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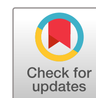
POINT-COUNTERPOINT



Clinical Microbiology Laboratories' Adoption of Culture-Independent Diagnostic Tests Is a Threat to Foodborne-Disease Surveillance in the United States

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INTRODUCTION In November 2015, the Centers for Disease Control and Prevention (CDC) sent a letter to state and territorial epidemiologists, state and territorial public health laboratory directors, and state and territorial health officials. In this letter, culture-independent diagnostic tests (CIDTs) for detection of enteric pathogens were characterized as "a serious and current threat to public health surveillance, particularly for Shiga toxin-producing *Escherichia coli* (STEC) and *Salmonella*." The document says CDC and its public health partners are approaching this issue, in part, by "reviewing regulatory authority in public health agencies to require culture isolates or specimen submission if CIDTs are used." Large-scale foodborne outbreaks are a continuing threat to public health, and tracking these outbreaks is an important tool in shortening them and developing strategies to prevent them. It is clear that the use of CIDTs for enteric pathogen detection, including both antigen detection and multiplex nucleic acid amplification techniques, is becoming more widespread. Furthermore, some clinical microbiology laboratories will resist the mandate to require submission of culture isolates, since it will likely not improve patient outcomes but may add significant costs. Specimen submission would be less expensive and time-consuming for clinical laboratories; however, this approach would be burdensome for public health laboratories, since those laboratories would need to perform culture isolation prior to typing. Shari Shea and Kristy Kubota from the Association of Public Health Laboratories, along with state public health laboratory officials from Colorado, Missouri, Tennessee, and Utah, will explain the public health laboratories' perspective on why having access to isolates of enteric pathogens is essential for public health surveillance, detection, and tracking of outbreaks and offer potential workable solutions which will allow them to do this. Marc Couturier of ARUP Laboratories and Melissa Miller of the University of North Carolina will explain the advantages of CIDTs for enteric pathogens and discuss practical solutions for clinical microbiology laboratories to address these public health needs.

KEYWORDS *Campylobacter jejuni*, PulseNet, STEC, *Salmonella*, *Shigella*, culture independent, food-borne pathogens

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POINT

Some of the greatest advances in public health—immunizations, clean water, safe food—have their roots in the science of microbiology. Data from clinical microbiology laboratories are continuously collected, analyzed, and interpreted as the back-

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bone of public health surveillance efforts. The success of public health surveillance for infectious diseases, including enteric diseases, is founded on a strong collaborative partnership between public health laboratories and clinical laboratories.

A revolution is taking place in the field of enteric microbiology that will test the strength of these long-standing partnerships. Culture-independent diagnostic tests (CIDTs) are improving diagnostics in ways that greatly benefit patient care. CIDTs can test for an array of clinically important infections, including respiratory, bloodstream, and enteric infections, more quickly and effectively than other methods can. Many of the benefits and challenges to CIDT implementation were discussed at a CIDT Forum organized by APHL and CDC in April 2012 (1). APHL lauds the benefits of CIDT technology while suggesting steps all players can take to avoid unintended negative consequences (2).

Limited data are available on the current use of CIDT tests in clinical laboratories. Observations from state public health scientists tell us many clinical laboratories are in the process of switching to CIDTs for the detection of enteric organisms. In 2015, CDC found a significant increase in the percentage of enteric infections diagnosed only by a CIDT compared to the average of such diagnoses between 2012 and 2014 in 10 sites. Specifically, for 4 pathogens, published data show an increase in positive CIDT reports in 2015 of 92% for *Campylobacter*, 284% for *Shigella*, 247% for *Salmonella*, and 120% for Shiga toxin-producing *Escherichia coli* (STEC) compared with the 2012 to 2014 averages; the overall increase in CIDT-only reports for these four pathogens was 122% (3). Accelerated uptake of these tests is expected to continue in the future. APHL encourages our member laboratories to stay in close contact with clinical laboratory partners to determine planned implementation of any CIDT, particularly for enteric diseases.

Public health approach. To protect, promote, and advance population health in the absence of traditional culture methods, new technologies must be developed that do not rely on the recovery of isolates. Until such technologies are developed, validated, and implemented, public health laboratories face a critical need to preserve access to clinical sources of enteric microbial isolates. Sending stools or other clinical material to the public health laboratory for isolation of the detected pathogen is not a tenable solution for several reasons. By mandate and by practice, public health laboratories are not operated with the intention of handling the work flow associated with routine culture of large numbers of clinical samples. While any one clinical laboratory may not encounter a high case count of enteric disease, the total number of enteric isolates referred to a public health laboratory from across a city, county, or state can become a large volume of work. For example, the Missouri State Public Health Laboratory receives over 1,000 *Salmonella* isolates a year, compared to the 300 to 400 stool samples they process annually for enteric bacteria. If as many as half of those *Salmonella* isolates began coming in as stool samples from CIDT-positive reactions, the increase in stool processing would be more than double the current stool enteric processing for that pathogen. Delaying culture until a specimen can be transported to the public health laboratory is also problematic, particularly for traditionally labile organisms, such as *Campylobacter* and non-O157 STEC.

Public health relies on clinical partners to perform timely isolation from patient specimens and submit pure cultures, which are then further characterized at the public health laboratory. With the advent of whole-genome sequencing (WGS) technology and increased epidemiological capacity to interview ill patients, enteric outbreaks are being investigated and sources of contamination are being determined quickly based on a very small number of confirmed related illnesses (Table 1). The loss of even one patient isolate due to nonviability could be the difference between quickly identifying a causative food item and letting a contaminated product remain on the grocery store shelves until more people are made ill.

Public health laboratories have historically used many tools to convey needs and requirements to our stakeholders. Public health law is one of those tools. State and local governments use public health law to convey requirements and define roles in a

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TABLE 1 Selected food-related recalls by contaminant and case count[a]

Recalled product	Contaminant	Case count (reference)
Alfalfa and onion sprouts	O157 STEC	7 cases in Minnesota and 2 cases in Wisconsin (4)
1.8 million lbs of ground beef	O157 STEC	1 case in Massachusetts, 5 cases in Michigan, 1 case in Missouri, and 5 cases in Ohio (5)
Several sizes and varieties of flour	O121 STEC	42 cases in 21 states, with most states having 1 or 2 cases (6)
Pistachios sold across the U.S. and in Canada, Mexico, and Peru	*Salmonella enterica* serovars Montevideo and Senftenberg	11 cases from 9 states (1 or 2 cases per state) (7)
358 frozen vegetable and fruit products sold under 42 separate brands	*Listeria monocytogenes*	1 case in Maryland, 1 case in Washington, and 6 cases in California (8)

[a]Selected list of recent food-borne investigations that traced ill patients to a contaminated source more quickly because of available data from 1 or 2 cases in a given state.

concrete and public manner. Such laws provide a level of clarity that enhances collaborative and long-standing relationships. Given the lack of enforcement provisions in most public health laws, they should be viewed in the light of effective communication and standard setting, not as punitive measures. These laws provide clinical partners who want to do the right thing easy access to the latest rules to help them proceed accordingly. An analysis of current rules and regulations for all 50 states and the District of Columbia pertaining to isolate and other clinical material submission was published by APHL in 2016 (9). This analysis shows that 43 states mandate submission of isolates or other clinical materials for at least three of the eight pathogens reviewed, and two-thirds or more of states require submission of five of the eight pathogens (STEC, *Listeria monocytogenes*, *Salmonella*, *Shigella*, and *Vibrio*). The majority of states mandate submission in their administrative rules and regulations; a few states address submission of isolates or clinical materials in statutes.

PulseNet: effective but in jeopardy. One driving force toward ensuring a safer U.S. food supply is PulseNet, the National Molecular Subtyping Network for Foodborne Disease Surveillance (10). PulseNet is a national laboratory network that uses bacterial DNA fingerprints to connect cases of foodborne illness that may be from a common food or environmental source. Through PulseNet, public health professionals typically detect well over one hundred local and multistate foodborne outbreaks each year. In existence since 1996, PulseNet revolutionized foodborne outbreak investigations by allowing for faster outbreak detection and effective industry response, thereby protecting American consumers from contaminated products ranging from produce to peanut butter to meat and poultry. Since 1996, more than 1 billion pounds of contaminated food have been recalled—saving lives, time, and money—thanks to PulseNet (11).

PulseNet is deemed a public health success because it supports public health action to control outbreaks and elucidate new food hazards. The network has also proven to be highly cost-effective. A recently published economic evaluation of PulseNet demonstrated the efficiency and value of this network in terms of cost savings (an estimated $507 million saved every year, an economic benefit about 70 times its cost) and illness prevention (prevents over 270,000 illnesses a year from *Salmonella*, STEC, and *Listeria*) (12). PulseNet's success, in large part, can be attributed to front-line clinical laboratory partners who obtain and submit isolates from ill patients.

Meeting public health needs. The public health community is committed to meeting our own needs related to the collection of surveillance data as best we can. We accept that we will bear some costs of maintaining our systems and have shown a willingness to pay for this. For example, courier service and/or complementary shipping materials may be available through your state or local public health laboratory. In many states, such as Colorado, Missouri, and Tennessee, when a clinical partner is unable to bear the costs of reflex culture, the public health laboratory accepts primary specimens. The key to finding the best solution in your city/county/state is open communication with the public health laboratory that serves your jurisdiction.

CDC has supported significant efforts to preserve isolate submission from clinical laboratories, with an aim to ensure that existing surveillance systems continue to

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operate. In the summer of 2015, CDC funded work in 5 jurisdictions to determine the most efficient methods for isolation of *Salmonella* and STEC from CIDT-positive specimens. APHL and CDC will publish cost-effective approaches based on this work in 2017. Additionally, both CDC and the Food and Drug Administration (FDA) are investing heavily in the development of WGS as a subtyping method for enteric pathogens and a wide array of other infectious agents. This transition to WGS will lead to cost savings by streamlining work flows and eliminating the need for tests such as traditional serotyping and targeted virulence and antimicrobial resistance marker detection. The WGS transformation will drive the expansion of both workforce and information technology capacities, building a more efficient and modern public health system.

Even with the initial success realized through WGS-based subtyping, this method relies on isolates and is therefore considered an interim technology for PulseNet. As a long-term solution, CDC is applying resources to develop enteric surveillance systems built on metagenomics, amplicon sequencing, and other technologies that do not require bacterial isolates. This research is in the early stages of development. Today's transitional work establishes WGS-derived pathogen databases that are necessary for the post-isolate era, leading to a public health system that is better prepared to migrate to culture-independent subtyping methods, such as metagenomics. In the meantime, isolate recovery efforts remain an important focus.

Meeting clinical needs. We believe clinical laboratories have incentives for performing reflex culture on a majority of positive CIDT specimens. Completing antimicrobial susceptibility test requests on *Salmonella*, *Shigella*, and *Campylobacter* isolates will require culture isolation in the clinical laboratory. The cost of adding culture isolation of *E. coli* O157:H7, or all STEC in those laboratories capable of recovering them, to this list of reflexed pathogens is not a huge burden given the low incidence of this pathogen. Furthermore, at least in large academic centers, the cost of reflex culture of positive CIDT specimens is minimal compared to the cost savings of the hundreds of stool requests tested with a multianalyte panel instead of culture and an ova and parasite exam. One institution estimated annual costs of $250,000 to $500,000 for molecular tests, with reimbursement at $2 to $2.5 million (13). For a relatively minimal expense, shared among clinical and public health partners, together we can achieve goals that are in everyone's best interest.

PulseNet is but one surveillance system built to decrease disease burden that relies on access to clinical isolates. NARMS, the National Antibiotic Resistance Monitoring System, is the only nationwide surveillance system that monitors antimicrobial resistance in select enteric bacteria from ill persons, retail meat, and food animals. NARMS is dependent upon bacterial isolates for susceptibility testing and other subtyping studies, such as WGS. For example, the NARMS team at CDC is currently using WGS, plasmid transformation studies, and mutational analysis to investigate the recent emergence of infections caused by a strain of *Salmonella enterica* serovar Infantis that expresses a CTX-M-type extended-spectrum beta-lactamase (ESBL). In this strain, a large multidrug-resistant plasmid confers resistance to ampicillin and clinically important third-generation cephalosporins, including ceftriaxone (CTX). The plasmid is capable of spreading antibiotic resistance among bacterial species. Another example of the utility of isolate-based surveillance is the recent discovery of the MCR-1 gene in human and pig isolates (14, 15). Since phenotypic and genotypic testing rely on isolation of an organism and cannot currently be performed on clinical material, obtaining isolates is an imperative part of the short-term solution to identifying and understanding the evolution of antimicrobial resistance.

We are pleased that our position aligns with the new "Guideline for Prevention and Management of Acute Diarrhea" from the American College of Gastroenterology (ACG). While recognizing that FDA-approved CIDTs can find a causal organism when "traditional methods" cannot, this ACG guideline supports doing both culture and CIDT and says that "Before bacterial culture is discarded entirely, it is important to acknowledge

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that multiplex molecular diagnostics do not yield isolates that can be forwarded to public health laboratories" (16). A *New England Journal of Medicine Journal Watch* article summarizes the first ACG recommendation as follows: "In acute diarrhea (duration, 1–14 days), perform stool cultures and new culture-independent molecular assays (if available) when a patient is at high risk of spreading disease or during outbreaks" (17). We hope additional medical societies and professional organizations take an interest in this issue in the future.

Path forward. How can the clinical and public health microbiology community benefit from CIDT technology without disrupting the extensive and beneficial public health systems that defend our nation from foodborne illness outbreaks? The primary recommendation from APHL and ASM is frequent and early communication between public health laboratories and clinical laboratories when a change in test offerings is being considered. Some public health laboratories are proactively contacting their submitting laboratories and are learning that almost 100% of those adopting CIDTs are willing and able to continue submitting isolates of *Salmonella*, *Shigella*, and STEC (S. Gladbach and R. Atkinson-Dunn, personal communications). Additionally, some clinical laboratory leaders have conveyed the value that continued submission of isolates to the public health laboratory for epidemiologic investigations holds for them (18). Interim guidelines have been released by APHL, CDC, and ASM that can help clinical laboratories efficiently recover these pathogens while minimizing costs (19). The three partners will collaborate on final guidelines in 2017, following analysis of newly available data.

Conclusions. In the near future, molecular microbiologists will be able to determine a wealth of valuable information about a pathogen from its DNA sequence. Identity, serotype, virulence factors, antibiotic resistance markers, and molecular subtype will all be available by reading A's and T's and C's and G's. Long-term solutions lie in novel advanced testing methods that provide the above-described information without an isolate. Developing these solutions will require the efforts of many partners over several years. In the meantime, we must maintain the effective culture-based surveillance activities that have served us so well.

What is at stake? The ability to connect ill patients to one another and to definitively link ill patients to the common source of their foodborne illness, and the ability to link dispersed cases caused by widely distributed products. Without isolates, many outbreaks will go undetected, contaminated products will remain on the market, and important gaps may reopen in our food safety system. In essence, we will lose the most effective tool we have for improving the safety of the U.S. food supply.

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COUNTERPOINT

It was not so long ago that the medical and laboratory communities' view of Shiga toxin-producing *E. coli* (STEC) was narrowly limited to the O157:H7 serotype. This perception was multifactorial but was largely due to the limitations of culture methods that selected only for sorbitol-nonfermenting strains, which were prototypical strains of O157. As such, traditional culture using sorbitol MacConkey agar dramatically skewed public health laboratory (PHL) reporting data and clinical perceptions of STEC, mainly the perception that O157:H7 STEC is the only STEC that matters. It is only as a result of STEC detection methods that are not primarily dependent on culture (so-called culture-independent diagnostic tests [CIDTs]) that we subsequently discovered the multitude of different serotypes of STEC that can produce Shiga toxins 1 and/or 2. With the adoption of toxin detection via immunocapture methods, such as enzyme-linked immunosorbent assay (ELISA) or lateral flow assays, in many laboratories in the United States, the incidence and detection rates of non-O157 serotypes of STEC associated with acute diarrhea and hemolytic uremic syndrome rose prominently (http://www.cdc.gov/ecoli/outbreaks.html). Presumably, these serotypes were always there, but our test approach was woefully inadequate. These increased detections were aptly exemplified in the state of Washington, where the adoption of FDA-approved antigen detection CIDTs led directly to increased detection of STEC, with significantly more recovery of both O157 and non-O157 serotypes (1). The PHL that published these data acknowledged that this increased detection posed a burden of effort on PHLs to subsequently identify the causative non-O157 types through follow-up cultures using enrichment broths or primary specimens (1). As we reflect on whether improved detection of outbreak pathogens can reasonably be considered a "burden," it would be illogical to argue that a return to O157 culture only would be prudent simply because it would be less burdensome. In fact, the opposite is true: with Shiga toxin detection being a CDC-recommended standard for clinical laboratories, in addition to O157 selective culture (guidance that was expertly and cooperatively drafted by PHLs and sentinel laboratory constituents) (2), our ability to detect outbreaks and critical cases of STEC in the sentinel laboratory has greatly improved clinical care. And with newer CIDTs, we can do even better!

Although antigen detection CIDTs for STEC have increased detection rates, one limitation is the requirement of 18 h of preenrichment in liquid broth to maximize

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clinical sensitivity. This was one driving force for retaining O157 selective culture in standard sentinel laboratory practice, since putative O157 colonies could be rapidly detected in selective/differential culture in less time than the antigen testing could be performed. However, in the era of rapid molecular detection methods for Shiga toxin genes (stx_1 and stx_2), the turnaround time is dramatically reduced due to removing the need for broth enrichment. Samples could therefore be routed to a PHL for culture and identification of the offending STEC strain in potentially less time than is currently possible using antigen detection CIDTs. Essentially, the downstream recovery process for STEC is largely unchanged (though possibly improved due to earlier transport to the PHL), while screening sensitivity is enhanced through superior technology.

If we think more broadly with regard to fastidious enteric pathogens, such as *Campylobacter* and *Shigella*, the discussion becomes slightly more complicated, since delays in transport and delays in setting up cultures can have marked deleterious effects on isolate recovery for these pathogens (3, 4). It is important to recognize that the discrepancies seen between delayed culture of fastidious pathogens and molecular-CIDT-positive results should not be viewed as false-positive molecular-test results, as Van Lint and colleagues have demonstrated that *Shigella* recovery in culture is impaired after 3 days of refrigerated storage but *Salmonella* is not significantly affected. Recent studies have shown increased detection rates for all of the aforementioned pathogens using molecular CIDTs (4, 5), and it is well known that our current culture practices, particularly for *Campylobacter*, are suboptimal and largely unstandardized (3, 6). This then leads to a practical consideration of whether delaying culture set up is potentially worth the improved detection that can be achieved with molecular CIDTs, even if all of the specimens cannot be optimally cultured thereafter (a reasonable concern for *Campylobacter* and *Shigella*). One must address the philosophical debate of whether it is of greater utility to recover isolates for only a fraction of "true cases" by maintaining insensitive predicate cultures or to detect a greater proportion of true cases at the risk of sacrificing a subset of samples to suboptimal isolate recovery. These challenges, in part, sparked a joint effort between key players in PHLs and sentinel laboratories to draft unified guidelines and recommendations for *Campylobacter* (in final preparation), akin to what was drafted for STEC. This will likely also force us to revisit or revise the case definition for more fastidious enteric pathogens like *Campylobacter*, to include molecular CIDTs and clear recommendations for isolate/specimen submission.

Antigen detection CIDTs, in particular for the detection of *Campylobacter*, have shown disputed clinical utility due to false-positive results that cannot be confirmed by culture or molecular assays (5). This could realistically lead to a significant burden to perform culture for these potentially low-yield samples. However, with highly sensitive and specific molecular CIDTs in place for routine clinical care and improved detection rates for samples containing enteric pathogens, the spectrum of samples that would require culture for outbreak investigation should become higher in yield than with previous generations of CIDT technology, albeit false-positive results will still occasionally be encountered. The critical question becomes, "Who should assume responsibility for culturing isolates for outbreak investigation purposes?"

In recent years, this has become a worrisome and polarizing subject in published works and conference proceedings, unfortunately (and unnecessarily) pitting PHL mandates against those of sentinel laboratories in a seemingly adversarial tone (7–9). PHLs have publicly expressed concern for poor financial resources to support these efforts and generally view CIDTs as a threat to their longstanding procedures for outbreak investigations despite the opportunities that come with these technologies (7–9). On the other side of this issue, sentinel laboratories are under greater pressure from hospital administrators to perform more testing with fewer staff and to reduce costs. In fact, outcome measures are rapidly becoming a metric for which hospitals hold physicians and laboratories accountable. If a process incurs expense and provides no direct clinical benefit to the patient, it essentially should not be performed (e.g., culturing a sample that already has a diagnostic CIDT result on a validated assay). Some

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laboratories that have adopted expensive CIDT molecular assays were required to outright cease stool culture to maintain cost-effectiveness. If culturing for isolates is simply a service to support public health outbreak investigations and plays no direct role in clinical care to the index patient, then this extra cost is difficult to justify in the sentinel laboratory. Another way to look at this would be to ask whether a private hospital laboratory or a private payer should be incurring expenses that are not of clinical necessity. When considered in this context, the discourse rapidly evolves away from practical laboratory discussions and toward government policy/potential legal recourse if culture enforcement is sought through forced legislation rather than collaboration and compromise.

How can this potential quagmire be avoided? It is paramount that we engage this in the same way we have for STEC and *Campylobacter*: collaboratively and through frank, open, constructive discourse between key stakeholders in PHLs and sentinel laboratories. Interim guidelines have already been collaboratively drafted between the American Society for Microbiology and the Association of Public Health Laboratories (10) and serve as a prime example of the advances we can achieve by working collaboratively to address these challenges. Lobbying for government intervention to force the hand of sentinel laboratories to perform reflex cultures is unconstructive and divisive. Likewise, outright refusal by sentinel laboratories to consider any compromise that includes selective culturing of stool samples that test positive by CIDTs will not move the discussion toward a reasonable solution either. PHLs and sentinel laboratories are a team (despite sometimes skewed perceptions to the contrary), and it is imperative that we continue to work together to best serve the individual patient, as well as the community at large.

How can we achieve this? Sentinel laboratories and their partners in PHLs must have discussions IN ADVANCE of implementing a CIDT to find a practical solution. Some discussion points to address include the following.

- Does the CIDT allow for subsequent culture of samples (i.e., preserved stools are collected)?
- Does the sentinel laboratory intend to maintain any stool culture capabilities? If not, would they consider directed culture on a limited basis for samples that test positive by CIDTs?
- Can PHLs solely assume the responsibility for culturing all samples with positive CIDTs?
- If the PHL cannot handle the burden of culturing all positives, as has been stated in several texts, can sentinel laboratories and PHLs establish a system for remuneration (perhaps via appropriated government funding) to maintain selective media as necessary for directed cultures in the sentinel laboratory? This could potentially be accomplished through the use of regional laboratory services.

This final point is likely the most practical option and should be explored. Directed cultures would involve only setting up a selective media for the organism(s) identified by the CIDT and submitting the subsequent growth to the PHL for further characterization. It would be illogical to perform an entire conventional stool culture interrogation when the laboratory knows what the offending pathogen is that needs to be targeted (this would also reduce the associated expenses). In the case of STEC, sentinel laboratories could continue to simply submit preserved stools or an enrichment broth. For *Salmonella*/*Shigella*, an appropriate medium (e.g., Hektoen enteric agar) could be set up for culture, and likewise for *Campylobacter* (e.g., Campy CVA). This could be a realistic solution if we cooperatively utilize our combined strengths and interests to jointly lobby for government resources to fund these important efforts. This could be pursued on a state or federal level as deemed appropriate, with support from professional societies. Along these same lines, the public health sector must pursue new technologies for culture-independent strain typing directly from stool samples in order to parallel the enhanced detection realized by molecular CIDTs. This cannot be

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achieved without adequate funding from appropriate government agencies and should be an effort supported at the federal, state, and local levels.

These technologies should not be feared but, rather, should be viewed as an opportunity. There are multiple studies that have highlighted the sensitivity increase seen when molecular CIDTs are tested against antigen CIDTs, and this is likely the future method of choice for most sentinel laboratories, as part of "syndromic panels" (11–14). In fact, early adopters of these technologies have experienced more frequent identification of reportable gastrointestinal pathogens than with traditional methods, which carries the potential to identify more outbreaks, identify outbreaks earlier, and aid in reducing additional or secondary transmission events (15). Norovirus is one such example of the positive impact to public health reporting and outbreak detection that can be realized through the use of syndromic panel testing. This should be viewed as an opportunity to increase diagnosis and subsequent isolate recovery in the case of bacterial pathogens, rather than a threat to public health surveillance.

Are CIDTs a threat to public health surveillance? They certainly could be IF we collectively fail to collaboratively find a solution for this challenge that meets the needs of the patient and the greater community. We've been successful before, we've jointly drafted interim guidance; so what is stopping us from executing this further?

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SUMMARY

Points of agreement

1. PulseNet has played an irreplaceable role in the detection and control of numerous foodborne outbreak in the United States. The current technology available to PulseNet requires bacterial isolates for analysis.
2. Culture-independent diagnostic tests (CIDT) enhance the detection of the major foodborne pathogens under surveillance by PulseNet: *Campylobacter*, *Salmonella*, *Shigella*, and Shiga toxin-producing *Escherichia coli*.
3. Having to recover organisms that have already been detected by CIDT will add unreimbursed expense for laboratories, a cost that many health care systems will not want to bear. Solutions to this problem will require agreement between diagnostic and public health laboratories.
4. Molecular methods of typing foodborne pathogens directly from clinical specimens are on the horizon, but this is clearly a long-term solution. A short-term solution is essential, since the bacterial isolates are essential for public health surveillance and diagnostic laboratories are becoming increasingly dependent on CIDTs.

Points requiring further consideration

1. Is it reasonable to expect public health laboratories to perform culture isolation from CIDT-positive stool specimens when they are already facing staffing and financial challenges?
2. Would rules or statutes which require diagnostic laboratories to subculture CIDT-positive specimens be the most cost-efficient means of providing isolates to public health laboratories?
3. What role do government agencies have in mandating how these organisms are recovered? For example, can a Current Procedural Terminology (CPT) code be established specifically for subculture of CIDT-positive specimens so that some level of reimbursement can be obtained? Alternatively, does the public value the safety of the food supply sufficiently to agree to a tax on food purchases to support public health laboratories' surveillance of foodborne outbreaks?

Peter H. Gilligan, Point-Counterpoint Editor, *Journal of Clinical Microbiology*

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