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# **An Intro to Culture- Independent Diagnostic Tests for Gastrointestinal Pathogens**

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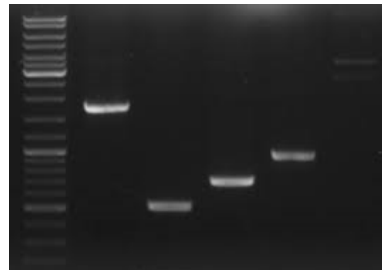
# Objectives of the Session

- Discuss the importance of reviewing and modifying local/state laws for mandatory isolate or clinical material submission
- Describe validation studies and workflow practices within public health laboratories in response to uptake of CIDT testing in clinical laboratories
- Explain current studies to address isolate recovery practices and long-term solutions for culture-independent public health surveillance testing



# What is “CIDT”?

- “Culture-Independent Diagnostic Test”
- Any diagnostic test that does not require the culture or isolation of a microorganism in order to arrive at a diagnostic test result
- May be any number of commercially- available or laboratory-derived test methodologies





# **Commercially Available CIDT's- Multi-target GI Pathogens**

- A handful of multi-target assays are available and more are in development
- Variation among the available multi-target CIDT's in which GI pathogens are targeted (Bacteria only vs bacteria and viruses vs bacteria, viruses and parasites)
- Common aspects of multi-target CIDT's:
  - Same day result
  - Molecular/ PCR-based



# Devices with GI Panels in Development or FDA Clearance Process

CLEARED



BD Max

CLEARED



BioFire FilmArray



GenMark Dx eSensor XT-8

CLEARED



Nanosphere's Verigene Enteric Pathogens (EP) Test



Cepheid GeneXpert



Applied Biocode

CLEARED



CLEARED



Luminex xTag GPP



# BioFire FilmArray® System



- Sample preparation, amplification, detection and analysis combined
- Add patient sample and reagents and walk away
- Detects 22 common bacterial, viral and parasitic GI pathogens
- Low throughput (single sample- can chain 8 instruments to a PC)
- Results in one hour





# Prodesse Progastro™ SSCS Assay



- Detects the four common bacterial agents of gastrointestinal disease: *Salmonella*, *Shigella*, *Campylobacter* and Shiga toxin-producing *E. coli*
- Real time PCR kit run on the Cepheid SmartCycler II platform
- Results in four hours





# BD MAX<sup>®</sup> Enteric Bacterial Panel



- Detects the 4 common enteric bacterial pathogens
- Virus and Parasite panels in development
- PCR-based
- Fully automated; 24 tests
- Flexibility to target pathogen class (B, V or P)
- Result in three hours



# Nanosphere Verigene® Enteric Pathogens (EP) Test



- Detects 9 common bacterial and viral GI pathogens
- Combines automated extraction, purification, amplification and hybridization
- Single throughput; can chain up to 8 instruments
- Result in two hours
- Most recent platform to become available



# Luminex xTAG GPP



- Both ASR and RUO kits available
- Detects 14-15 common bacterial, viral and parasitic gastrointestinal pathogens
- Bead-based technology
- Higher throughput; 96 well\*
- More significant hands-on time
- Results in 5 hrs (~24 tests)



# Advantages to CIDT Use

- Generally faster to result than traditional tests
- Classically-trained microbiologists not needed in many cases
- May be more cost-effective than traditional, conventional tests
- Syndromic-based testing approach possible with multi-target tests
- Ability to detect non-cultureable or fastidious pathogens



# Advantages to CIDT Use

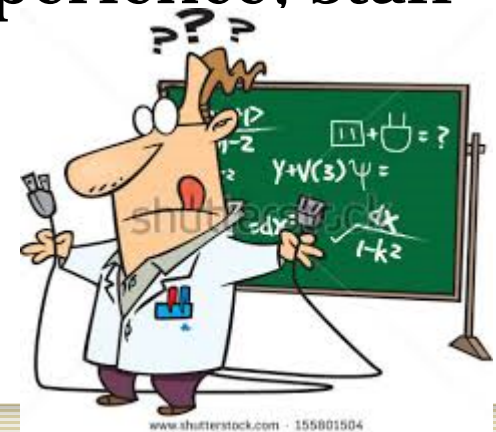
- Improved sensitivity and specificity?
  - Compared with culture
  - Need to assess the validity of the developer validation studies; specimens and/or isolates used may not have been optimal
- Detection of nonviable organisms\*
  - Only advantageous if truly pathogenic or a significant cause of GI illness





# Disadvantages to CIDT Use

- Price of some CIDT platforms may be cost-prohibitive for laboratories
- **Loss of culture isolates**
  - To clinical laboratories and PHL's for AST
  - To public health for surveillance
- Loss of classical microbiology experience; staff unable to determine when CIDT results don't make sense





# Disadvantages to CIDT Use

- Detection of nonviable organisms\*
  - Problematic if not significant; not the cause of illness
  - Ineffective for test of cure; patient may shed nonviable organism or organism DNA well after the infection has passed



Red Herring!





# Considerations of CIDT Results

- Interpretation of results
  - What do the findings mean in relation to the clinical picture of the patient?
  - What is the significance of multiple pathogens detected?
  - How do epidemiologists apply the current reportable conditions guidelines to CIDT results?
    - Confirmed?
    - Suspect?
    - Probable?





# PHL Strategies for CIDT

- Partner with clinical laboratories in your jurisdiction
  - Work to ensure isolate/ specimen submission continues
  - Communicate regularly- know who is using CIDT
- Assess impact of clinical lab CIDT implementation on your laboratory
  - Calculate number of additional cultures you will need to perform
  - Pursue funding (grants, general revenues, etc.) to cover rising costs of PH surveillance



# PHL Strategies for CIDT

- Partner with epidemiologists
  - Discuss reporting issues
  - Educate them on what results may mean
- Monitor CIDT use and performance
  - What CIDT's have become available?
  - Have there been published performance issues?
- Pursue mandatory **specimen** submission in your jurisdiction (in addition to isolate submission mandates)
- Partner with CIDT industry representatives



# Summary

- There are a number of multi-target CIDT's that have become available for detection of GI pathogens
- These CIDT's offer definite advantages over traditional culture-based testing methods but considerations still must be taken into account when assessing their utility
- PH labs and epidemiologists must adapt to the ever-changing world of clinical diagnostics
- There are strategies PHL can utilize to address and adapt to the effects CIDT have on them