For more information contact: Missouri State Public Health Laboratory | labweb1@health.mo.gov | 573-751-3334

INTRODUCTION

Identifying influenza-like illnesses (ILI) of unknown etiology is essential to a fast and effective response to a pandemic event. Early identification of these novel pathogens is dependent on sampling and testing of initial clinical cases associated with the pandemic. Laboratory testing plays a crucial role as many symptoms of ILIs are nonspecific. The Missouri State Public Health Laboratory (MSPHL) maintains testing capability and capacity to assist with early identification of novel pathogens in a pandemic event.

OBJECTIVES

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

BACKGROUND

The MSPHL collaborates with the Centers for Disease Control and Prevention to conduct statewide influenza surveillance. Year-round, ILI specimens from designated sentinel laboratories are sent to MSPHL for influenza A and B subtyping and genotyping using real-time reverse transcription polymerase chain reaction (rRT-PCR). A representative number of influenza specimens are then sent to the Centers for Disease Control and Prevention (CDC), or designated reference center, for further antigenic characterization. In addition, a representative number of samples subtyped are sent to CDC for antiviral resistance testing and next generation sequencing. Specimens that cannot be subtyped 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).

The MSPHL maintains a fully trained virology and molecular staff. In the summer of 2007, the laboratory 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 CDC's Influenza SARS-CoV-2 (Flu SC2) Multiplex Assay and Human Influenza Virus Real-Time RT-PCR Diagnostic Panel methods to increase capacity and support during a pandemic or other public health emergency. MSPHL participates in year-round laboratory-based surveillance and contributes to the National Respiratory and Enteric Virus Surveillance System (NREVSS).

Training and exercises are part of the preparedness activities that MSPHL participates in or conducts 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 the MSPHL or at off-site locations. These sessions cover information related to diseases of unknown etiology; seasonal and pandemic influenza; data collection and interpretation; laboratory testing issues; and vaccinations. Training may also include a review of packaging and shipping protocols, safe specimen collection, testing procedures, and MSPHL reporting mechanisms.

PLANNING ASSUMPTIONS

- As a member of the Association of Public Health Laboratories (APHL), MSPHL utilizes laboratory tests and methods recommended by the CDC in cooperation with APHL. MSPHL utilizes all testing algorithms as disseminated by APHL and CDC.
- MSPHL maintains year-round capability to perform virus isolation and rRT-PCR testing for ILI pathogens. MSPHL will continue characterization of circulating influenza strains and monitoring for novel influenza subtypes.
- MSPHL will provide advanced testing, utilizing laboratory tests and reagents supplied by the CDC and the WHO. These testing procedures are not available to most clinical laboratories.
- During a pandemic, MSPHL will work with the 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 scientists are cross trained to assist with testing of the greatest need. There is an acknowledgement that certain testing may be delayed or redistributed to other laboratories to meet more critical testing demands. The laboratory works with program staff to develop plans for specimen referral and triage.
- MSPHL will utilize the Missouri Laboratory Response Network (MOLRN) to disseminate current testing recommendations and information to member laboratories throughout the state.
- Pandemic intervals will determine testing strategies and testing algorithms. Highest test load is expected to occur during early stages when a novel virus demonstrates efficient human-to-human transmission. During the pandemic peak, laboratory testing is expected to decrease, as more patients will be treated without confirmatory laboratory testing. During the peak, testing will be provided for the purpose of diagnostics and surveillance of the viral strain and for antiviral resistance.
- MSPHL continues to participate in the Wadsworth Center specimen exchange program, College of American Pathologists (CAP) proficiency testing program, CDC Influenza and SARS-CoV-2 Molecular Diagnostic and Performance Evaluation Panel, Wisconsin State Laboratory of Hygiene proficiency testing program, and the LRN bioterrorism challenge panel program.
- MSPHL will maintain compliant registration with the Federal Select Agent Program.
- As part the LRN, if MSPHL cannot perform required testing or lacks capacity, the laboratory can transfer samples to another appropriate laboratory partner for testing.
- 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.

LABORATORY RESPONSE NETWORK (LRN)



The LRN was established in 1999 to ensure an effective laboratory response to biological and chemical threats and other public health emergencies. This integrated network includes local clinical laboratories (sentinel labs), state and local public health laboratories (reference labs) and federal laboratories (CDC, United States Army Medical Research Institute for Infectious Diseases, U.S. Food and Drug Administration). MOLRN is an extension of the national LRN and consists of governmental and private laboratories throughout the state, including MSPHL, which serves as Missouri's reference laboratory. See the CDC website for additional information about the LRN role in emergency preparedness and response.

LABORATORY TESTING

ILI specimens are received from multiple sources including:

- Clinical laboratories.
- Local public health agencies.
- ILI 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.

Testing Capabilities:

- <u>CDC Influenza SARS-CoV-2 (Flu SC2) Multiplex Assay</u>: Utilizes rRT-PCR for the detection of SARS-CoV-2 and influenza A and B viruses; CDC's recommended methodology for influenza A/B and SARS-CoV-2 identification.
- <u>CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (CDC Flu rRT-PCR Dx</u> <u>Panel)</u>: 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; CDC FDA-approved influenza rRT-PCR assay for detection and characterization of influenza A and B viruses.
- <u>BioFire Respiratory panel</u>: Rapid detection of 22 viral and bacterial respiratory targets including Influenza A, AH1, AH3, AH1 2009, B, and SARS-CoV2.
- <u>BioFire Pneumonia panel</u>: Rapid detection of 33 viral and bacterial targets causing pneumonia including influenza A and B.
- <u>Influenza A subtyping</u>: Specimens identified as influenza A by rRT-PCR are further characterized by subtype including, human seasonal H3, Pandemic 2009 H1N1, H5 (Asian lineage), H7 (Eurasian lineage including H7N9), and H3N2 Variant Virus. This assay has the capability of detecting other novel influenza viruses as they arise.
- <u>Coronavirus PCR assays</u>: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV).
- <u>Influenza B lineage</u>: Specimens identified as influenza B by rRT-PCR are further characterized by lineage including, Victoria and Yamagata.
- <u>Highly Pathogenic Avian Influenza (HPAI)</u>: If suspected, rRT-PCR identification is the only test performed.

If the results of rRT-PCR suggest the presence of a novel influenza virus, the sample is sent to CDC for additional testing.

PANDEMIC INFLUENZA: LABORATORY ROLES AND RESPONSIBILITES

Sentinel and other private laboratories:

Pandemic Planning

- Inventory current levels of diagnostic supplies, including personal protective equipment.
- Assess anticipated need for equipment and supplies to determine trigger point for ordering additional resources. Consider back-up and alternate sources for supplies.
- Identify laboratory personnel are critical to maintaining laboratory operations.
- Institute surveillance for ILI among laboratory personnel.
- Train/cross-train employees in management of ILI specimens.
- Cross-train employees to perform rapid diagnostic tests and report results.
- Qualified personnel should be identified to staff laboratory for 24/7 capabilities.
- Train employees on the proper packaging and shipping of ILI specimens to MSPHL.
- Determine the surge capacity of the laboratory and develop and maintain a plan for implementation.

Pandemic Response

- Follow current DHSS guidelines for collection, testing, and reporting of persons with suspected ILI.
- Implement surge protection plan as necessary.
- Expedite specimens from clinical cases associated with the pandemic for testing at the MSPHL.
- Conduct ILI surveillance among laboratory personnel.

Missouri State Public Health Laboratory:

Pandemic Planning

- Inventory current levels of diagnostic supplies, including personal protective equipment.
- Assess anticipated need for equipment and supplies to determine trigger point for ordering additional resources. Consider back-up and alternate sources for supplies.
- The laboratory receives testing supplies through the CDC International Reagent Resource (IRR) which helps 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.
- Enhance lab-based surveillance by increasing designated sentinel sites.
- Utilize the MOLRN and Health Alert Network to inform external partners how to notify DHSS if novel illness is suspected.
- Institute surveillance for ILI among laboratory personnel.
- Educate sentinel laboratories with BSL-3 facilities on the highly pathogenic nature of certain emerging novel viruses. ILI cultures should not be performed in most clinical laboratories.
- Train MORLN laboratories and LPHAs in proper influenza specimen collection, handling, packaging, and shipping procedures.

• Maintain supply of specimen collection kits and courier service to all counties to facilitate receipt of influenza specimens to the MSPHL.

Pandemic Response

- Monitor and implement CDC guidance related to emerging novel viruses. This may include implementation of new testing algorithms, changes to laboratory procedures, changes in testing reagents due to availability, etc. Testing protocols will be determined by the CDC algorithms and may be modified throughout the pandemic.
- Notify MOLRN laboratories of CDC guidance related to emerging novel viruses. This may include implementation of new testing algorithms, changes to laboratory procedures, changes in testing reagents due to availability, etc. Testing protocols will be determined by the CDC algorithms and may be modified throughout the pandemic.
- Cross-train laboratory staff to assist in areas of need during periods of increased testing requests. This May include specimen collection kit assembly, extraction, reporting, and telephone call triage.
- Hire temporary staff to meet workload needs as appropriate.
- Notify the DHSS Division of Community Public Health (DCPH) of confirmation of a novel influenza strain within the state and trends as the pandemic evolves.
- Maintain supply of specimen collection kits and courier service to all counties to facilitate receipt of influenza specimens to the MSPHL.

LABORATORY INFORMATION MANAGEMENT SYSTEM (LIMS)

The MSPHL uses a laboratory information management system (LIMS) to support testing and reporting activities. LIMS provides for the electronic transfer of patient demographics, specimen information, and results within DHSS as well as to local and federal partners. 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 Pandemic Influenza Response Plan

Missouri State Public Health Laboratory

MSPHL – Avian Influenza (H5N1)

DHSS Health Alerts, Advisories, and Updates

CDC - Influenza

Laboratory Response Network (LRN)