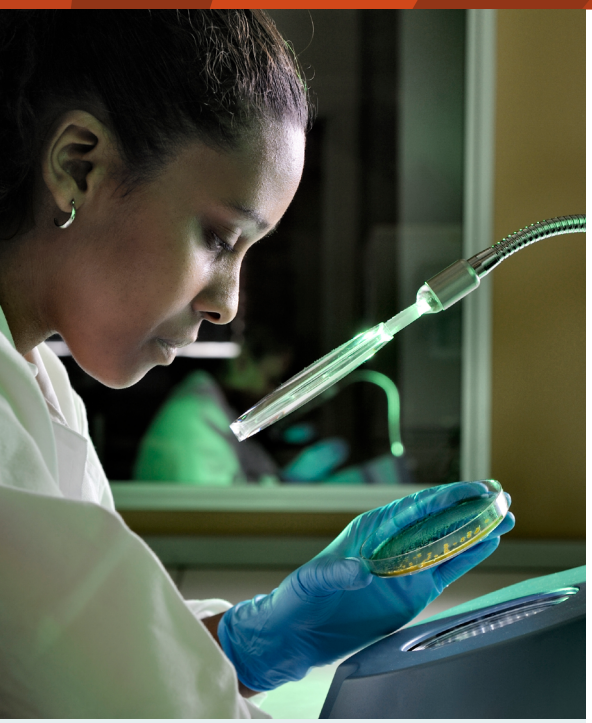
FoodCORE Model Practice:

Laboratory Timeliness and Completeness



Introduction:

Laboratory activities are a critical component of enteric disease surveillance and cluster and outbreak detection. Identification of the etiologic agent causing illness requires testing of specimens at local hospitals, clinics, and private and public health laboratories. Laboratory-based surveillance identifies confirmed cases of enteric disease infection and can help guide pathogen-specific response activities. Further characterization of pathogens (e.g., subtype, virulence determinants, antimicrobial susceptibility, etc.) at public health laboratories (PHLs) enhances the ability to identify patterns and trends, including clusters of disease that may represent unrecognized outbreaks. Additionally, PHLs provide primary diagnostic functions in event-associated outbreaks of undetermined etiology. PHLs also offer testing for rare pathogens and provide enhanced or novel characterization of pathogens that are not offered by commercial laboratories.

This FoodCORE Model Practice summarizes the successful laboratory practices utilized by PHLs in the FoodCORE centers for improving and maintaining the timeliness and completeness of isolate or specimen submissions to the PHLs, the subtyping of enteric pathogens, and the communication of laboratory results and cluster detection reports. FoodCORE centers maintain PHL capacity through the acquisition and maintenance of equipment, reagents, supplies, and trained staff.

The activities described would apply to various pathogens but are focused on those that are likely transmitted via food. A checklist is provided that may be used to determine if current PHL practices align with the FoodCORE model practices.

Appendices:

Appendix A. Checklist for FoodCORE Laboratory Practices

Appendix B. Training and Resources

Aligning with other initiatives:

The laboratory model practice document is not intended to replace guidance about laboratory test protocols or participation in reporting to surveillance systems. These FoodCORE laboratory model practices may help develop future guidance documents and workflows.

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Receiving and processing specimens:

FoodCORE centers use various practices and systems to help ensure timely and complete submission of isolates/specimens from these external sources. These practices include:

- Utilizing data interoperability to accession isolates and specimens rapidly and accurately
- Rapidly transporting isolates/specimens to the PHL for testing to ensure prompt receipt of all requested or required bacterial, viral, or parasitic specimens from clinical and commercial laboratories
    - Rapid transport can be supported with a variety of services such as the provision of mailing containers, a contract courier service, or other means of specimen transport to the PHL
    - Transport time (e.g., collection date to received date at the PHL) should be monitored to identify gaps and areas for improvement
- Providing current guidance for
    - Submitting patient, food, or environmental isolates/specimens to the PHL as part of routine surveillance and when investigating outbreaks, including outbreaks of undetermined etiology
    - When and how to submit enrichment broths and other primary clinical specimens that are found positive by culture-independent diagnostic tests (CIDT) for Shiga toxin-producing *E. coli* (STEC) or other pathogens that meet submission requirements in your jurisdiction

FoodCORE centers also work closely with the clinical and commercial laboratories that submit specimens so any delays or gaps in submissions can be identified. Laboratory scientists at FoodCORE PHLs work with epidemiologists as needed to reach out to laboratories to encourage submissions and help eliminate barriers to submission if they are identified.

FoodCORE centers also conduct training for local health department (LHD) partners.[1] As part of this training, submission protocol documents (manuals, standard operating procedure documents, etc.) and shipping materials can be provided to help ensure all partners know the testing capabilities of the PHL, what type of specimens should be collected, as well as when and how to collect and submit them to the PHL.

To help streamline the receipt and testing of specimens, outreach, resources, and training for clinical and commercial laboratories and LHD partners should include guidance stating that the PHL should be notified when specimens/samples will be submitted for outbreak investigations. PHLs should discuss capacity and prioritization with epidemiologists and environmental health partners during investigations where testing is needed, especially if a large number of environmental samples may require testing.

[1] Epi-Ready Team Training. Integrated Food Safety Centers of Excellence. Accessed March 9, 2023. https://foodsafetycoe.org/product/1440/.

Subtyping specimens:

Public health laboratories should reference current PulseNet Standard Operating Procedures (SOPs) and protocols for whole genome sequencing (WGS).

Reporting results and cluster detection:

FoodCORE centers capitalize on the completeness and timeliness of specimen subtyping to quickly identify clusters of illness. All subtyping results are reported to the appropriate surveillance network in real-time whenever possible. To enhance reporting and cluster detection, FoodCORE centers use the following practices:

- Submitting all WGS data and metadata to the PulseNet national databases within 24 hours of results; submitting raw sequences to the National Center for Biotechnology Information (NCBI) for accessibility to those outside PulseNet
- Routinely analyzing subtyping data from PHL testing to determine if there is an increase of a specific subtype or strain
    - Conducting surveillance and cluster detection using WGS data
        - Following PulseNet's recommended thresholds for detecting WGS clusters
            - Look for three or more cases differing within 10 alleles by cgMLST, of which two differ within five alleles.[2] Upload dates for all cases should be within the past 60 days of detection (120 days for *Listeria*). It is recommended that at least 30% of isolation dates fall within the past 50 days, except for *Listeria*.
        - Utilizing the 'Find Clusters Tool' (as referenced in PulseNet SOPs and protocols) to detect local clusters
        - Creating routine and ad hoc cgMLST dendrograms and/or similarity matrices to view allele differences
- Routinely comparing subtyping results to centralized databases to determine whether there are additional subtype matches
- Utilizing subtyping results to link pathogens identified from product testing to persons infected with the same subtype or strain
- Utilizing shared data systems that permit routine rapid sharing of laboratory information and results for human, food, and environmental isolate testing to inform and facilitate response activities. These shared data systems allow for real-time sharing of specimen testing and subtyping information during an investigation:
    - System for Enteric Disease Response, Investigation, and Coordination (SEDRIC)
        - Utilizing SEDRIC to facilitate secure electronic data-sharing among partners during outbreak investigations. SEDRIC's cluster detection tool enables users to set easy parameters to find clusters of isolates based on allele codes.

[2] Some jurisdictions may use a narrower cluster definition that detects two or more clinical cases within 60 days.

        - Utilizing SEDRIC to visualize trees via NCBI's Pathogen Detection pipeline (see note under NCBI below)
        - Utilizing SEDRIC's Genomic Data Visualization Application to show genotypic and phenotypic characteristics of a chosen group of isolates.
    - NCBI
        - Utilizing NCBI's Pathogen Detection Pipeline (https://www.ncbi.nlm.nih.gov/pathogens/) to visualize trees (differences are in single nucleotide polymorphisms, or SNPs, not alleles)
    - PulseNet SharePoint Site
        - Posting initial clusters that have not already been coded by PulseNet at CDC and continuing their follow up even if they are not given an official outbreak code.
        - Posting clusters with isolates, bundle files, and potential other state involvement as needed to identify additional isolates or common exposures. For example, cases clustering near a border to another state could be posted to request information on cases in the neighboring state.

- Routinely exchanging cluster detection reports
    - At a minimum, weekly reporting with more frequent reporting (i.e., twice weekly, daily, etc.) if possible
        - It is suggested that cluster detection reports describe:
            - Number of isolates included
            - Outbreak code (if available) and allele code(s) involved in the cluster (downloaded from the national database)
            - Allele differences for the cluster
            - Information regarding any relevant historical matches (past outbreaks, non-human, etc.)
            - Matches in other states
            - Genotyping information such as resistance or virulence data
            - Line lists containing allele codes and relevant demographic information
            - Dendrograms or similarity matrices
    - Integrating reports with routine data analyses to determine if there is an increase in the number of cases of infection with a specific subtype or strain within your state
    - Establishing methods for exchanging information about potential clusters that are detected between scheduled reports
    - Having standing meetings and trainings that include laboratory and epidemiology staff so all staff have a working understanding of the needs and capabilities of each group and can interpret laboratory results with interview data
        - Providing technical assistance to epidemiology staff on the interpretation of subtyping results, as needed

Appendix A. Checklist for FoodCORE Laboratory Practices–Table 1a

Receiving Specimens

Yes	No	Partial	Will be implemented (Date)	Practice
				1. Utilize data interoperability to accession isolates and specimens rapidly and accurately
				2. Utilize a courier or equivalent system for rapid transport of specimens/isolates to the PHL
				3. Monitor transport time (e.g., collection date to received date at the PHL) to identify gaps and areas for improvement
				4. Provide guidance for the submission of specimens under conditions of undetermined etiology
				5. Provide guidance for the submission of clinical specimens that are positive by CIDT for pathogens that meet submission requirements in your jurisdiction
				6. Conduct outreach to clinical or commercial labs with submission delays
				7. Provide guidace materials for PHL testing capabilities/services
				8. Conduct trainings and/or provide reference materials for appropriate specimen collection (type of specimen, how to collect and submit, etc.)
				9. Provide guidance stating that clinical and commercial labs and LHD partners notify the PHL when submitting specimens/samples for outbreak investigations

Appendix A. Checklist for FoodCORE Laboratory Practices–Table 1b

Subtyping Specimens

Yes	No	Partial	Will be implemented (Date)	Practice
				10. Reference current PulseNet Standard Operating Procedures and protocols for performing WGS and meet PulseNet's turnaround time for real-time subtyping (from the receipt/recovery of an isolate in the PHL to upload to the PulseNet national database)

Appendix A. Checklist for FoodCORE Laboratory Practices–Table 1c

Reporting Results and Cluster Detection

Yes	No	Partial	Will be implemented (Date)	Practice
				11. Submit all WGS data and metadata to PulseNet national databases within 24 hours of results
				12. Submit raw sequences to NCBI for accessibility to those outside PulseNet
				13. Routinely analyze subtyping results for cluster detection (follow PulseNet's recommended thresholds for detecting WGS clusters, utilize 'Find Clusters Tool' to detect local clusters, and create cgMLST dendrograms and/or similarity matrices to view allele differences)
				14. Routinely compare subtyping results to centralized database results
				15. Link, by subtype, pathogens identified in non-human sources to human illness with the same strain
				16. Utilize shared data systems (SEDRIC, NCBI, PulseNet SharePoint Site) that permit rapid sharing of laboratory information across the core areas of response
				17. Exchange subtyping results in real-time during an investigation across the core areas of response
				18. Exchange routine cluster detection results at least weekly and more frequently if possible
				19. Utilize established methods for exchanging information about potential clusters that are detected between scheduled reports
				20. Participate in meetings and trainings that include laboratory and epidemiology staff so that all staff can interpret laboratory results with interview data

Appendix B. Training and Resources

General PulseNet Resources

PulseNet is a national laboratory network that connects foodborne, waterborne, and One Health–related illness cases to detect outbreaks. PulseNet uses the DNA fingerprints of bacteria making people sick to detect thousands of local and multistate outbreaks. Since the network began in 1996, PulseNet has improved food safety systems through identifying outbreaks early. This allows investigators to find the source, alert the public sooner, and identify gaps in food safety systems that would not otherwise be recognized.

For more information about PulseNet USA, visit https://www.cdc.gov/pulsenet/index.html.

For more information about PulseNet International, visit https://www.aphl.org/programs/food_safety/Pages/PulseNet-International.aspx.

For PulseNet Standard Operating Procedures, visit https://www.aphl.org/programs/food_safety/Pages/PulseNet-International-SOPs.aspx.

Other Resources

Association of Public Health Laboratories (APHL)

The Association of Public Health Laboratories (APHL) works to strengthen laboratory systems serving the public's health in the United States and globally. APHL has a wide array of training and education options to support the growth and development of public health laboratory scientists, including conferences and meetings, webinars, workshops, on-demand courses, toolkits, and other training documents. PulseNet has free courses available via APHL's Training Portal, a new digital repository for online courses and archived webinars, on PulseNet workflow for analysis and data reporting.

For more information about APHL's Laboratory Training Program, visit https://www.aphl.org/training/Pages/About-Laboratory-Training.aspx.

Submission of Enteric Pathogens from Positive Culture-Independent Diagnostic Test Specimens to Public Health: Interim Guidelines

In 2016, APHL published interim recommendations for clinical laboratories on public health submission of specimens that have tested positive using culture-independent diagnostic tests to ensure accurate pathogen surveillance and monitor disease trends.

For APHL's "Submission of Enteric Pathogens from Positive Culture-Independent Diagnostic Test Specimens to Public Health: Interim Guidelines," visit https://www.aphl.org/aboutAPHL/publications/Documents/FS-Enteric_Pathogens_Guidelines_0216.pdf.

Campylobacter Isolation and Characterization from Clinical Specimens Guidance for Public Health Laboratories

In 2023, APHL published guidance to provide a framework for the isolation and characterization of *Campylobacter* infections by public health laboratories. Accurate identification of *Campylobacter*-attributed illnesses will provide robust and comprehensive data to support surveillance activities, outbreak investigations and guide prevention and policy efforts.

For APHL's "*Campylobacter* Isolation and Characterization from Clinical Specimens Guidance for Public Health Laboratories," visit https://www.aphl.org/aboutAPHL/publications/Documents/FS-Campylobacter-Diagnosis-Recommendations.pdf.

To search APHL technical and informational publications, visit https://www.aphl.org/Pages/reportsbriefsresults.aspx.

CaliciNet

CaliciNet is a national norovirus outbreak surveillance network of federal, state, and local public health laboratories in the United States. CDC launched CaliciNet in 2009 to collect information on norovirus strains associated with gastroenteritis outbreaks in the United States. Public health laboratories electronically submit laboratory data, including genetic sequences of norovirus strains, and epidemiology data from norovirus outbreaks to the CaliciNet database. The norovirus strains can be compared with other norovirus strains in the database, helping CDC link outbreaks to a common source, monitor norovirus strains that are circulating, and identify new emerging norovirus strains.

For more information about CaliciNet, visit https://www.cdc.gov/norovirus/reporting/calicinet/index.html.

CaliciNet data are updated monthly here: https://www.cdc.gov/norovirus/reporting/calicinet/data.html.

CIFOR Outbreaks of Undetermined Etiology (OUE) Guidelines

The CIFOR Outbreaks of Undetermined Etiology (OUE) Guidelines include recommendations on "universal" collection, shipment, testing and retention of foodborne outbreak specimens, even in the early stages of an investigation. Based on syndromes and specific outbreak profiles, the guidelines are designed to provide adequate specimens for second-tier testing and pathogen discovery should an etiology prove elusive.

The OUE Guidelines cover both infectious and non-infectious agents. A companion OUE Agent List provides detailed information including incubation period, primary signs and symptoms, primary specimen(s) and key epidemiological information.

For more information about CIFOR's Outbreaks of Undetermined Etiology (OUE) Guidelines, visit https://cifor.us/products/outbreaks-of-undetermined-etiology-oue-guidelines.

Guidelines for Specimen Collection

CDC published instructions for collecting stool specimens. The guidelines cover when to collect specimens, how much to collect, method for collection, storage of specimens after collection, and transportation of specimens.

For more information, visit https://www.cdc.gov/foodsafety/outbreaks/investigating-outbreaks/specimen-collection.html.

Integrated Food Safety Centers of Excellence (Food Safety CoEs) Online Trainings and Resources

The Food Safety CoEs have developed numerous online trainings and resources related to foodborne illness. Resources span all disciplines and topics and are available online at no cost. Some of the trainings, videos, and guidance documents may be especially helpful when improving subtyping, reporting results, and cluster detection. Resources are continually being updated and added, so check back often.

For more information about Food Safety CoE resources, visit https://foodsafetycoe.org/.

National Respiratory and Enteric Virus Surveillance System (NREVSS)

The National Respiratory and Enteric Virus Surveillance System (NREVSS) is a laboratory-based system that monitors temporal and geographic circulation patterns (patterns occurring in time and place) of respiratory syncytial virus (RSV), human parainfluenza viruses (HPIV), human metapneumovirus (HMPV), respiratory adenoviruses, human coronavirus, rotavirus, and norovirus. In this surveillance system, participating U.S. laboratories voluntarily report weekly to CDC the total number of weekly aggregate tests performed to detect these viruses, and the weekly aggregate positive tests. They also report the specimen type, location, and week of collection. NREVSS allows for timely analysis of data to monitor viral seasons and circulation patterns.

For more information about NREVSS, visit https://www.cdc.gov/surveillance/nrevss/index.html.

State Public Health Bioinformatics group (StaPH-B)

StaPH-B is a consortium of public health scientists interested in addressing the common barriers of impeding bioinformatics implementation in state public health laboratories. Their mission is to support the construction and maintenance of bioinformatics infrastructure within regional state PHLs; provide training for public health scientists on the fundamentals and practice of bioinformatics; develop bioinformatics resources including tools, pipelines, and documentation; and partner with CDC and APHL to ensure compatibility and utility of their efforts. Training materials from previous workshops and seminars are available on their website.

For more information about StaPH-B trainings, visit https://staphb.org/training.html.

System for Enteric Disease Response, Investigation, and Coordination (SEDRIC)

CDC has worked with a private-sector partner to develop SEDRIC, a secure, web-based system to streamline and coordinate outbreak investigations. SEDRIC allows outbreak response teams in many different locations to work together faster and more effectively through real-time data sharing. SEDRIC is used by state, local, and federal health departments and regulatory agencies.

For more information about SEDRIC, visit https://www.cdc.gov/foodsafety/outbreaks/investigating-outbreaks/sedric.html.