

Culture-Independent Diagnostic Tests: Paving the Way for Improved Diagnostics and the Future of Foodborne Disease Surveillance

Improvements in foodborne disease surveillance systems, such as PulseNet, have enhanced public health food safety programs by enabling the rapid identification of foodborne outbreaks. PulseNet is a national, laboratory-based surveillance system which uses molecular subtyping methods (i.e. “DNA fingerprinting”) to identify clusters of disease caused by bacterial pathogens such as *Salmonella*, *Listeria* and *E. coli* O157 from patients. The essential step in the process is the production and availability of the cultured isolate. Identification of disease clusters by PulseNet triggers epidemiological investigations into possible common sources, such as foods. The information gained from outbreak investigations gives the food industry and regulators additional information they need to keep our food safe. Preservation of the flow of culture isolates from the clinical laboratory to the public health laboratories (PHLs) is essential to maintaining this and other laboratory-based surveillance systems for early detection and limiting the spread of foodborne diseases.

Laboratory tests that detect the molecular signature of pathogens and do not depend on obtaining a culture are rapidly being adopted by laboratories that test human specimens. These culture-independent diagnostic tests (CIDTs) represent a major shift in microbiology practice with important implications for physicians, patients, and public health. How are CIDTs changing diagnosis and surveillance of foodborne pathogens?

- A new generation of molecular CIDTs for the detection and identification of multiple gastrointestinal (GI) pathogens at the same time are now entering the marketplace. The adoption of this technology will likely be accompanied by a major shift away from performing bacterial culture and classical microbiological techniques in clinical laboratory settings.
- CIDTs are faster than culture, and provide data to physicians and their patients in a more clinically useful timeframe.
- New culture-independent products are syndrome-based and can simultaneously detect a wide range of pathogens which traditionally required multiple microbiology procedures.
- New GI panel CIDTs offer information about uncultivable agents such as *Cryptosporidium* and norovirus, or agents for which traditional culture techniques have been less sensitive, complex or exceedingly slow.
- Molecular CIDTs in the marketplace do not require classically trained microbiologists to conduct testing. Interpretation of the clinical significance of some CIDT results require expertise in clinical microbiology and/or infectious diseases.
- The use of CIDTs in the clinical laboratory may be more cost-effective than classical microbiological techniques and require less staff.
- As clinical laboratories utilize CIDTs, the number of bacterial cultures being performed in the clinical laboratory will likely be reduced or eliminated.
- Clinical laboratories that cannot afford the cost outlay to purchase and maintain CIDT instrumentation may choose to contract with health network partners to test patient samples.

Taken together, these facts suggest that we may be approaching a tipping-point, where there could be a rapid change from performing culture to implementing culture-independent testing in clinical laboratories. **Public health surveillance programs at local, state and federal levels depend on cultured isolates in order to maintain current foodborne surveillance programs.** Isolates are further characterized by PHLs and the resulting DNA fingerprint profiles are used to detect clusters of foodborne pathogens. Additionally, surveillance data are used to study food attribution and other applied public health questions related to food safety practices. The consequences to public health of not addressing the challenges posed by the increased use of CIDTs are severe. The number of foodborne

disease clusters and outbreaks that can be identified is directly related to the number of culture isolates available, and with the projected decline of culture many opportunities for prevention of foodborne illness will be lost. In the long run, the loss of information generated by the public health laboratory about what is making people sick will result in a measurable reduction in the safety of the nation's food supply.

Recommended actions for clinical laboratories and public health agencies:

Clinical Laboratories

- Ideally, continue to obtain and submit isolates of foodborne pathogens to local and state PHLs. Isolates are the cornerstone of current foodborne illness surveillance practices in the United States.
- If isolates are not available, due to implementation of CIDTs, submit clinical material (stool, broths) to local or state PHLs.
- Review your state's disease reporting and/or mandatory isolate submission regulations to understand submission requirements in your state.
- If needed, courier service and/or shipping materials may be available from a PHL in your jurisdiction to facilitate the submission of isolates or clinical material for surveillance.
- Maintain effective and open communication with the PHLs in your state or jurisdiction. Notify the PHL of your intent to implement a CIDT for foodborne pathogens.

Public Health Departments

- Review existing regulations and guidance for isolate/clinical material submissions by clinical laboratories.
- Meet with State Board of Health or other governing entity to determine if regulations need to be revised or updated to include mandatory submission of clinical material and/or isolates for reportable diseases. This should be undertaken as a collaborative effort between state public health epidemiologists and laboratorians in order to demonstrate cooperative use of resources and the broad impact of the issue.
- Conduct a survey of clinical laboratories within your state to identify current use and implementation of CIDTs. The survey should elicit responses that will indicate clinical laboratories' future plans regarding bacterial culture. Communicate and work with clinical partners to determine the best approach for retrieving isolate/clinical material from them.
- Develop a cost analysis tool that can be used to support funding requests to pay for the expected increase in isolate recovery efforts from clinical material.

Centers for Disease Control and Prevention

- Work with CIDT manufacturers during the assay development process to assure specimen and process compatibility with isolate recovery efforts.
- Help to identify and overcome barriers to reflex culture (i.e. culture of CIDT-positive specimens) at clinical laboratories and isolate recovery at PHLs.
- Use whole genome sequencing to help identify and investigate foodborne outbreaks. This effort will build reference databases and a sequence-based infrastructure needed for development of culture-independent metagenomic applications for future public health surveillance activities.
- Identify genetic targets and develop assays for surveillance testing to serve as a culture-independent transition to the metagenomics era.

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