts Contact Information for Texas Counties

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Andrews County	Andrews City-CO Health Dept	211 NW 1st Street	Andrews	79714	432-524-1434	432-524-1461	Lubbock
Angelina County	Angelina CO & Cities Health Dist	503 Hill Street	Lufkin	75904	936-632-1139	936-632-2640	Tyler/East Texas
Archer County							Tarrant
Anderson County							Tyler/East Texas
Angelina County							Tyler/East Texas
Aransas County							Corpus Christi
Armstrong County							Lubbock
Atascosa County							San Antonio
Austin County							Houston
Bailey County							Lubbock
Bandera County							San Antonio
Bastrop County							Austin
Baylor County							Tarrant
Bee County							Corpus Christi
Bell County	Bell CO Public Health Dist	201 North 8th Street	Temple	76501	254-773-4457	254-773-7535	Austin
Bexar County	San Antonio Metropolitan Hlth Dist	332 W Commerce, Ste 307	San Antonio	78205-2489	210-207-8731	210-207-8999	San Antonio
Blanco County							Austin
Borden County							Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Bosque County							Austin
Bowie County	Texarkana-Bowie CO Fam Hlth Cntr	902 West 12th	Texarkana	75501	903-798-3255	903-793-2289	Tyler/East Texas
Brazoria County	Brazoria CO Health Department	432 East Mulberry	Angleton	77515- 4736	281-756-1484	979-864-1456	Houston
Brazos County	Brazos CO Health Dist	201 North Texas Ave	Bryan	77803- 5317	979-361-4440	979-823-2275	Austin
Brewster County							El Paso
Briscoe County							Lubbock
Brooks County							Harlingen/South Texas
Brown County	Brownwood-Brown CO Health Dept	510 East Lee	Brownwood	76801	325-646-0554	325-643-8157	Tarrant
Burleson County							Austin
Burnet County							Austin
Caldwell County							Austin
Calhoun County	Calhoun CO Health Dept	117 West Ash	Port Lavaca	77979	361-552-9721	361-552-9722	Corpus Christi
Callahan County							Tarrant
Cameron County	Cameron CO Health Dept	1122 Morgan Blvd	Harlingen	78550	956-427-8037	956-427-8107	Harlingen/South Texas
Camp County							Tyler/East Texas
Carson County							Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Cass County	Cass County Health Dept	123 South Kaufman	Linden	75563	903-756-7051	903-756-5146	Tyler/East Texas
Chambers County	Chambers CO Health Dept	1204 Stowell Street	Anahuac	77514	409-267-8356	409-267-4276	Houston
Cherokee County	Cherokee CO Health Dept	1209 N Main Street	Rusk	75785	903-683-4688	903-683-4899	Tyler/East Texas
Childress County							Lubbock
City of Beaumont	Beaumont Public Health Dept	950 Washington Blvd	Beaumont	77705	409-832-4000	409-832-4270	Houston
City of Dallas	Dallas Envirn & Hlth Svcs Dept (City of)	1500 Marilla Street, Ste 7AN	Dallas	75201	214-670-5711	214-670-3863	Dallas
City of Fort Worth	Fort Worth (City of) Public Health Dept	1800 University Dr, Rm 232	Fort Worth	76107	817-871-7201	817-871-7335	Tarrant
City of Houston	Houston Dept of HHS	8000 N Stadium Drive, 8th Flr	Houston	77054	713-794-9311	713-798-0862	Houston
City of Port Arthur	Port Arthur City Health Dept	449 Austin Avenue	Port Arthur	77640	409-983-8800	409-983-8870	Houston
Clay County							Tarrant
Cochran County							Lubbock
Coke County							Lubbock
Coleman County							Tarrant
Collin County	Collin CO Health Care Servcs	825 N McDonald St, Ste 130	McKinney	75069	972-548-5500	972-548-5550	Dallas
Collingsworth County							Lubbock
Colorado County							Houston
Comal County							San Antonio
Comanche County							Tarrant

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Concho County							Austin
Cooke County							Tarrant
Corvell County							Austin
Cottle County							Lubbock
Crane County							Lubbock
Crockett County							Austin
Crosby County							Lubbock
Culberson County							El Paso
Dallam County							Lubbock
Dallas County excluding City of Dallas	Dallas CO Health & Human Servcs	2377 N Stemmons Freeway	Dallas	75207	214-819-6070	214-819-6022	Dallas
Dawson County	South Plains Public Health Dist	922 East Main Street	Brownfield	79316- 0115	806-637-2167	806-637-4298	Lubbock
Deaf Smith County							Lubbock
Delta County							Tyler/East Texas
Denton County	Denton CO Health Dept	306 N Loop 288, Ste 183	Denton	76209	940-349-2900	940-349-2905	Tarrant
DeWitt County	Cuero-DeWitt CO Health Dept	106 N Gonzales Street	Cuero	77954	361-275-3461	361-275-5732	San Antonio
Dickens County							Lubbock
Dimmit County							San Antonio

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Donley County							Lubbock
Duval County							San Antonio
Eastland County							Tarrant
Ector County	Ector CO Health Dept	221 North Texas	Odessa	79761	432-498-4141	432-498-4143	Lubbock
Edwards County							San Antonio
Ellis County							Dallas
El Paso County	El Paso City-CO Hlth & Envirn Dist	5115 El Paso Drive	El Paso	79905	915-771-5701	915-771-5729	El Paso
Erath County							Tarrant
Falls County							Austin
Fannin County							Dallas
Fayette County							Austin
Fisher County							Lubbock
Floyd County							Lubbock
Foard County							Tarrant
Fort Bend County	Fort Bend CO Health Dept (HHS)	4520 Reading Road, Ste A	Rosenberg	77471	281-342-6414	281-342-7371	Houston

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Franklin County							Tyler/East Texas
Freestone County							Austin
Frio County							San Antonio
Gaines County	South Plains Public Health Dist	921 East Main Street	Brownfield	79316-0114	806-637-2166	806-637-4297	Lubbock
Galveston County	Galveston CO Health Dist	1207 Oak Street	La Marque	77568-5925	409-938-2401	409-938-2243	Houston
Garza County							Lubbock
Gillespie County							San Antonio
Glasscock County							Lubbock
Goliad County							Corpus Christi
Gonzales County							San Antonio
Gray County							Lubbock
Grayson County	Grayson CO Health Dept	515 North Walnut	Sherman	Physical	903-893-0131	903-892-3776	Dallas
Gregg County	Gregg County Health Department	405 East Marshall	Longview	75601	903-237-2620	903-237-2608	Tyler/East Texas
Grimes County							Austin
Guadalupe County							San Antonio
Hale County	Plainview-Hale CO Health Dist	111 East 10th Street	Plainview	79072	806-293-1359	806-293-5741	Lubbock
Hall County							Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Hamilton County							Austin
Hansford County							Lubbock
Hardeman County							Tarrant
Hardin County	Hardin CO Health Dept	440 West Monroe	Kountze	77625	409-246-5188	409-246-4373	Houston
Harris County excluding City of Houston	Harris CO Public Health & Environ Servcs	2223 West Loop South	Houston	77027	713-439-6016	713-439-6080	Houston
Harrison County	Marshall-Harrison CO Health Dist	1900 S Washington	Marshall	75670	903-938-8338	903-938-8330	Tyler/East Texas
Hartley County							Lubbock
Haskell County							Tarrant
Hays County	Hays CO Health Dept	401-A Broadway Drive	San Marcos	78666	512-393-5520	512-393-5530	Austin
Hemphill County							Lubbock
Henderson County							Dallas
Hidalgo County	Hidalgo CO Health Dept	1304 South 25th Street	Edinburg	78539	956-383-6221	956-383-8864	Harlingen/South Texas
Hill County							Austin
Hood County							Tarrant
Hockley County							Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Hopkins County							Tyler/East Texas
Houston County							Tyler/East Texas
Howard County							Lubbock
Hutchinson County							Lubbock
Hudspeth County							El Paso
Hunt County	Greenville-Hunt CO Health Dept	2700 Johnson Street	Greenville	75401	903-408-4140	903-454-3721	Dallas
Irion County							Lubbock
Jack County							Tarrant
Jackson County	Jackson CO Health Dept	411 N Wells, Rm 102	Edna	77957	361-782-5221	361-782-7312	Corpus Christi
Jasper County	Jasper-Newton CO Public Health Dist	140 West Lamar Street	Jasper	75951	409-384-6830	409-384-7862	Tyler/East Texas
Jeff Davis County							El Paso
Jefferson County							Houston
Jim Hogg County							Harlingen/South Texas
Jim Wells County							San Antonio
Johnson County							Tarrant

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Jones County							Tarrant
Karnes County							San Antonio
Kaufman County							Dallas
Kendall County							San Antonio
Kenedy County							Harlingen/South Texas
Kent County							Lubbock
Kerr County							San Antonio
Kimble County							Austin
King County							Lubbock
Kinney County							San Antonio
Kleberg County							Corpus Christi
Knox County							Tarrant
La Salle County							San Antonio
Lamar County	Paris-Lamar CO Health Dept	740 SW 6th	Paris	75460	903-785-4561	903-737-9924	Tyler/East Texas
Lamb County							Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Lampasas County							Austin
Lavaca County							San Antonio
Lee County							Austin
Leon County							Austin
Liberty County							Houston
Limestone County							Austin
Lipscomb County							Lubbock
Live Oak County	Live Oak CO Health Dept	305 Guadalupe St-Crths Annex	George West	78022	361-449-2733 x118	361-449-1013	San Antonio
Llano County							Austin
Loving County							Lubbock
Lubbock County	Lubbock City Health Dept	1902 Texas Avenue	Lubbock	79411	806-775-2899	806-775-3209	Lubbock
Lynn County							Lubbock
Madison County							Austin
Marion County							Tyler/East Texas
Martin County							Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Mason County							Austin
Matagorda County							Houston
Maverick County							San Antonio
McCulloch County							Austin
McLennan County	Waco-McLennan CO Public Health Dist	225 West Waco Drive	Waco	76707	254-750-5450	254-750-5452	Austin
McMullen							San Antonio
Medina County	Medina CO Health Dept	3103 Avenue G	Hondo	78861	830-741-6191	830-426-4202	San Antonio
Menard County							Austin
Midland County	Midland Health Dept	3303 W Illinois, Space 22	Midland	79703	432-681-7613	432-681-7634	Lubbock
Milam County	Milam CO Health Dept	209 South Houston Street	Cameron	76520	254-697-7039	254-697-4809	Austin
Mills County							Austin
Mitchell County							Lubbock
Montague County							Tarrant
Montgomery County	Montgomery CO Health Dept	701 East Davis, Suite A	Conroe	77301	936-525-2800	936-539-9272	Houston
Moore County							Lubbock
Morris County							Tyler/East Texas

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Motley County							Lubbock
Nacogdoches County							Tyler/East Texas
Navarro County	Corsicana-Navarro Public Health Dist	618 North Main	Corsicana	75110	903-874-6731	903-872-7215	Dallas
Newton County	Jasper-Newton CO Public Health Dist	139 West Lamar Street	Jasper	75951	409-384-6829	409-384-7861	Tyler/East Texas
Nolan County	Sweetwater-Nolan CO Health Dept	301 East 12th Street	Sweetwater	79556	325-235-5463	325-236-6856	Lubbock
Nueces County	Corpus Christi-Nueces CO PH Dist	1702 Horne Road	Corpus Christi	78416	361-851-7200	361-851-7295	Corpus Christi
Ochiltree							Lubbock
Oldham							Lubbock
Orange County	Orange CO Health Dept	2014 North 10th Street	Orange	77630	409-883-6119	409-883-3147	Houston
Palo Pinto County							Tarrant
Panola County							Tyler/East Texas
Parker County							Tarrant
Parmer County							Lubbock
Pecos County	Pecos County Health Department	461 S. Highway 285, Suite 2	Ft. Stockton	79735	432-336-2738	432-336-3552	El Paso
Polk County							Tyler/East Texas
Potter County	Amarillo (City of) Dept of Health	1411 Amarillo Blvd, East	Amarillo	79105	806-351-7220	806-351-7275	Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Presidio County							El Paso
Rains County							Dallas
Randall County	Amarillo (City of) Dept of Health	1412 Amarillo Blvd, East	Amarillo	79105	806-351-7221	806-351-7276	Lubbock
Reagan County							Lubbock
Real County							San Antonio
Red River County							Tyler/East Texas
Reeves County							El Paso
Refugio County							Corpus Christi
Roberts County							Lubbock
Robertson County							Austin
Rockwall County							Dallas
Runnels County							Tarrant
Rusk County							Tyler/East Texas
Sabine County							Tyler/East Texas
San Augustine County							Tyler/East Texas

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
San Jacinto County							Houston
San Patricio County	San Patricio CO Dept of Health	313 North Rachal Street	Sinton	78387	361-364-6208	361-364-6117	Corpus Christi
San Saba County							Austin
Schleicher County							Austin
Scurry County	Scurry CO Health Unit	911 26th Street	Snyder	79549	325-573-3508	325-573-0380	Lubbock
Shelby County							Tyler/East Texas
Smith County	Smith CO Public Health Dist	815 North Broadway	Tyler	75702-4507	903-535-0036	903-535-0052	Tyler/East Texas
Shackelford County							Tarrant
Sherman County							Lubbock
Somervell County							Tarrant
Starr County							Harlingen/South Texas
Stephens County							Tarrant
Sterling County							Lubbock
Stonewall County							Lubbock
Sutton County							Austin
Swisher County							Lubbock
Tarrant County excluding City of Fort Worth	Tarrant CO Public Health Dept	1101 S. Main, Rm 2412	Fort Worth	76104	817-321-5300	817-321-5302	Tarrant

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Taylor County	Abilene-Taylor CO Health Dept	2241 South 19th Street	Abilene	79605	325-692-5600	325-690-6707	Tarrant
Terrell County							El Paso
Terry County	South Plains Public Health Dist	919 East Main Street	Brownfield	79316-0112	806-637-2164	806-637-4295	Lubbock
Throckmorton County							Tarrant
Titus County							Tyler/East Texas
Tom Green County	SanAngelo-TomGreen CO Hlth Dept	2 City Hall Plaza	San Angelo	76903	325-657-4235	325-657-4553	Lubbock
Travis County	Austin-Travis CO HHS	Post Office Box 1088	Austin	78767	512-972-5000	512-972-5016	Austin
Trinity County							Tyler/East Texas
Tyler County							Tyler/East Texas
Upshur County							Tyler/East Texas
Upton County							Lubbock
Uvalde County	Uvalde CO Health Dept	1021 Garnerfield Road	Uvalde	78801	830-278-1705	830-278-1881	San Antonio
Val Verde							San Antonio
Van Zandt County							Dallas
Victoria County	Victoria City-CO Health Dept	2805 North Navarro	Victoria	77901	361-578-6281	361-578-7046	Corpus Christi
Walker County							Houston

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Waller County							Houston
Ward County							Lubbock
Washington County							Austin
Webb County	Laredo (City of) Health Dept	2600 Cedar Avenue	Laredo	78043	956-795-4901	956-726-2632	San Antonio
Wharton County							Houston
Wheeler County							Lubbock
Wichita County	Wichita Falls-Wichita CO PH Dist	1700 Third Street	Wichita Falls	76301-2199	940-761-7800	940-767-5242	Tarrant
Wilbarger County							Tarrant
Willacy County							Harlingen/South Texas
Williamson County	Williamson CO & Cities PH Dist	100 West 3rd Street	Georgetown	78626-5030	512-930-4387	512-943-1499	Austin
Wilson County							San Antonio
Winkler County							Lubbock
Wise County							Tarrant
Wood County	Wood CO Health Dept	213 Bermuda Road	Quitman	75783	903-763-5406	903-763-5407	Tyler/East Texas
Yoakum County	South Plains Public Health Dist	920 East Main Street	Brownfield	79316-0113	806-637-2165	806-637-4296	Lubbock

Area Served	Local Health Dept.	Address	City	Zip Code	Telephone	Fax	LRN region
Young County							Tarrant
Zapata County							Harlingen/South Texas
Zavala County							San Antonio

Appendix B: Packaging and Shipping Instructions

PACKING AND SHIPMENT OF SPECIMENS:

Timely transport to the laboratory will increase the likelihood of recovering the influenza virus from specimens; overnight delivery is the preferred method of shipment.

Packaging Materials

All infectious substances and diagnostic specimens must be packaged under “triple pack” conditions. The three following packaging descriptions detail each component of the “triple pack” system.

Primary Packaging:

- The primary receptacle must be water tight (e.g., screw cap sealed with adhesive tape or similar positive means to prevent the cap from loosening).
- When shipping more than one fragile primary receptacle in a single secondary package, each receptacle must be individually wrapped to prevent breakage. The total content amount for the primary package will be determined by adding each of the primary receptacle content amounts together.
- Individual primary receptacles shall be capable of withstanding, without leakage, an internal pressure of 95 kPa (0.95 bars) in the range of -40°C to 55°C.
- Primary packages **must not** contain more than 1.0 L of contents.

Secondary Packaging:

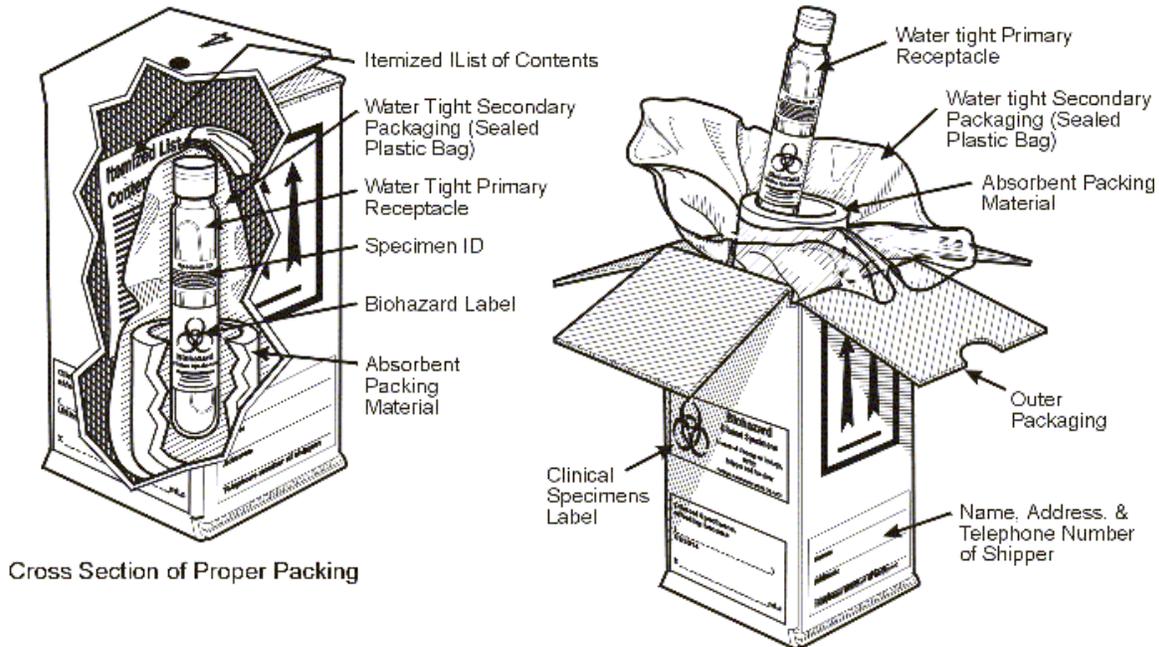
- Use enough absorbent material in the secondary container to absorb the entire contents of all primary receptacles in case of leakage or damage.
- Secondary packaging must be watertight. Follow the packaging manufacturer or other authorized party’s packing instructions included with the secondary packaging.

Outer Packaging:

- The outer package may be made of cardboard or paper fiberboard and must meet the IATA packaging 1.2 meter drop test procedure.
- Either dry ice or wet ice must be placed outside the secondary packaging for samples that must be transported frozen or cold, respectively.
- **Dry ice:** packaging must permit the release of carbon dioxide gas. Therefore, **do not tape** the Styrofoam chest closed to allow venting of carbon dioxide gas. The packaging must also meet requirements for packages under IATA and DOT regulations.
- **Ice packs:** packaging must be leak-proof. Ice packs are preferred over wet ice.
- The outer packaging must be no less than 100 mm (approx. 4 inches) in the smallest overall external dimension and must be large enough to accommodate shipping documents.

- The outer packaging must not contain more than 4 L or 4 Kg
- Place shipping documents between the secondary packaging and the outer packaging in a watertight bag.

Diagram of a triple packed parcel containing a diagnostic specimen



Cross Section of Proper Packing

Required Labeling:

The outer packaging will have the required UN specification markings. A circle containing a “U” above an “N” indicates United Nations specifications have been met. The additional text indicates: the type of package, class of goods the package may carry, manufacturing date, authorizing agency, and the manufacturer, respectively.

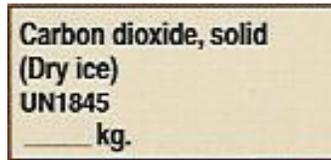
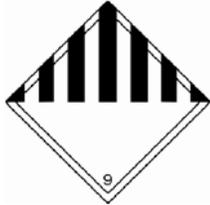


4G/CLASS 6.2/2001
USA/6-20 SHIPPCO

For diagnostic specimens, each package and the air waybill must be marked with the following exact wording:

**UN 3373
BIOLOGICAL SUBSTANCE, CATEGORY B
PACKED IN COMPLIANCE WITH
IATA PACKING INSTRUCTION 650**

If packed with dry ice - Class 9: Black on white diamond label and UN 1845 Carbon dioxide dry ice amount label (to convert to kg divide pounds by 2 using whole numbers)



Appendix C: Specimen Submission Instructions for the DSHS Laboratory

To submit specimens to the DSHS (Austin) laboratory for influenza culture surveillance, please contact Stacy Davlin at 512-458-7111 x6364 or Wendy Sessions at 512-458-7594. Viral transport media, packaging and shipping materials, and shipping costs can be provided to laboratories or health care providers interested in submitting specimens as part of the influenza surveillance program. The following protocol contains guidelines on how to properly collect and ship specimens to the DSHS laboratory.

TEXAS DEPARTMENT OF STATE HEALTH SERVICES INFLUENZA CULTURE SURVEILLANCE PROTOCOL

- Beginning January 1, 2007, the shipping regulations for diagnostic specimens will change. Boxes containing diagnostic specimens must now be labeled, “Biological Substance, Category B”. Air Shipments must display the UN3373 Label with the adjoining words, “Biological Substance, Category B”. The phone number and name of a person must be listed on the box and on the airbill for both the shipper and the recipient. **All materials sent by DSHS will comply with the new regulations.**
- DSHS will now pay for all shipping of influenza surveillance specimens; however, the submitter must either use the FedEx airbill provided by DSHS or fill out their own airbill correctly with the DSHS-IDCU FedEx account number. Submitters who do not follow these instructions **will not** be reimbursed by DSHS.
- DSHS will be providing sterile, polyester-tipped, plastic shaft swabs with all flu transport media. This is an attempt to further reduce costs incurred by our surveillance sites and to prevent the improper use of wooden shaft and calcium alginate swabs for specimen collection. **The DSHS supplied swabs are not intended for use as a nasopharyngeal swab, and should be used as throat swabs only.**
- In addition to the swabs, DSHS will be supplying a limited number of cold storage boxes (Styrofoam box inside a cardboard box) for continual use throughout the season. Please keep the Styrofoam box inside the outer cardboard shipping box (do not discard the cardboard box). This is the shipping container unit you will use to ship your specimens to the DSHS lab throughout the season. DSHS will return these shipping units (cold box kits) to you after receipt of each shipment of specimens.

STORAGE OF DSHS-SUPPLIED VIRAL SPECIMEN TUBES:

1. Storage **Before** Specimen Collection:

- DSHS removes specimen tubes from freezer storage and sends to the surveillance sites overnight at room temperature. Before sending, DSHS places each receptacle specimen tube inside a plastic liner with screw cap that is then placed inside a Styrofoam cold box.
- When received at the sites, the specimen tubes should be stored frozen (-20° C or below).

- If a freezer is unavailable at the site, then the specimen tubes should be refrigerated (2-8° C) and used as soon as possible.

Note: Freezer storage of specimen tubes (media) before specimen collection is preferred, because it provides the temperature ideal for stability. If freezer storage is not available and specimen tubes are stored in refrigerator, avoid storing the tubes for long periods of time. Instead, shipments of media can be mailed, as needed, during the season. Sites should save the plastic liners with screw caps, Styrofoam boxes as well as any fiberboard cylinder containers (if received), and the outer cardboard box for shipping the specimens back to DSHS, as these DSHS-provided containers meet the shipping rules for triple containment of diagnostic specimens. Media that is expired should not be used.

2. Storage **After** Specimen Collection:

- Refrigerate specimen tubes immediately after collection. Ship specimen tubes to the DSHS laboratory as soon as possible after collection; overnight delivery is preferred.
- **If collected specimens will arrive at the DSHS laboratory less than 3-4 days after collection, store at 2-8° C. If collected specimens will arrive greater than 3-4 days after collection, freeze at -70° C.**
- Specimens should be stored in an upright position.

COLLECTION OF SPECIMENS:

1. Collect specimens from patients who present with clinical symptoms of upper respiratory infection (one swab per patient). Please do not include patients with allergy symptoms, strep throat, common colds, or any other confirmed diagnosis that explains symptoms.
2. Symptoms of influenza infection generally include: fever (typically > 100°F), malaise, myalgia, (muscle aches), cough, coryza (runny nose), sore throat, chills, and headache.
3. Select patients who present with recent onset (patients whose symptom onset was within three days of presenting to the clinic).
4. If the specimen tube has been stored frozen, the media should be thawed (at either refrigeration or room temperature) completely before specimen collection. **Do not** overheat, microwave, or incubate media prior to use as this may cause inactivation of the virus.
5. Use the DSHS-supplied sterile, polyester-tipped, plastic shaft swabs and flu transport media for specimen collection. Dacron or rayon-tipped swabs with a plastic shaft or any other commercially available sterile collection system intended for virus isolation may be used. Calcium alginate swabs or swabs with wooden shafts are **not acceptable** for specimen collection as they may inhibit recovery of the virus.
6. Nasopharyngeal swabs, throat swabs, nasal washes, or other respiratory specimens are acceptable as clinically appropriate; however, the swabs provided by DSHS are intended for use as throat swabs only. They should not be used for collection of nasopharyngeal specimens.
7. After specimen collection, insert the fiber tip of the swab into the specimen tube and break off the shaft so that the swab fits completely within the tube and the cap can be securely tightened.

SPECIMEN LABELING AND G-2A LAB FORM COMPLETION:

1. Ensure that the patient name and date of collection are written on each specimen tube that is submitted. A corresponding G-2A must accompany each specimen tube. ***The patient name and date of collection on the specimen tube must match the name and date on the corresponding lab form.***
2. Each surveillance site submitter should have a master G-2A specimen submission lab form that includes their unique submitter number, name, and address. This master lab form should be reserved to make copies for specimen submission. If the submitter has not yet established a unique submitter number with DSHS, they must contact Lab Reporting at: (512) 458-7578.
3. Complete the G-2A lab form. Section 5 and section 10 must be completed as instructed on page 6 of this document. ***It is imperative that this form be completed correctly to avoid receiving a bill. Submitters who do not complete the form correctly and are billed, will not be reimbursed.***

PACKING AND SHIPMENT OF SPECIMENS TO DSHS:

*Timely transport to the laboratory will increase the likelihood of recovering the influenza virus from specimens; overnight delivery is the preferred method of shipment.

1. **If the specimens will arrive at the DSHS laboratory less than 3-4 days after the date of collection, ship specimens on cold or freezer packs.**
2. **If the specimens will arrive at the DSHS laboratory greater than 3-4 days after the date of collection, ship specimens frozen on dry ice. If dry ice is used, it should be noted on the outer cardboard box.**

Note: Whichever shipping method is used, be sure to pack enough coolant (i.e. freezer packs or dry ice) in the Styrofoam box to ensure that the specimens remain either cold or frozen until they arrive at DSHS.

3. It is important to follow the triple container rules for the shipment of all clinical diagnostic specimens. The DSHS-provided containers meet the triple container rules and may be used for shipping as noted below:
 - Primary container = the DSHS-provided receptacle specimen tube containing the media that the specimen swab is placed in.
 - Secondary container = the DSHS-provided plastic liner with screw cap.
 - Outer shipping container = the DSHS-provided Styrofoam box placed inside of the cardboard shipping box or the DSHS fiberboard cylinder with metal screw cap (if used).

Note: Please refer to diagram of packing and shipping instructions.

4. The primary container (the specimen) should be placed into the secondary container (the plastic liner with screw cap) with enough absorbent material to absorb the entire contents if leakage/breakage occurs. The secondary container must then be placed in the Styrofoam chest

(or cylinder fiberboard container if supplied) or other suitable container for controlled-temperature shipment. The Styrofoam chest is then placed in a corrugated cardboard box (provided), which is taped for shipping. If dry ice is used, do not tape the Styrofoam chest to allow venting of the carbon dioxide as it melts. Place the G-2A lab form on top of the Styrofoam box inside the cardboard box. ***You must submit a completed G-2A lab form for each specimen in the shipment.***

Note: To avoid specimen warm up during packing and shipment, it is helpful if the plastic liners and fiberboard cylinder containers (if used) are cold before placing the specimen inside.

5. Be certain that all three containers: the receptacle specimen tube, the plastic liner with screw cap, and the Styrofoam box or fiberboard cylinder with metal screw cap (if used) are securely sealed. Not only does this prevent leaks, but it also prevents carbon dioxide vapors from coming into contact with the specimen if the specimens are shipped on dry ice.

Note: If substitutions of any of the DSHS-provided containers are made, it is your responsibility as the shipper to make sure that all packaging and labeling meet the current criteria.

6. Specimens should arrive at DSHS laboratory within five (5) days of collection. Sites might want to collect specimens on Monday for Tuesday shipment, or on Friday for Monday shipment to meet the time requirements. Ship specimens no later than Tuesday of the week for regular delivery, and no later than Wednesday for overnight delivery. This will ensure that specimens are delivered before the weekend so they can be properly stored and viral isolation procedures can begin as soon as possible.
7. Use the DSHS-provided “Biological Substance, Category B” mailing label and send specimens to:

Texas Department of State Health Services
Laboratory
1100 West 49th Street
Austin, TX 78756-3194

Note: The lab forms and specimen tubes provided are intended for use for influenza surveillance activities only. In general, these materials are best suited for focused attempts to culture influenza viruses from specimens, although occasionally other viruses (parainfluenza, adenovirus, herpes simplex virus, and enterovirus) have been isolated using this system. Specimens submitted through the influenza virus surveillance program generally **do not receive a comprehensive viral diagnostic work-up** to intentionally look for other viruses.

Instructions for Filling Out the G-2A Specimen Submission Form for Influenza Culture Surveillance

Ensure Section 1, "Submitter Information" has your correct submitter name, address, phone, and contact information. This section should already be pre-populated on your master form. Please make copies of you master. **Do not send in your master form.****

Complete Section 2, "Patient Information" with date of specimen collection, patient name, address, date of birth, and any other pertinent information (i.e. diagnosis/symptoms)

Complete Section 3, "Specimen Source or Type" by checking appropriate box.

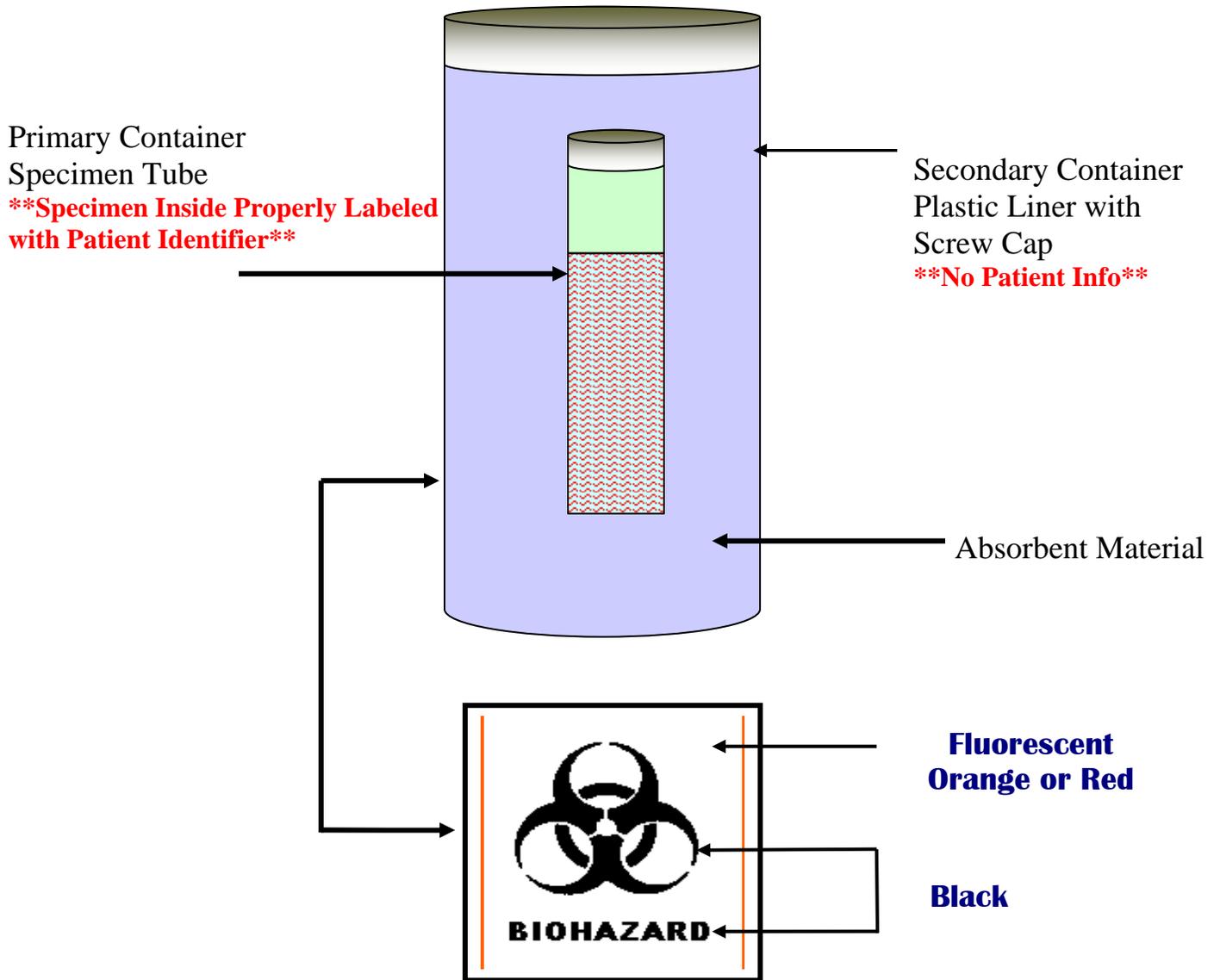
Complete Section 5, "Payor Source" by checking the box marked, "IDEAS". If you do not check this box, you will be billed.

Section 5. PAYOR SOURCE – (REQUIRED)	
Indicate whether we should bill the submitter, Medicaid, Medicare, private insurance, or DSHS Program. If Medicaid or Medicare is indicated, the Medicaid/Medicare number is required and the copy of the card must be attached. If private insurance or DSHS Program is indicated, the required billing information below is designated with an asterisk (*). If required information is not provided, THE SUBMITTER WILL BE BILLED.	
<input type="checkbox"/> Submitter	<input type="checkbox"/> Private Insurance
<input type="checkbox"/> Medicaid	<input type="checkbox"/> Medicare
Medicaid/Medicare #: _____ (attach copy of card)	
DSHS Programs:	
<input type="checkbox"/> THSteps	<input type="checkbox"/> Title V – Family Planning
<input type="checkbox"/> BT Grant	<input type="checkbox"/> Title V – MCH
<input type="checkbox"/> HIV / STD	<input type="checkbox"/> Title X – Family Planning
<input type="checkbox"/> Immunizations	<input type="checkbox"/> Title XX – Family Planning
<input checked="" type="checkbox"/> IDEAS	<input type="checkbox"/> Tuberculosis
<input type="checkbox"/> Refugee	<input type="checkbox"/> Zoonosis
	<input type="checkbox"/> Other: _____

Section 10. VIROLOGY
<input type="checkbox"/> Electron microscopy
<input checked="" type="checkbox"/> Influenza surveillance
Vaccine received: <input type="checkbox"/> Yes <input type="checkbox"/> No
<input type="checkbox"/> Reference culture (Virus ID on isolate)
Suspected: _____
Submitted on: _____
<input type="checkbox"/> Virus isolation (comprehensive)
<input type="checkbox"/> Other: _____

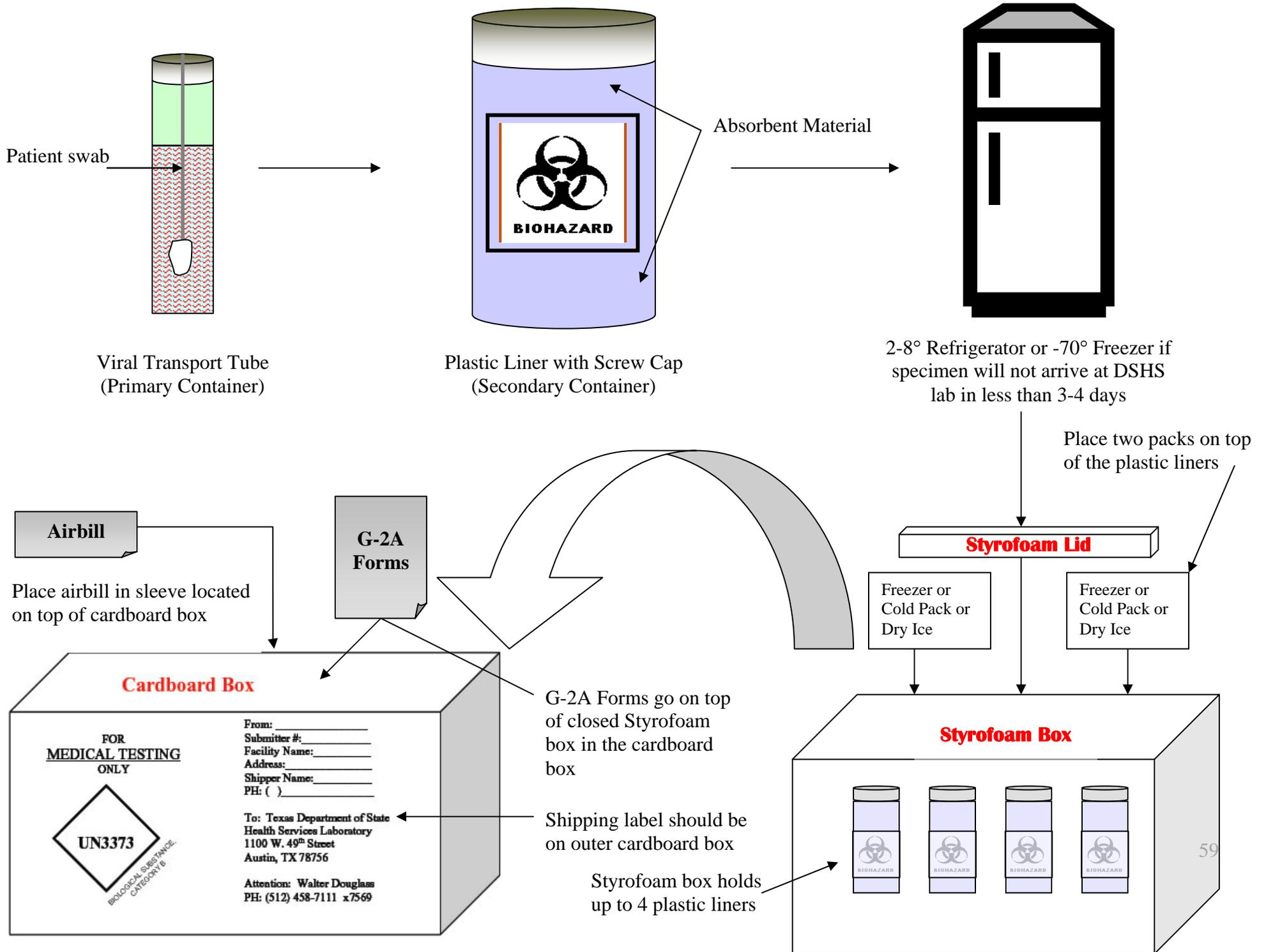
****If you are not registered as a submitter with DSHS, you must contact: (512) 458-7578 to receive a submitter identification number before you can submit specimens.**

Packaging and Labeling of Clinical Diagnostic Samples
**Do Not Put Any Patient Information on Outer or
Secondary Containers or Lids**



Biohazard Label should already be on Secondary
Container.

DO NOT put Biohazard label on Outer Container.



Resources:

TX DSHS Infectious Disease Control Unit:

<http://www.dshs.state.tx.us/idcu/disease/influenza/surveillance/2007/>

http://www.dshs.state.tx.us/preparedness/pandemic_flu/

http://www.dshs.state.tx.us/idcu/disease/influenza/pandemic/Draft_PIPP_10_24_web.pdf

TX DSHS Public Health Laboratory--Austin

<http://www.dshs.state.tx.us/lab/default.shtm>

Current WHO Pandemic Phase, see

http://www.who.int/csr/disease/avian_influenza/phase/en/index.html

List of influenza H5N1-affected countries

<http://www.cdc.gov/flu/avian/outbreaks/current.htm>

http://www.oie.int/eng/en_index.htm

http://www.who.int/csr/disease/avian_influenza/en/

Laboratory Biosafety Level Criteria

<http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4s3.htm>

CDC Guidelines for Persons Exposed to Avian Influenza

<http://www2a.cdc.gov/han/ArchiveSys/ViewMsgV.asp?AlertNum=00246>

CDC Guidelines for Handling Avian Influenza Viruses

<http://www.cdc.gov/flu/h2n2bsl3.htm>

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