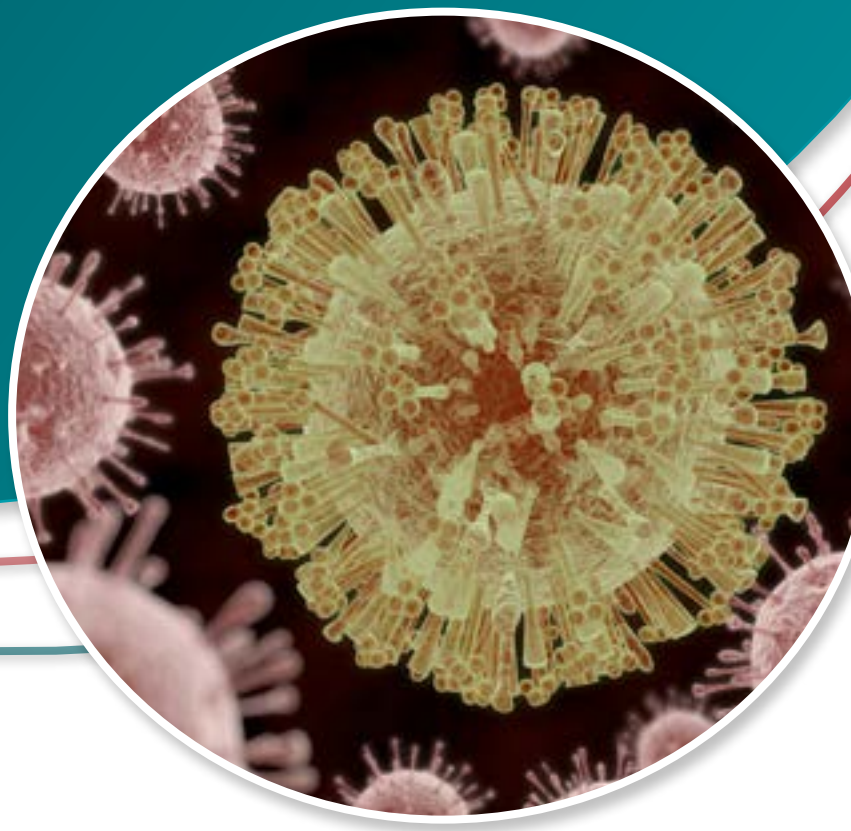
Essential Laboratory Capabilities for Arbovirus Testing in the United States



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Introduction

This document outlines five essential laboratory capabilities to support the control and prevention of arboviral diseases in the US. For each essential capability we define baseline and enhanced capabilities for public health laboratories. All public health laboratories should meet the baseline capabilities and ensure access to enhanced capabilities. Collectively, this capability is necessary to maintain an effective public health laboratory network that can detect and respond to current and emerging arboviral threats.

Maintaining broad testing capability for arboviruses and the ability to detect and respond to travel-associated cases and emerging threats is a persistent challenge for public health laboratories. Public health laboratories in collaboration with their public health partners—including epidemiology, surveillance and vector control programs—must determine how to prioritize allocation of limited resources to ensure readiness despite these challenges. Determining which arboviral pathogens of public health significance are prioritized will vary by jurisdiction. The program should have knowledge about of the unique circumstances of their jurisdiction, such as which hosts (humans and other animals), vectors and pathogens are endemic in the area they serve (i.e., city, county, state, etc.) and neighboring jurisdictions, how host and vector ranges are shifting, and the incidence of travel-associated cases. Based on these factors, the program, including the public health laboratory, should assess and document where all relevant testing will be conducted keeping in mind that public health laboratories must maintain sufficient capacity to perform routine testing as well as respond to an outbreak. To help guide these decisions, five essential laboratory capabilities are outlined below. Capabilities should align with jurisdictional needs based upon the identified pathogens of public health significance.

The five essential laboratory capabilities are aligned with the goals of the National Public Health Framework for the Prevention and Control of Vector-Borne Diseases in Humans including:

- Promoting the need for building and sustaining testing capacity with appropriate methods, reagents, supplies and equipment to provide timely and accurate answers
- Funding to support a well-trained workforce
- Proper infrastructure to support the sharing of resources and results.[1]

In 2023, federal leaders used the framework to write the policy: A National Public Health Strategy to Prevent and Control Vector-Borne Diseases in People. The strategy was published in February 2024.[2]

Background

National surveillance capacity for arboviral diseases was largely developed in response to widespread West Nile virus (WNV) outbreaks across the US in the early 2000s.[3] Because arbovirus testing was not a national priority before this time, public health laboratories were underfunded, understaffed and underprepared. In response, federal funding was crucial to enable public health laboratories to expand their capabilities to meet the increased testing demand. Federal funds made available through cooperative agreements such as the Epidemiology and Laboratory Capacity for Prevention and Control of Emerging Infectious Diseases (ELC) program made it possible for laboratories to hire skilled personnel, purchase necessary equipment and maintain reagents and supplies to meet testing needs. As a result, a basic competency for arbovirus testing was achieved in all 50 states by 2004.[3]

Despite the continued activity of WNV and increased spread of arboviruses and vectors into non-endemic areas, federal funding to state public health laboratories peaked in 2004 then steadily and significantly declined. With this decline, the capability and capacity to perform testing using multiple methods for arboviruses and their vectors also declined. When faced with the Zika virus outbreak in 2016-2017, the previous years of funding cuts left public health laboratories

lacking capacity to meet testing demand. Specifically, many laboratories had switched from the US Centers for Disease Control and Prevention's (CDC) MAC-ELISA platform to other commercially available arbovirus serology test methods in the intervening years. This meant that not only was the test method not performed, but staff competency lapsed and relationships with manufacturers that supplied the critical reagents weakened.[4] Even laboratories that were able to the MAC-ELISA faced challenges in scaling up to meet the testing demands required for the Zika outbreak response. Since MAC-ELISA is the serology platform utilized by CDC for known and emerging arboviruses and due to the typically short viremic periods of arboviruses, it is a critical test method to ensure our continued ability to detect and respond to arboviral threats. In a 2018 survey conducted by APHL, laboratories reported an increase in capacity and capability due in part to the Zika outbreak response. While a bit dated, this survey is a reasonable estimation of testing being performed in US public health laboratories including endemic and imported or travel associated arboviruses.[5]

The public health laboratory system must have the capability and capacity to monitor and test clinical specimens and samples from animal and vector sources for arboviral pathogens to maintain adequate surveillance and to protect the public from emerging arboviral disease threats. These essential capabilities must be restored and maintained within the public health laboratory system to support the National Public Health Framework for the Prevention and Control of Vector-Borne Diseases in Humans.[1]

How to Use this Document

For each of the five essential laboratory capabilities we define baseline and enhanced capabilities to allow for flexibility in planning and to make best use of limited financial and staff resources (**Table 1**). All public health laboratories should meet baseline capabilities and therefore be able to effectively test and monitor for jurisdictionally defined arboviruses of public health significance in human specimens. Additionally, public health laboratories should ensure access to enhanced capabilities through in-house testing for referral. Enhanced capabilities are above and beyond those defined for baseline. A laboratory may have some enhanced capabilities in one area (e.g., certain components of one or more capability but not every component) but not in all capabilities. The goal is that each public health laboratory may have some enhanced capacity and that all aspects of all enhanced capabilities would be assured across the public health system. Laboratories maintaining enhanced capabilities should consider providing services to other public health laboratories through existing regional consortia, a shared service model or other partnering relationships to the extent possible.

Public health laboratories need to coordinate and communicate with a large, diverse number of partners to establish, maintain and regularly review their arboviral disease testing program. In addition to traditional partners such as epidemiologists, state and local jurisdictions and federal partners, public health laboratories may find themselves interfacing with vector control programs, commercial and clinical laboratories, veterinary laboratories and academic partners. To facilitate these ongoing conversations all partners should meet regularly (at least once per year) to collectively define the needs for the jurisdiction in a collaborative working session. If needed, public health laboratories may use the **Partner Worksheet (page 18)** in the Appendix to document and maintain a list of all necessary partners and to consolidate contact information.

Public health laboratories, in collaboration with their programmatic partners (as defined previously or within the **Partner Worksheet**), should use this document to review their arboviral disease testing program. This will include reviewing and completing the **Testing Needs Assessment (page 19)** in the Appendix (as part of **Essential Capability 1**) which is a needs assessment tool to assist in defining jurisdictional needs and identifying gaps in testing. Additionally, as you review each capability you will be able to identify whether the testing performed in-house meets baseline or whether you also have enhanced services that could be offered to the broader public health system. Lastly, reviewing this document and the current services your laboratory provides may enable you to identify gaps that need to be addressed or services that could be offered to other laboratories.

Table 1: Summary of Five Essential Laboratory Capabilities

#	Capability	Baseline	Enhanced
1	**Develop and Maintain Arbovirus Testing Portfolio***	• Use the needs assessment tool to guide portfolio development. • Ensure access to diagnostic and surveillance testing for endemic, imported and travel-associated arboviruses (in-house or referral).	
2	**Build and Sustain Testing Capacity**	• Human Specimens • Serologic (IgM ELISA, ideally MAC-ELISA) • Molecular methods (real-time RT-PCR) • Access to BSL-3 laboratory • Multipurpose instrumentation (ideally some surge capacity)	• Animal and vector samples • Serologic (IgM ELISA and PRNT) • Molecular methods (real-time RT-PCR, sequencing) • Virus culture/isolation • BSL-3 laboratory in-house • Automated, high throughput platforms ensuring surge capacity
3	**Develop and Retain Skilled and Competent Personnel**	• Staff trained to perform baseline testing (i.e., IgM ELISA, nucleic acid extractions and real-time RT-PCR) • Sufficient staff cross-trained across methods	• Staff trained to perform enhanced testing (i.e. Virus culture, PRNT, sequencing) • Staff trained to manipulate and handle mosquito pools and ticks. • Sufficient staff cross-trained across confirmatory and advanced methods • Access to bioinformaticians for sequence analysis
4	**Prepare for Implementing New Test Methods, Technologies and Approaches**	Validate or verify new technologies, methods or reagents	• Evaluate new test methods and technologies • Share specimens with other labs for validation • Conduct applied research to develop new methods or assays on existing instruments
5	**Establish and Maintain IT Infrastructure**	• Utilize a laboratory information management system (LIMS) • Provide a secure electronic test order and result (ETOR) mechanism. • Share results electronically with submitters and epidemiologists. • Report results to ArboNet	• Require use of ETOR • Establish and maintain ELR reporting. • Consider reporting directly to EMR/epi surveillance system • Share animal and vector testing results with partners and entered into ArboNet

* **Essential Capability 1** is considered foundational and is therefore not divided into baseline or enhanced.

The Essential Capabilities

1. Develop and Maintain Arbovirus Testing Portfolio

Public health laboratories should work with their public health program to develop a comprehensive testing portfolio to ensure access to diagnostic and surveillance testing for all arboviruses of public health significance as defined by the jurisdiction including endemic, imported and travel-associated arboviruses which should be reviewed annually. The testing portfolio should include testing for human specimens as well as animal and vector samples for each of the jurisdictionally defined arboviruses. Testing for these arboviruses on specific specimens or samples may be performed within your jurisdiction at the public health laboratory or within a vector control program or through other partnerships. Additionally, testing may also be performed by referring specimens to another laboratory (e.g., another public health laboratory, commercial laboratories, CDC, amongst others).

☐ **Determine or review which arboviruses, vectors or hosts may impact your jurisdiction.**

The prevalence and distribution of arboviruses, their vectors and hosts vary widely across the US. Additionally, the risk for imported and/or travel-associated arboviruses or cases will also vary based on your location and population dynamics. Public health laboratories and programmatic partners should take into consideration the arthropod species present in their jurisdictions and regions and which viruses they may harbor or transmit as well as how climate affects their abundance and distribution. This data may be gathered through local, regional and national surveillance data and well as case reports, meetings and peer-reviewed publications. Testing can occur in-house, aligning with the baseline capabilities below, or can be sent to partner labs (another public health laboratory, CDC or commercial laboratory) for testing. For those specimens sent to partner laboratories, a formal or informal agreement should be entered into by both parties.

☐ **Generate a prioritized list of arboviruses of public health significance for the jurisdiction.**

Public health laboratories and programmatic partners will need to define a prioritized list of arboviruses for which a testing portfolio will be developed based on the current or risk for arboviruses, vectors or hosts defined above. Prioritized pathogens for the jurisdiction should be considered "baseline" for the rest of this document and will be referred to as "jurisdictionally defined arboviruses of public health significance."

☐ **Develop a testing portfolio to ensure readiness to detect or respond to future threats.**

Public health laboratories and programmatic partners likely already have an arbovirus testing program which addresses this aspect. If this is the case, please review that document along with the questions above and in the **Testing Needs Assessment (page 19)** to create your portfolio.

If your jurisdiction does not have a testing portfolio, we suggest starting with ensuring you have addressed the two bullets above and taking a look at the testing needs assessment in the **Testing Needs Assessment**. The testing portfolio should include a plan for testing all jurisdictionally defined arboviruses of public health significance, but consideration should also be made for arboviruses that are of concern to the larger region to ensure that your jurisdiction has a plan to ensure readiness to detect and respond to the most likely arboviral threats. Testing for jurisdictionally defined arboviruses of public health concern should be performed within your jurisdiction to the extent possible. However, given limited resources this may not be possible. Therefore, take into consideration ensuring access to testing through referral to clinical or commercial laboratories, other public health laboratories in the region, CDC or

potentially academic/veterinary laboratories for animal and vector testing. For any specimens or samples tested at partner laboratories, a formal or informal agreement should be entered into by both parties that outlines how specimens/samples will be handled, how data will be shared and any other items of concern.

☐ **Develop a strategy to ensure adequate surveillance of jurisdictionally defined arboviruses of public health significance within your jurisdiction.**

In addition to the testing portfolio, jurisdictions should ensure they have a complete surveillance strategy that ensures the testing of animals and vector samples. Testing data should be shared as described in later capabilities so informed decisions can be made for the jurisdiction.

☐ **Develop a strategy to ensure collaboration across the jurisdiction to address testing needs to meet demands for surge capacity or outbreak response.**

Laboratories are encouraged to maintain communication with and awareness of neighboring jurisdictions' capabilities. This can be addressed by engagement with regional consortia and establishing partnerships to address testing needs during a surge in testing demand or outbreak. Public health laboratories should engage in ColLABorate communities* (e.g., Lab Director, Microbiology) and use the Public Health Laboratory Systems Database,* a data repository of all testing in public health laboratories.

Best Practices for Building and Sustaining Testing Capacity

- **Consider space when determining what testing can be performed (i.e., equipment, instrumentation)**
- **Perform risks assessment to determine whether it has the appropriate biosafety and engineering controls to perform any testing being considered.**
- **Laboratories must maintain sufficient quantities of in-date reagents, controls and consumables to perform all testing.**
- **All assays must be properly validated or verified using appropriate specimen types for the pathogen and documented.**
- **All required quality control must be conducted, documented and data maintained.**
- **Properly documented training and annual competency assessments are required for all personnel performing testing.**
- **Proficiency must be demonstrated through commercial panels, specimen sharing with another laboratory or creating a panel using previously tested specimens.**

2. Build and Sustain Testing Capacity

Baseline Capability

Public health laboratories should maintain serologic (IgM ELISA, ideally MAC-ELISA) and molecular methods (real-time RT-PCR) for the detection of jurisdictionally defined arboviruses of public health significance in human specimens. Instrumentation that can be used broadly for other clinical testing should be strongly considered and ideally would allow some surge capacity.

Maintaining instruments and reagents that can be utilized for multiple diseases allows public health laboratories to add testing for emerging arboviruses with minimal effort. As examples, instrumentation used for West Nile Virus (WNV) testing has subsequently been used for Chikungunya Virus (CHIKV) and Zika Virus (ZIKV) testing. Instruments used for influenza testing were able to be used at the start of the COVID-19 pandemic.

☐ Perform diagnostic testing and surveillance for jurisdictionally relevant arboviruses.

Testing and surveillance for jurisdictionally defined arboviruses of public health significance are performed in-house for all human specimens.

☐ Serologic detection of jurisdictionally relevant arboviruses in humans using paired sera and CSF.

IgM ELISA is the most important diagnostic method to detect a recent infection with arboviruses endemic to the US. There are some commercially available IgM ELISA kits for arboviruses which can be utilized; however, it is important to also maintain staff competency and proficiency with MAC-ELISA since it is the platform utilized by CDC for known and potentially emerging arboviruses. Due to cross-reactivity, confirmation of IgM ELISA results is frequently required. Confirmation of infection can be accomplished by detection of a four-fold increase in titer between paired sera (acute and convalescent phase sera)[6] using an IgM or IgG-based assay, or by using a plaque reduction neutralization test(PRNT).6 Serologic detection is important because for several arboviruses (e.g., WNV, EEEV, SLEV) the viremia is fleeting and it is difficult to detect infection using molecular methods.

☐ Molecular detection of jurisdictionally relevant arboviruses in humans using appropriate specimen types.

Real-time RT-PCR has the potential to detect infections where a detectable viremia is produced in humans (e.g., DENV, ZIKV, CHIKV). When real-time RT-PCR assays are appropriate, they may be preferred due to their sensitivity and specificity.

☐ Maintain access to a certified biosafety level 3 (BSL-3) laboratory.

The BMBL[7] recommends BSL-3 precautions for several arboviruses (e.g., CHIKV, EEEV and YFV) due to their infectivity and ability to cause laboratory-associated infections (LAIs) in laboratorians as well as for diagnostic specimens without an identified etiologic agent. Handling of these viruses requires containment facilities and enhanced safety and work practices, including the use of properly fit-tested respiratory protection. Access to a BSL-3 may be necessary in certain situations and therefore a plan should exist for how and when it could be utilized.

☐ Utilize instrumentation that can be used for arboviral testing and other clinical testing performed in the laboratory.

Whenever possible, laboratories should prioritize acquiring equipment that serves multiple purposes. Efficient use of equipment can reduce or eliminate the need for redundant equipment with similar capabilities, save on instrument maintenance and repair costs, and provide public health laboratories with the capability to adopt new assays more easily during a response. Additionally, public health laboratories should consider equipment and instrumentation that not only supports daily testing but would allow for some amount of surge capacity. This could mean validating manual procedures as well as semi-automated or automated instruments/equipment.

Enhanced Capability

Public health laboratories should maintain baseline serologic (IgM ELISA, MAC-ELISA) and molecular methods (real-time RT-PCR) for the detection of jurisdictionally defined arboviruses of public health significance in human specimens. In addition, laboratories may have enhanced capabilities if they also:

- Perform serologic or molecular testing for animal and/or vector samples.
- Perform advanced or confirmatory methods such as PRNT, virus isolation and/or sequencing.
- Maintain a BSL-3 laboratory within the facility.
- Maintain capability and capacity for testing additional arboviruses beyond those defined as priority for the jurisdiction.
- Maintain automated and/or high throughput instrumentation which can be used for multiple pathogens and to handle surge capacity for jurisdiction and broader region.

Laboratories with enhanced capabilities should consider providing services to other public health laboratories through existing regional consortia, a shared service model or other partnering relationships to provide surge capacity or to aid in investigations to the extent possible.

☐ Perform serologic and molecular testing for human specimens.

Public health laboratories should maintain testing for additional arboviruses beyond those defined as priority for the jurisdiction that would be helpful for regional or national testing capacity.

☐ Perform serologic and/or molecular testing for jurisdictionally or regionally relevant arboviruses in animal samples.

Public health laboratories should maintain methods to support testing in animal samples as needed for their jurisdiction or region for ongoing surveillance. Testing may also be provided for surge capacity or to support outbreak investigations if requested.

☐ Perform molecular testing of vectors known to transmit jurisdictionally or regionally relevant arboviruses.

Public health laboratories should maintain methods to support testing in vectors as needed for their jurisdiction or region for ongoing surveillance. Testing may also be provided for surge capacity or to support outbreak investigations if requested.

☐ Maintain a certified biosafety level 3 (BSL-3) laboratory.

For many arboviruses, or for diagnostic specimens without an identified etiologic agent, initial processing must be performed in a properly maintained and certified BSL-3 laboratory. Perform a full biological risk assessment (Best Practices and Zika Risk Assessment are both great resources) and viability study following your facility policies to determine if specimens may be tested outside the BSL-3 laboratory.

☐ Perform confirmatory testing by Plaque Reduction Neutralization Testing (PRNT).

PRNT is the gold-standard test for detecting and measuring neutralizing antibodies. It is more sensitive and specific than other serologic tests. The test is complex and time-consuming (5–7 days) because it requires viral growth in cell culture. PRNT can discriminate between recent infection or cross-reactivity from related viruses and is used to confirm presumptive positive results from other serological methods (e.g., IgM ELISA).

☐ Perform additional advanced methods such as viral culture and isolation and sequencing.

Virus culture is necessary for PRNT, but virus isolation is also an important method to ensure access to in the public health system. Sequencing (e.g., Sanger, next-generation sequencing (NGS), etc.) is a valuable tool to characterize outbreaks, understand pathways of spread, understand drivers of change and improve diagnostic tests. Sequencing can identify genotype/lineage and relatedness. Laboratories that perform sequencing should maintain sufficient data storage and computing power to support analysis or have access to a partner to perform analysis and ensure data is shared to public repositories.

☐ Ensure access to automated and/or high throughput testing platforms.

The ability to test large numbers of samples quickly and the ability to test one sample for multiple pathogens rapidly are key components of an outbreak response and considered enhanced capabilities. These goals can be achieved by using more automation at various steps in the testing process such as nucleic acid extraction biorobots (molecular), liquid handlers (serologic, molecular, viral isolation, sequencing etc.), cell culture (virus isolation/PRNT) and high-throughput PCR platforms (molecular). Additionally, testing for multiple pathogens at one time using multiplexing principles can be especially helpful in outbreaks of unknown etiology and/or in testing vector populations.

3. Develop and Retain Skilled and Competent Personnel

Baseline Capability

Public health laboratories should hire and/or develop and retain staff that are trained and competent to perform baseline testing identified in **Essential Capability 2**: serologic and molecular detection of jurisdictionally defined arboviruses in human specimens. They should be able to work safely in biosafety cabinets and in the appropriate biosafety level laboratories as needed. This includes all relevant pre- and post- analytical skills. Sufficient staff should also be cross-trained to ensure a rapid response to public health emergencies of new and emerging threats.

☐ **Ensure sufficient staff are trained and competent to perform baseline testing as outlined in Essential Capability 2.**

Laboratories should maintain sufficient staff who are trained and competent in IgM testing, ideally MAC ELISA and molecular detection including nucleic acid extraction and real-time RT-PCR. This includes proper operation of instrumentation, troubleshooting and analysis and interpretation of results. Laboratories must also include redundancy to guard against turnover and to scale up capacity if needed for a response.

During the initial response to the 2016 Zika virus outbreak, some public health laboratories lacked skilled staff who could perform, analyze and interpret results of the Zika MAC-ELISA assay appropriately. This lack of expertise is a direct result of reduced funding and led to delayed testing implementation and outsourcing of testing to other public health laboratories, which increased the testing burden on these laboratories.

☐ **Ensure staff are trained and competent to safely work in a biosafety cabinet and in relevant biosafety level laboratories.**

Staff must demonstrate competency to perform work in a biosafety cabinet and to perform baseline testing in appropriate biosafety level laboratories.

☐ **Ensure sufficient staff are trained and competent in pre- and post-analytical skills such as accessioning samples, reporting results and data management.**

Specific assay competencies should include pre- and post-analytical activities such as sample accessioning, operation and troubleshooting of instrumentation/equipment, analysis and interpretation, and proper reporting of results. Some of the major bottlenecks in surge capacity are these pre- and post-analytic aspects so ensuring that sufficient staff are trained in these tasks is crucial for being prepared for an emerging threat.

☐ **Cross-train staff to more rapidly respond to public health emergencies (i.e., outbreaks and/or situations requiring surge capacity).**

Public health laboratories should seek opportunities to expand staff competencies and training as well as increase workforce size. Additional staff who are not dedicated to arbovirus testing should be able to perform arbovirus testing when the need exists.

Furthermore, training of staff to address surge capacity should be included in public health laboratory emergency response plans to safeguard continued testing capacity during surge or outbreak response activities.

☐ **Support staff in continuing education and ongoing training to maintain competency and be able to adopt new technologies.**

Staff should be encouraged to participate in continuing educational opportunities to stay current on best practices, methodologies and technologies.

Enhanced Capability

Public health laboratories should hire and/or develop and retain staff that are trained and competent to perform baseline testing as well as any enhanced capabilities identified in **Essential Capability 2: Perform Serology on Human and Animal Specimens**. They should be able to work safely in biosafety cabinets and in the appropriate biosafety level laboratories, including BSL-3 as needed. Sufficient staff should also be cross-trained on any advanced methods performed in the laboratory to ensure a rapid response to public health emergencies of new and emerging threats.

☐ **Ensure staff are trained and competent to baseline and enhanced testing practices outlined in Essential Capability 2.**

Laboratories should maintain trained and competent staff to perform serology, specifically MAC ELISA, molecular detection and any enhanced capabilities such as mosquito pool testing or handling ticks, virus culture and isolation, PRNT, and sequencing. This includes proper operation of instrumentation (including all automated or high-throughput equipment), troubleshooting and analysis and interpretation of results. Laboratories must also include redundancy to guard against turnover and to scale up capacity if needed for a response.

☐ **Ensure adequate staff are trained and competent to perform advanced or confirmatory methods.**

Many of the techniques such as sequencing are cross-cutting and public health laboratories are well positioned currently to have trained and competent staff for wet lab aspects. However, they should be familiar with and able to perform sequencing methods for arboviruses specifically as well as access to bioinformaticians to analyze and interpret results as well as ensuring proper data storage and depositing data into public repositories. Laboratories that are offering virus culture/isolation or PRNT will require which is a skillset that may not otherwise be needed in the public health laboratory and cross-training and ensuring sufficient staff are trained may be a challenge.

4. Prepare For Implementing New Test Methods, Technologies and Approaches

Baseline Capability

Laboratories should be able to verify or validate and implement new test methods, technologies and approaches that improve their testing portfolio for diagnostics and surveillance and/or to respond to an emerging threat.

☐ **Laboratories should maintain the capability to validate or verify new technologies, test methods, or reagents as they are made available.**

While classical techniques have been instrumental in the detection of arboviruses, technology continues to advance. New test methods or technologies must be implemented as they are developed for laboratories to be able to maintain the most accurate and timely results. This is especially important when responding to a new or emerging threat.

☐ **Laboratories must adhere to all necessary quality control and regulatory requirements such as ensuring proficiency testing prior to implementing new methodologies.**

Laboratories must follow requirements outlined by federal and state regulatory agencies such as the Center for Medicare and Medicaid Services (CMS), the Clinical Laboratory Improvement Act (CLIA) and the College of American Pathology (CAP).

Enhanced Capability

Laboratories should evaluate new test methods, technologies and testing approaches to improve testing of arboviruses from human specimens, as well as animal and vector samples. Additionally, laboratories with enhanced capabilities in this area should maintain archives and contribute to repositories that help the public health laboratory system such as ArboShare to aid in validations by other laboratories, engage in applied research to develop and optimize new test methods and share findings and outcomes from above activities within the public health system.

☐ **Laboratories should evaluate new test methods, technologies and testing approaches.**

Laboratories should be willing and able to evaluate new methods or reagents, technologies or testing approaches such as different specimen types or algorithms as they are available. They should be evaluated against existing methods with defined performance characteristics. Results should be shared with CDC and other partner laboratories.

☐ **Laboratories should share specimens within the public health system for validation and verification of new methods.**

To facilitate ongoing validation and verification of methods or evaluation of new methods, laboratories with enhanced capabilities should retain primary specimens or samples, nucleic acid extracts and unique isolates to be shared with partner laboratories if requested. Relevant data such as: specimen type, date of symptom onset, collection date, test date, testing performed and results as well as relevant epidemiologic data should be stored and shared along with any specimens or samples.

☐ **Laboratories should conduct applied research to develop new methods or new assays on existing instruments.**

Laboratories should engage in applied research to develop new technologies to prepare for detection of emerging threats. This work can be done in-house or in partnership with national reference laboratories, research universities and biotech companies. Through collaboration with outside partners, public health laboratories may also engage in ongoing clinical studies and receive specimens and epidemiological data for further research.

5. Establish and Maintain the IT Infrastructure Used to Share Data Among Key Partners

Baseline Capability

Laboratories must utilize a laboratory information management system (LIMS). Laboratories should also establish and provide a secure electronic test orders and results (ETOR) mechanism for receiving test orders and reporting results electronically to the submitter and public health program. Ideally the LIMS would be integrated with the ETOR system to seamlessly integrate test orders and reporting. Public health laboratories must also ensure a mechanism for electronic laboratory reporting (ELR) which is capable of transmitting data electronically to state epidemiologists, CDC and other partners as relevant.

☐ Laboratories must maintain a secure LIMS for patient information and testing data, as well as quality metrics and results.

Laboratories must maintain a secure electronic LIMS to capture all pertinent submitted information and to record all test results. All associated quality assurance metrics must be captured in the LIMS or other secure manner in accordance with written protocols.

☐ Laboratories must provide a secure ETOR mechanism.

ETOR allows the laboratory to receive orders electronically and report results in real-time to the submitter and potentially other partners It enables a more complete set of information (both orders and results) to be exchanged rapidly which is essential for patient care. At a high level, there are three possible ETOR implementation paths available – web portal, system integrated (direct), and system integrated (indirect). Laboratories interested in learning more can find information from APHL or CDC. Note that while secure fax is still used, it is not considered a best practice and does not meet the goal of electronic reporting. Test results may also need to be shared with relevant partners by the same or different electronic mechanisms.

☐ Share ELR with the public health program.

ELR results in more complete information than mailing and faxing and is exponentially faster and more accurate. Technical assistance is available through APHL for implementing or updating ELR messaging.

☐ Report results from human specimens to CDC ArboNet by relevant partners.

Jurisdictional level data should be reported to CDC ArboNet to inform broader regional and national surveillance efforts. Jurisdictions will follow their own previously established guidelines for reporting data to ArboNet. However, this may be part of the initial conversations in completing **Essential Capability 1** and could be updated as needed.

Enhanced Capability

Laboratories should require use of a ETOR for human specimens and work towards implementation of a system integrated ETOR approach that would interface with clinical electronic medical or health record systems (EMR/EHR). Additionally, laboratories should leverage systems (LIMS and ETOR) established for human testing for electronically handling test orders and results for animal and vector samples.

☐ Laboratories should require use of ETOR for human specimens and work towards implementation of a system integrated ETOR approach.

Laboratories should require all submitters to utilize their ETOR system for all human testing. For laboratories that do not have an ELR interface from their LIMS to submitters' EHRs, a web portal can be a vast improvement over paper test orders and results. However, a system integrated approach may be ideal—when laboratories are able to connect to submitters via an ETOR Intermediary, each entity is able to send and receive messages in their preferred formats, and the laboratory no longer must build and maintain several disparate single-use connections. This minimizes the burden on both the public health laboratories and healthcare organizations. Additionally, a system integrated implementation is better equipped to handle multiple submitters and high-volume submissions which would be important in general as well as for public health emergencies.

☐ Laboratories should leverage secure LIMS and ETOR for animal and vector testing, as well as quality metrics and results.

Laboratories should leverage systems (LIMS and ETOR) established for human testing for electronically storing relevant information, accepting test orders and reporting results for animal and vector samples testing to submitters and the public health program. If this testing takes place in a different facility than human testing, those facilities should consider establishing their own LIMS and ETOR systems that are compatible with the system.

☐ Share results electronically with the public health program and partners.

Laboratories should report results from animal and vector testing to all relevant partners via secure electronic means, ideally utilizing ELR.

☐ Report results from animal and vector samples to CDC ArboNet by relevant partners.

Jurisdictional level data should be reported to CDC ArboNet to inform broader regional and national surveillance efforts. Jurisdictions will follow their own previously established guidelines for reporting data to ArboNet. However, this may be part of the initial conversations in completing **Essential Capability 1** and could be updated as needed.

Discussion/Conclusions

State and local public health laboratories are on the front line in protecting the health of their communities including preventing disease as well as addressing and responding to outbreaks. The implementation of these essential capabilities in each public health laboratory will provide the framework to build and sustain a comprehensive program as well as the foundation for a regional and national system. The public health system is most effective when there is considerable collaboration amongst all partners including vector control, epidemiology and surveillance programs. Through implementation of these capabilities and collaboration with partners, the public health laboratories will be positioned to maintain surveillance of pathogens and vectors, provide critical diagnoses, and detect emerging threats. With this strong foundation, public health laboratories will maintain the ability to influence and inform necessary public health action.

Additional Resources

- Risk Assessment Best Practices, APHL (2016).
- Zika Risk Assessment, APHL (2016)
- Laboratory Information Management System Infographic, APHL (2020)
- Electronic Test Order and Results, APHL (2019)
- Electronic Laboratory Reporting Infographic, APHL (2020)
- APHL ETOR Implementation Handbook (see Solution Description section)
- CDC's Public Health Laboratory ETOR Initiative
- APHL Technical Assistance Information (Informatics)
- Verification and Validation Toolkit, APHL (2024)

References

1 Brochure_National_Framework_VBDs-P.pdf [Internet]. [cited 2024 Oct 8]. Available from: www.cdc.gov/vector-borne-diseases/media/pdfs/Brochure_National_Framework_VBDs-P.pdf

2 CDC. National Public Health Strategy to Prevent and Control Vector-Borne Diseases in People [Internet]. Vector-Borne Diseases. 2024 [cited 2024 Oct 8]. Available from: www.cdc.gov/vector-borne-diseases/php/data-research/national-strategy/index.html

3 Hadler JL, Patel D, Bradley K, Hughes JM, Blackmore C, Etkind P, et al. National capacity for surveillance, prevention, and control of West Nile virus and other arbovirus infections--United States, 2004 and 2012. MMWR Morb Mortal Wkly Rep. 2014 Apr 4;63(13):281–4.

4 Association of Public Health Laboratories. A Complex Virus, A Coordinated Response: Public Health Laboratories Battle Zika [Internet]. 2018. 92 p. Available from: www.aphl.org/aboutAPHL/publications/Documents/APHL_A-Complex-Virus_A-Coordinated-Response_Public-Health-Laboratories-Battle-Zika_150ppi_web.pdf

5 Arbovirus Testing in Public Health Laboratories: 2018 Survey Report.

6 Piantadosi A, Kanjilal S. Diagnostic Approach for Arboviral Infections in the United States. J Clin Microbiol. 2020 Nov 18;58(12):e01926-19.

7 CDC. Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition [Internet]. CDC Laboratories. 2024 [cited 2024 Jul 1]. Available from: www.cdc.gov/labs/bmbl/index.html

Appendix

Partner Worksheet

Partner Name	**Point(s) of Contact** Name, Email, Phone Number	**Role in VBD Surveillance**	**Describe Communication Channels** Mechanism, Frequency, What Information, etc.	**Additional Notes**

Testing Needs Assessment

The Arbovirus Testing Needs Assessment is designed to be used by labs to identify jurisdictional testing needs and to identify gaps in testing. Complete each sheet in this workbook to outline current capabilities, facilities, IT infrastructure, equipment and staffing. If you need any assistance, please contact us at infectious.diseases@aphl.org.

Download the Arbovirus Testing Needs Assessment:
www.aphl.org/programs/infectious_disease/Documents/APHL-Arbovirus-Testing-Needs-Assessment.zip

Glossary

ArboNet: ArboNet is the National Arboviral Surveillance System. It is managed by CDC and maintains data on arboviral infections among humans, animals and vectors.

Arboviral Pathogens of Public Health Significance: Pathogens known or suspected to cause illness or disease in humans including but not limited to: West Nile virus (WNV), Eastern equine encephalitis virus (EEEV), Zika virus (ZIKV), dengue virus (DENV) and chikungunya virus (CHIKV).

Arbovirus: The term for a group of viruses which are transmitted to humans by the bite of an infected arthropod such as a mosquito or tick.

Arthropod: Invertebrate animals including insects such as mosquitoes and ticks.

Biosafety Level (BSL): There are four biosafety levels for laboratories as defined by CDC's Biosafety in Microbiological and Biomedical Laboratories (BMBL) which consistent of combinations of facility design features and safety equipment, facility practices and procedures and personal protective equipment.

Capability: Having the necessary personnel, access to appropriate equipment, access to specimens or other considerations to perform a specific test method.

Capacity: The total volume of testing that a laboratory can perform or absorb with no or minimal operational changes, within normal hours of operation, using existing staff and without impacting other laboratory activities.

Clinical: Term used to refer to specimens collected from humans for detection of microorganisms causing infection or disease.

Electronic Laboratory Reporting (ELR): The transmission of required results/reports for reportable conditions (and more) to public health departments from laboratories and supports disease surveillance and response capabilities

Enzyme-linked Immunosorbent Assay (ELISA): An assay designed for detecting antibodies; may also be used quantitatively or semi-quantitatively.

Emerging: A disease or pathogen that is new or previously unrecognized or rapidly increasing in incidence or geographic range.

Electronic Medical Record (EMR) or Electronic Health Record (EHR): Two different terms commonly used to refer to the software used by healthcare organizations to manage patient level data in their systems.

Endemic: A disease or pathogen that is maintained or regularly occurring within an area or community without introduction from outside areas.

Host: Human, animal or vector in which a pathogen normally lives and reproduces and causing minimal to zero disease.

IgM Antibody Capture Enzyme-Linked Immunosorbent Assay (MAC-ELISA): A specific type of ELISA developed by CDC to detect virus-specific IgM antibody.

Immunoglobulin G (IgG): A type of antibody that persists long-term to protect against an antigen. The detection of IgG is used as part of the diagnosis of longer term, chronic or prior illness.

Immunoglobulin M (IgM): The first type of antibody that appears after initial exposure to an antigen as well as subsequent exposure(s), though to a lesser extent, but does not typically persist long-term. The detection of IgM is used as part of the diagnosis of early or acute illness.

Imported: A disease or pathogen that is introduced to an area where it is not endemic. This term is frequently used in conjunction with or instead of "travel-associated."

Isolate: A single species of growing microorganism (e.g., virus) that was isolated from an infected host (e.g., human, animal or vector) and propagated in culture.

Jurisdiction: The state, territory, county, city or other government-defined area that the public health program or laboratory serves. This document can be used by various levels of governmental public health programs, so the term "jurisdiction" is used to define the area rather than a more specific term such as state or county.

Laboratory: The physical location where analytic tests are performed on human specimens, animal and vector samples, or other samples as needed.

Laboratory Information Management System (LIMS): The system used to store information associated with test orders, test results and other related quality metrics.

Molecular: A general term referring to methods that detect the nucleic acid of a pathogen including RNA and DNA, would include real-time RT-PCR.

Multiplex: A multiplexed assay is one in which multiple analytes can be measured and reported at the same time.

Real-time Reverse Transcriptase-PCR (real-time RT-PCR): A method for detection of RNA that is based on the ongoing detection of DNA that is being amplified following an initial step that transcribes the DNA from RNA (reverse transcription) in the sample.

Pathogen: A microorganism capable of causing disease.

Program/Public Health Program: Group of public health officials, epidemiologists and laboratorians who collaborate to address and respond to diseases and disease outbreaks.

Sample: In this document, referring to material from animals and vectors used for testing.

Serologic: A general term referring to methods that detect antibody generated by the immune system in response to a pathogen or antigens from the pathogen. Includes methods such as ELISA and PRNT.

Specimen: In this document, referring to human clinical material used for testing.

Surge Capacity: The capacity for sudden and sustained increase in the volume of testing that a laboratory can perform in an emergency or outbreak situation. It may require implementing substantial operational changes. This can be applicable within a laboratory (internal) or in the entire system by utilizing shared services/reference centers (overall).

Plaque Reduction Neutralization Test (PRNT): A test method used to measure virus-specific neutralizing antibody titers.

Travel-associated (cases): Arboviral infections occurring in persons when visiting an area outside of where they live and identified upon their return to their home jurisdiction. These cases may also result in onward transmission in their home jurisdiction if the appropriate vector(s) is also present.

Validation: The process used to confirm with objective evidence that a laboratory-developed test (LDT) or modified FDA-cleared or approved test method or instrument system delivers reliable results for the intended application.

Vector: An organism that can transmit a pathogen from one animal to another, including to humans.

Verification: The one-time process by which a laboratory determines that an unmodified FDA-cleared or approved test performs according to the manufacturer's specifications when used as directed.

Association of Public Health Laboratories

The Association of Public Health Laboratories (APHL) works to strengthen laboratory systems serving the public's health in the US and globally. APHL's member laboratories protect the public's health by monitoring and detecting infectious and foodborne diseases, environmental contaminants, terrorist agents, genetic disorders in newborns and other diverse health threats.

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