Culture-Independent Diagnostic Initiative & Molecular Multi-Analyte Gastrointestinal Detection Panels Update —Public Health and Industry Efforts

U.S. FOOD & DRUG ADMINISTRATION

FDA Perspective on Clearance of Multiplexed Molecular Tests for Gastrointestinal Pathogens

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CDRH/OIR/DMD/BAC2

Regulatory Review Process for GI Panel Devices

- **Pre-submission:** We strongly encourage manufacturers to use the pre-sub process to receive FDA feedback on analytical and clinical study design. We find that pre-subs help to streamline the review process.

http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf

- **510(k) submission**: Establish substantial equivalence to a predicate device

- **Regulation:** CFR 866.3990, Class II, 510(k), Product code PCH

Device Indications for Use Guides the Data Review

- Name of assay system
- A brief description of the type of test or technology used (i.e., NAAT)
- Microorganisms detected
- Specimen Type (e.g., unpreserved and preserved stool)
- The Intended Use population (e.g., aid in the diagnosis of gastrointestinal infections in patients with signs and symptoms)
- Results to be used in conjunction with other available clinical and laboratory information

Review Totality of Scientific Evidence

- **Clinical:** Well designed and executed multi-site clinical study including all claimed specimen types
  - High sensitivity and specificity for each claimed analyte
  - High level of reproducibility with analyte concentrations near the limit of detection

- **Analytical:** Demonstration of analytical performance using simulated specimens prepared in claimed matrices (e.g., LoD, Inclusivity, Cross-Reactivity, Competitive Interference, Interfering Substances, Carryover/Cross-contamination, Specimen Stability, Fresh versus frozen)

- **Software/Instrumentation**

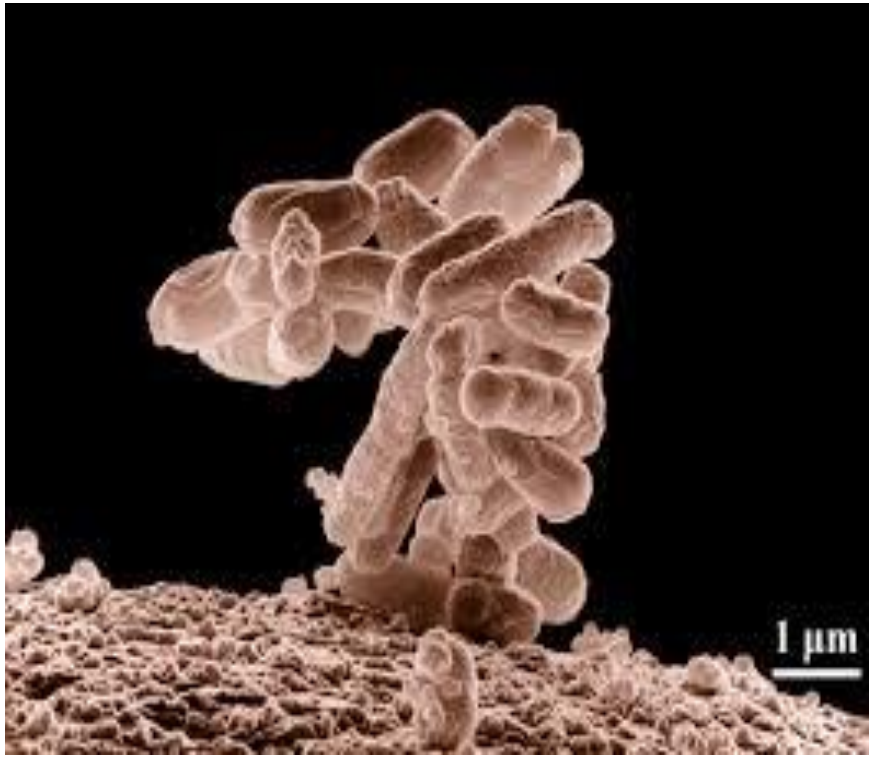
Clinical Study Design

- **Minimum three geographically diverse clinical collection and testing sites**
- **Specimens:**
  - Prospectively collected specimens, minimum 1,500, from IU population i.e., patients with signs and symptoms of gastrointestinal infection
  - Specimen types for cleared devices are unpreserved and/or preserved stool (e.g., Cary Blair)
  - Archived Positive specimens, if needed for low prevalence analytes
  - Contrived specimens for rare analytes

- **Reference/Comparator Methods:**
  - Bacterial analytes, comparison to culture
  - Viral analytes, comparison to composite of two PCRs/bi-directional sequencing
  - Parasitic analytes, comparison to microscopy or composite of two PCRs/bi-directional sequencing

- **Reproducibility Study:**
  - Three site study with large number of replicates evaluated on multiple runs/days

Cleared Multiplex Molecular Devices for Enteric Pathogens



- Luminex xTAG GI Pathogen Panel (*de novo*, 2013)
- Hologic ProGastro SSCS Assay
- FilmArray GI Panel
- BD MAX Enteric Bacterial Panel
- BD MAX Parasite Panel
- Verigene Enteric Pathogens Nucleic Acid Test
- Great Basin Shiga Toxin Direct Test

GI Panels and Reportable Analytes

- Several bacterial analytes on GI Panels (e.g., Salmonella, Shigella, Vibrio and STEC) are reportable/actionable analytes for reporting to public health authorities.
- Surveillance is a critical component of promoting public health.
- We understand the potential impact on CDC surveillance efforts as laboratories move from culture methods to molecular devices.
- Within the scope of FDA's mission, we have been working with CDC and the CIDT workgroup to develop language for package inserts to inform device users regarding this issue.

Package Insert Language

Suggested Public Health Language to be included in the precaution statement of package inserts for newly cleared or approved molecular multi-analyte (and single analyte) detection panels that detect "reportable analytes"

Precaution related to Public Health Reporting: Local, state, and federal rules and regulations for notification of reportable diseases are continually updated and include a number of organisms that are important for surveillance and outbreak investigations.[1-2]. Laboratories are responsible for following their state and/or local rules pertaining to reportable pathogens and should consult their local and/or state public health laboratories for isolate and/or clinical sample submission guidelines.

[1] *Summary of Notifiable Diseases.* available at <http://www.cdc.gov>

[2] *CIFOR Analysis of State Legal Authorities*. available at <http://www.cifor.us/>

Resources

- **FDA Guidance for Highly Multiplexed Devices**

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM327294.pdf

- **Special Controls Guideline for GI Panels**

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM470559.pdf

- **Decision Summaries posted in 510(k)/*de novo* database**
  - Search under product code PCH for Multiplex GI device)
  - Search under Microbiology (Panel) for all DMD cleared devices

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm

A 510(K) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR §807.92(a)(3)) that is not subject to premarket approval.

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Search Database

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510K Number | Type | Product Code: PCH

Center | Combination Products

Applicant Name | Cleared/Approved In Vitro Products

Device Name | Redacted FOIA 510(k)

Panel: Microbiology | Third Party Reviewed

Decision

Decision Date: 11/28/2014 to 11/29/2016 | Clinical Trials

Sort by: Decision Date (descending)

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Other Databases

- De Novo
- Medical Device Reports (MAUDE)
- CDRH Export Certificate Validation (CECV)
- CDRH FOIA Electronic Reading Room
- CFR Title 21
- CLIA
- Device Classification
- FDA Guidance Documents
- Humanitarian Device Exemption
- Medsun Reports
- Premarket Approvals (PMAs)
- Post-Approval Studies
- Postmarket Surveillance Studies
- Radiation-Emitting Products
- Radiation-Emitting Electronic Products Corrective Actions
- Recalls
- Registration & Listing
- Standards
- Total Product Life Cycle
- X-Ray Assembler

1 to 4 of 4 Results
Panel: *Microbiology* **ProductCode:** *PCH*
Decision Date From: *11/28/2014*
Decision Date To: *11/29/2016*

Results per Page 10

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Device Name	Applicant	510(K) Number	Decision Date
Filmarray Gastrointestinal Panel (Gi) Fo	Biofire Diagnostics, Llc	K160459	04/01/2016
Great Basin Shiga Toxin Direct Test	Great Basin Scientific, Inc.	K152955	03/22/2016
Bd Max Enteric Parasite Panel, Bd Max In	Becton, Dickinson And Company	K143648	08/25/2015
Filmarray Gastrointestinal (Gi) Panel Fo	Biofire Diagnostics, Llc	K143005	02/19/2015

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Device Classification Name	Gastrointestinal Pathogen Panel Multiplex Nucleic Acid-Based Assay System
510(K) Number	K160459
Device Name	FilmArray Gastrointestinal Panel (GI) For Use With FilmArray Torch
Applicant	BIOFIRE DIAGNOSTICS, LLC 390 Wakara Way Salt Lake City, UT 84108
Applicant Contact	Kristen J. Kanack
Correspondent	BIOFIRE DIAGNOSTICS, LLC 390 Wakara Way Salt Lake City, UT 84108
Correspodent Contact	Kristen J. Kanack
Regulation Number	866.3990
Classification Product Code	PCH
Date Received	02/19/2016
Decision Date	04/01/2016
Decision	Substantially Equivalent (SESE)
Regulation Medical Specialty	Microbiology
510k Review Panel	Microbiology
Summary	Summary
FDA Review	Decision Summary
Type	Special
Reviewed By Third Party	No
Combination Product	No