Department of Health and Human Services

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To: State and Territorial Epidemiologists, State and Territorial Public Health Laboratory Directors, and State and Territorial Health Officials

RE: Preserving access to clinical enteric microbial isolates for public health surveillance

CDC would like to provide you with an informational update and potential steps states could consider regarding recent developments in diagnostic laboratory technologies. Public health surveillance programs depend on isolates obtained by culture of clinical specimens. The growing use of new diagnostic technologies that do not produce isolates (culture independent diagnostic tests, or CIDTs) represents a serious and current threat to public health surveillance, particularly for Shiga toxin-producing *E. coli* (STEC) and *Salmonella*.

Isolates provide the information needed to characterize the organisms that cause infections in order to find outbreaks and monitor disease trends. Without isolates, we lose the most effective way much of our ability to identify and investigate dispersed outbreaks, track trends in subtypes or antimicrobial resistance, and attribute illnesses to their sources. CDC's recent findings have highlighted the growing impact of the loss of isolates of enteric pathogens.

Although future approaches may allow rapid bacterial subtyping and characterization directly from patient material, all current methods, including whole genome sequencing, require that a microorganism be isolated. Subtyping is an essential part of public health surveillance for enteric bacteria like *Salmonella*, STEC, and *Listeria*, and is a growing part of surveillance for other infections. CDC created PulseNet in 1996 as a nationwide subtyping system to help detect and investigate outbreaks. For these bacteria, improvements in subtyping have led to detection of outbreaks that would otherwise have been missed and helped link those outbreaks to specific sources. This work has resulted in safer foods. Without isolates, many outbreaks will go undetected, contaminated products will remain on the market, important gaps may open in our food safety systems.

To preserve access to isolates, some states are already taking action. For example, several states have changed their reporting regulations to require submission of either the isolate or the CIDT-positive specimen to the public health laboratory. Another state has created guidelines for recommended case reporting and submission of clinical material that they discuss with each clinical lab that adopts the new diagnostic technology. The Association of Public Health Laboratories (APHL) is developing recommendations for measures that will ensure the availability of clinical isolates for public health surveillance. A fact sheet outlines some of the challenges, with suggested actions for clinical labs and public health agencies.

CDC and our public health partners are approaching this issue in several additional ways:

- Tracking through public health surveillance how CIDTs are affecting the availability of culture isolates and public health surveillance.
- Reviewing regulatory authority in public health agencies to require culture isolate or specimen submission if CIDTs are used.
- Exploring language for package inserts, and other recommendations with the U.S. Food and Drug Administration (FDA), Centers for Medicare and Medicaid Services (CMS)

related to the Clinical Laboratory Improvement Act (CLIA), and diagnostic device manufacturers.

- Developing more efficient stool culture procedures to isolate *Salmonella* and STEC detected by CIDTs.
    - The "reflex culture" of specimens that are positive by CIDT could be performed by the clinical laboratory and the resulting isolates sent to the public health laboratory for subtyping. Culturing only those specimens that are positive by CIDT would reduce costs, and would allow testing for antimicrobial susceptibility if needed.
    - Some clinical laboratories may choose to send the CIDT-positive specimen to the public health laboratory for culture. This would increase the workload at the public health laboratory.
    - A CDC-led CIDT Workgroup is exploring opportunities for reimbursement of clinical laboratories for cultured that may not be medically indicated, but are critical for public health.

Public health partners need to prepare now for the time when isolates might not be available directly from many clinical laboratories. Preparations may include:

- Fostering communication between public health officials and clinical labs to promote better understanding of public health priorities.
- Contacting clinical labs serving your state to underline the importance of isolates and reflex culture, and to be kept informed when labs change to CIDTs.
- Reviewing procedures for specimen and isolate referral, particularly for STEC and *Salmonella*.
    - For STEC, previously issued guidelines for clinical laboratories can help with your review.
    - For *Salmonella*, reflex culture can be encouraged, with the alternative being specimen submission.
- In some states, adjusting reporting requirements to require or request reflex culture and referral of isolates may be possible.
- Providing routine courier service can lower the cost of transferring isolates or specimens.
- Introducing simpler culture methods optimized for specific pathogens, as noted above, to lower the burden of culturing CIDT-positive specimens.

Long-term solutions lie in novel advanced testing methods that provide information about subtype, antibiotic resistance, and virulence without an isolate. Developing these will need many partners and many years. In the meantime, effective surveillance must be maintained.

Thank you for your attention to this critical issue. CDC will provide updates on these matters and assistance when requested. We look forward to working with our state and local public health partners, diagnostic test manufacturers and clinical labs to ensure that our vital foodborne outbreak surveillance systems can be maintained to protect Americans from foodborne disease.

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