

Pandemic Influenza Plan – Laboratory Preparedness

For more information contact Russ Drury at russ.drury@health.mo.gov or 573-751-3334

INTRODUCTION

A well-organized network of laboratories, capable of rapidly and correctly identifying a novel disease of unknown etiology and subtyping influenza viruses is critical to recognizing and managing a pandemic. Recognition of novel strains of diseases will be dependent upon early detection and sampling of initial clinical cases associated with the pandemic. Since the symptoms of many illnesses are nonspecific and are similar to those caused by a number of respiratory pathogens, laboratory testing is crucial to identify the causative agent. It is essential that the Missouri Department of Health and Senior Services (DHSS), Missouri State Public Health Laboratory (MSPHL) be prepared for the emergence of novel pathogens and pandemic.

OBJECTIVES

- Provide laboratory resources for rapid detection of novel human or animal diseases.
- Monitor changes in the circulating viruses during the pandemic.
- Monitor development of antiviral resistance in novel virus strains.

BACKGROUND

MSPHL is a collaborating laboratory in the World Health Organization's (WHO) Global Influenza Surveillance Network. Year-round respiratory specimens from designated sentinel laboratories are sent to MSPHL where they are first tested by polymerase chain reaction (PCR) and subsequently by virus isolation. The PCR-positive influenza specimens are then sub-typed and a representative number of influenza A and B positives are then forwarded to the Centers for Disease Control and Prevention (CDC) for further antigenic characterization. In addition, a representative number of samples sub-typed are sent to CDC for antiviral resistance testing. All specimens that cannot be sub-typed are forwarded to CDC for further testing. Daily reports of laboratory-confirmed cases of Influenza A and B viruses are sent by HL7 messaging to CDC via the Public Health Laboratory Interoperability Project (PHLIP).

MSPHL maintains a fully trained technical virology and molecular staff. In the summer of 2007, MSPHL moved into a new state-of-the-art facility that contains an extensive biosafety level 3 (BSL-3) laboratory. Additional scientists have been trained in the CDC PCR testing methods to provide back-up and support during a pandemic or public health emergency. MSPHL participates in year-round laboratory-based surveillance via the National Respiratory and Enteric Virus Surveillance System (NREVSS). MSPHL continues the Sentinel Surveillance Program with providers participating in the CDC Influenza Sentinel Provider Network. Providers are expected to send up to nine specimens per season October through May and/or if the providers see any unusual influenza activity.

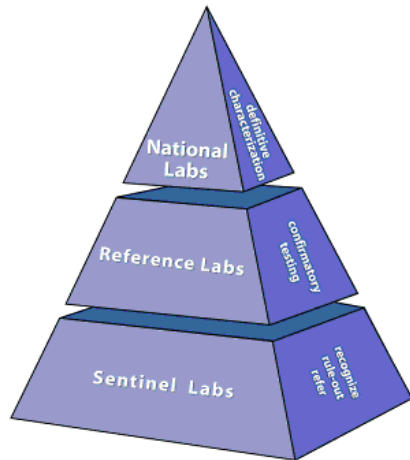
Trainings and exercises are part of the preparedness activities that MSPHL participates in throughout the year. MSPHL exercises the laboratory pandemic plan by maintaining scientist's competencies in polymerase chain reaction (PCR) testing and maintains Clinical Laboratory Improvement Amendments (CLIA) certification.

The MSPHL, Bureau of Communicable Disease Control and Prevention, and Bureau of Immunizations, in cooperation with local public health agencies (LPHAs), perform year-round outbreak and seasonal influenza surveillance. In support of this influenza surveillance, MSPHL and program staff conduct training sessions at DHSS area or district health offices. Such training provides hands on opportunities for LPHA staff to ask questions and gain knowledge on issues related to diseases of unknown etiology; seasonal, avian and pandemic influenza; data collection and interpretation; laboratory testing issues; and vaccinations. These trainings serve as an opportunity to review packaging and shipping protocols, safe specimen collection protocols, and testing procedures, as well as MSPHL reporting mechanisms and responsibilities.

PLANNING ASSUMPTIONS

- As a member of the Association of Public Health Laboratories (APHL), MSPHL will utilize laboratory tests and methods recommended by CDC in cooperation with APHL. MSPHL will utilize all testing algorithms as disseminated by APHL and CDC.
- MSPHL will continue to conduct year-round testing for influenza viruses in order to characterize circulating influenza strains and to monitor for novel influenza subtypes.
- MSPHL will provide advanced testing, utilizing laboratory tests and reagents supplied by CDC and WHO. These testing procedures are not available to most clinical laboratories.
- During a pandemic, MSPHL will work with CDC to provide guidelines for specimen management and diagnostic testing as the pandemic evolves.
- MSPHL will maintain testing supplies and the capacity to meet the public health surveillance needs of the state. MSPHL will not accept specimens solely for diagnostic purposes. MSPHL will process only specimens of public health significance.
- MSPHL scientists are cross-trained in an effort to assist with testing of greatest need. There is an acknowledgement that certain testing may be delayed or redistributed to other laboratories in order to meet more pressing or other critical testing demands. The laboratory has worked with program staff to develop plans for specimen referral and triage.
- MSPHL will utilize the Missouri Laboratory Response Network (MOLRN) to contact member laboratories throughout the state with up-to-date testing recommendations and information.
- The pandemic intervals will determine testing strategies and testing algorithms. Highest test load is expected to occur during the early stages when the novel virus demonstrates efficient human-to-human transmission. During the peak of the pandemic, laboratory testing is expected to decrease as more patients will be treated without laboratory confirmation. During the pandemic peak, testing will be provided for the purpose of surveillance of the pandemic strain and for antiviral resistance. Once the cases begin to decline, MSPHL will continue testing for surveillance of the pandemic pathogen as well as other circulating viruses.

LABORATORY RESPONSE NETWORK (LRN)



The LRN became operational in August 1999 with the objective to ensure an effective laboratory response to bioterrorism. The LRN is an integrated network of local clinical laboratories (sentinel labs), state and local public health laboratories (reference labs) and federal laboratories (CDC, The United States Army Medical Research Institute for Infectious Diseases, U.S. Food and Drug Administration). MOLRN is a network of Missouri laboratories that are fully equipped and trained to respond quickly to acts of chemical or biological terrorism, emerging infectious diseases and other public health threats and emergencies. MOLRN includes MSPHL, which serves as Missouri's LRN reference laboratory, plus sentinel laboratories within the state. See <https://emergency.cdc.gov/lrn/biological.asp>.

SENTINEL LABORATORIES

According to the 2019 MOLRN survey of sentinel laboratories within Missouri, 56% perform rapid diagnostic testing for influenza viruses on respiratory specimens. Of these, 30% have the capability to perform high-complexity viral testing, including the use of viral isolation techniques. In addition, 22% of Missouri's sentinel laboratories are capable of performing PCR or immuno-fluorescence (IF) testing for rapid detection and sub-typing. These laboratories could be utilized for surge capacity should the situation warrant the need. *Hospital laboratories should not attempt to isolate influenza viruses from patients with suspected novel influenza virus infections.*

MISSOURI STATE PUBLIC HEALTH LABORATORY TESTING CAPABILITIES

MSPHL receives samples for testing for respiratory viruses from multiple sources:

- Sentinel influenza surveillance sites.
- Respiratory outbreak investigations, including COVID-19.
- Suspected cases of novel influenza virus, including avian flu.
- As a reference laboratory, MSPHL receives influenza isolates from commercial and hospital laboratories.

MSPHL performs several different tests for diagnosis:

- Real-Time Polymerase Chain Reaction (RT-PCR): MSPHL performs the CDC FDA-approved influenza RT-PCR assay for detection of influenza A and B viruses. This test detects all influenza A and B viruses, including the highly pathogenic Influenza A/H5N1 (Asian lineage) and Influenza A/H7 (Eurasian lineage including H7N9) strains.
- All specimens that test positive for influenza A by PCR are further characterized by subtype. MSPHL can detect the following subtypes: human seasonal H3 and 2009 H1N1 pdm, H5 (Asian lineage), H7 (Eurasian lineage including H7N9), and H3N2 Variant Virus.
- A PCR assay for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Middle-Eastern Respiratory Syndrome Coronavirus (MERS-CoV).

- All specimens that test positive for influenza B by PCR are further characterized by lineage. MSPHL can detect the following lineage genotypes: Victoria and Yamagata.
- If the sample is from a patient who meets the criteria for a suspected case of highly pathogenic avian influenza virus, then RT-PCR testing is the only test performed. The sample is not inoculated into virus culture, where the virus would be amplified.
- If the RT-PCR test results suggest the presence of a novel influenza virus, the sample is sent to CDC for additional testing.

Laboratory procedures for testing may change depending on the characteristics of the circulating influenza strains.

- MSPHL maintains year-round capability to perform virus isolation and RT-PCR testing for influenza and other respiratory pathogens.
- MSPHL maintains testing capacity for outbreak investigations, reference testing, and testing for other influenza viruses.
- MSPHL continues to participate in a specimen exchange program with the Wadsworth Center in New York, the College of American Pathologists (CAP) proficiency-testing program, and the CAP bioterrorism proficiency testing program. MSPHL will maintain its status as a certified laboratory within the Select Agent Program.
- As part of the LRN, MSPHL has the capability of transferring samples to the nearest appropriate partner laboratory if MSPHL cannot perform the required tests or becomes overwhelmed.
- MSPHL has exercised and drilled the use of the Emergency Management Assistance Compact (EMAC). EMAC is another resource which could be employed should the need arise for additional testing beyond the capacity of MSPHL.

PANDEMIC INFLUENZA: LABORATORY ROLES AND RESPONSIBILITIES

Sentinel and Other Private Laboratories:

Pandemic Planning

- Inventory current levels of diagnostic supplies, including personal protective equipment. Assess anticipated needs for equipment and supplies, and determine trigger point for ordering additional resources. Consider a back-up source for supplies.
- Identify key laboratory personnel whose roles are critical to maintaining laboratory operations.
- Train employees in management of respiratory specimens.
- Institute surveillance for flu-like illnesses among laboratory personnel.
- Cross-train employees to perform rapid diagnostic tests and report results.
- Qualified personnel should be identified to staff laboratory for 24/7 capabilities.
- Ensure employees are trained in the proper packaging and shipping of suspected novel influenza strains to MSPHL.

Pandemic Response

- Follow current DHSS guidelines for collecting, testing, and reporting of persons with suspected infection with a novel pathogen. See updated health alerts at <http://health.mo.gov/emergencies/ert/alertsadvisories/> and guidance at <http://health.mo.gov/lab/respiratory.php>.
- Scale up to manage increased requests for testing.

- Continue to expedite specimens from possible pandemic illness patients to MSPHL.
- Maintain surveillance for flu-like illnesses among laboratory personnel.

Missouri State Public Health Laboratory

Pandemic Planning

- Follow CDC guidance related to possible emerging novel viruses, including implementation of new testing algorithms, changes in laboratory procedures, availability of testing reagents, etc. as pandemic evolves. Testing protocols will be determined by CDC algorithms and may be modified with each stage of the pandemic. The laboratory receives RT-PCR test kits and consumables through the CDC International Reagent Resource (IRR). These kits and consumables are supplied as a set to ensure the availability of necessary items during peak demand. Due to the highly variable nature of viruses, these kits are managed on a national level and cannot be stockpiled by the laboratory.
- Inventory current levels of supplies, assess anticipated needs for equipment and supplies, and determine trigger point for ordering additional resources. Include specimen mailing kits in assessment. Arrange for back-up manufacturer source for supplies and equipment.
- Enhance lab-based surveillance by increasing designated sentinel sites.
- Utilize the MOLRN **and** Health Alert Network to send out Health Alerts to educate sentinel laboratories, LPHAs, physicians, and other network partners on how to notify DHSS if novel illness infection is suspected.
- Institute surveillance for flu-like illnesses among laboratory personnel.
- Educate sentinel laboratories within Missouri which have BSL 3 facilities on the highly pathogenic nature of certain emerging novel diseases. Respiratory virus cultures should not be performed in most clinical laboratories, and such cultures should not be ordered for patients suspected of having highly pathogenic A/H5 (Asian Linage) virus infection. See <http://www.cdc.gov/flu>.
- Continue ongoing training of sentinel laboratories and LPHAs in proper specimen collection, handling and packaging, and shipping procedures. See http://health.mo.gov/lab/pdf/sphl_avianflu_instructions.pdf.
- Communicate expeditiously to the DHSS Division of Community Public Health (DCPH) any confirmation of a novel illness within the state.
- Continue to supply specimen collection kits and maintain courier service to all counties to facilitate receipt of novel influenza strain at the MSPHL.

Pandemic Response

- Educate sentinel laboratories on the evolving novel strain testing procedures as well as supply updated information received from CDC on an ongoing basis to MOLRN laboratories, LPHAs, and other associated partners using Health Alerts, MOLRN broadcasts, updated website information, and by other communication means as necessary. See <http://health.mo.gov/lab/respiratory.php>.
- Utilize technicians cross-trained in performing RT-PCR procedures to report results as requests for testing increase.
- Redirect laboratory staff to areas of greatest need, i.e., assist in specimen collection kit assembly, extraction, reporting, and telephone call triage.
- Utilize temporary staff as needed to meet increased staffing needs.

- Follow CDC guidance related to the novel pathogen, including institution of new testing algorithms, changes in procedures, electronic message/result reporting, availability of testing reagents, etc. as the pandemic evolves.
- Supply updated information received from CDC on an ongoing basis to MOLRN laboratories, LPHAs, and other associated partners using Health Alerts, MOLRN broadcasts, updated website information, and by other communication means as necessary. See <http://health.mo.gov/lab/respiratory.php>.
- Communicate expeditiously to DCPH initial confirmation of the novel pathogen within the state, and trends and movement of the pathogen throughout the state, as the pandemic evolves.
- Continue to supply specimen collection kits and maintain courier service to all counties to facilitate receipt of novel influenza strain at MSPHL.

LABORATORY INFORMATION MANAGEMENT SYSTEM (LIMS)

Beginning in 2009, MSPHL began the implementation of a Laboratory Information Management System (LIMS). Initially, LIMS provides for the electronic transfer of patient demographics, specimen information, and results within DHSS as well as to its federal partners. The long term capabilities and benefits of this system will be to interface with sentinel and other clinical laboratories, hospitals, health clinics, and healthcare institutions to facilitate the exchange of electronic laboratory information.

REFERENCES:

Missouri State Public Health Laboratory

<http://health.mo.gov/lab/>

Health Alerts and Updates for Novel Influenza A H1N1 and Avian Influenza A

<http://health.mo.gov/emergencies/ert/alertsadvisories/index.php>

Missouri Pandemic Influenza Response Plan

<http://health.mo.gov/emergencies/panflu/panfluplan.php>

CDC Influenza

<https://www.cdc.gov/flu/>

WHO Influenza Network

http://www.who.int/influenza/gisrs_laboratory/en/

CDC Laboratory Response Network Partner in Preparedness (LRN)

<https://emergency.cdc.gov/lrn/>