January 16, 2025

BioFire Diagnostics, LLC
Karli Plenert
Senior Director, Regulatory Affairs
515 Colorow Drive
Salt Lake City, Utah 84108

Re: K243885
Trade/Device Name: BIOFIRE FILMARRAY Gastrointestinal (GI) Panel Mid
Regulation Number: 21 CFR 866.3990
Regulation Name: Gastrointestinal Microorganism Multiplex Nucleic Acid-Based Assay
Regulatory Class: Class II
Product Code: PCH
Dated: December 18, 2024
Received: December 18, 2024

Dear Karli Plenert:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Bryan M. Grabias -S

Digitally signed by Bryan M. Grabias -S
Date: 2025.01.16 13:45:22 -05'00'

Bryan Grabias, Ph. D.
Acting Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K243885

Device Name
BIOFIRE FILMARRAY Gastrointestinal (GI) Panel Mid

Indications for Use *(Describe)*
The BIOFIRE FILMARRAY Gastrointestinal (GI) Panel Mid is an automated qualitative multiplexed nucleic acid-based in vitro diagnostic test intended for use with BIOFIRE FILMARRAY Systems. The BIOFIRE FILMARRAY GI Panel Mid is capable of the simultaneous detection and identification of nucleic acids from multiple bacteria, viruses, and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following bacteria, parasites, and viruses are identified using the BIOFIRE FILMARRAY GI Panel Mid:

- Campylobacter (C. jejuni/C. coli/C. upsaliensis)
- Clostridioides (Clostridium) difficile (toxin A/B)
- Salmonella
- Vibrio (V. parahaemolyticus/V. vulnificus/ V. cholerae)
- Yersinia enterocolitica
- Shiga-like toxin-producing Escherichia coli (STEC) stx1/stx2
- Shigella/ Enteroinvasive Escherichia coli (EIEC)
- Cryptosporidium
- Cyclospora cayetanensis
- Giardia lamblia (also known as G. intestinalis and G. duodenalis)
- Norovirus GI/GII

The BIOFIRE FILMARRAY GI Panel Mid is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness and results are meant to be used in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not included in the BIOFIRE FILMARRAY GI Panel Mid. The agent detected may not be the definite cause of the disease.

Concomitant culture is necessary for organism recovery and further typing of bacterial agents.

This device is not intended to monitor or guide treatment for C. difficile infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for Yersinia enterocolitica, were established primarily with retrospective clinical specimens.

Performance characteristics for Vibrio (V. parahaemolyticus, V. vulnificus, and Vibrio cholerae) was established primarily using contrived clinical specimens.

Negative BIOFIRE FILMARRAY GI Panel Mid results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.

A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute gastroenteritis in the context of outbreaks.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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BIOFIRE® FILMARRAY® Gastrointestinal Panel Mid

Special 510(k) Summary
BioFire Diagnostics, LLC

Introduction:

The purpose of this Special 510(k) submission is to obtain clearance for the BIOFIRE® FILMARRAY® Gastrointestinal Panel Mid (BIOFIRE FILMARRAY GI Panel Mid). The BIOFIRE FILMARRAY GI Panel Mid is compatible with the BIOFIRE® FILMARRAY® 2.0 System (K143178) and the BIOFIRE® FILMARRAY® TORCH System (K160068), a polymerase chain reaction (PCR)-based in vitro diagnostic system for infectious disease testing.

The BIOFIRE GI Panel Mid is an identical product to the BIOFIRE® FILMARRAY® Gastrointestinal Panel (K242367) except it uses modified labeling and modified software to mask and report only 11 of the 22 targets normally reported on the BIOFIRE FILMARRAY GI Panel.

Modifications to the BIOFIRE FILMARRAY GI Panel Mid labeling, which includes changes to the Instructions for Use and Quick Guide, have been made to reflect the change in panel name and reported analytes.

According to the requirements of 21 CFR 807.92, the information included with this submission provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitted by:

BioFire Diagnostics, LLC (bioMérieux)
515 Colorow Drive
Salt Lake City, UT 84108

Contact: Karli Plenert, MBA
Telephone: 385-414-4985
Email: Karli.Plenert@biomerieux.com

Date submitted: January 16, 2025

Device Name and Classification:

Trade name: BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel Mid

Primary Regulation Number for Device Classification: 21 CFR 866.3990

Regulation Number: 21 CFR 866.3990

Classification Name: Gastrointestinal microorganism multiplex nucleic acid-based assay

Predicate Device:

K242367– BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel

Intended Use:

The BIOFIRE® FILMARRAY® Gastrointestinal Panel Mid is an automated qualitative multiplexed nucleic acid-based *in vitro* diagnostic test intended for use with BIOFIRE® FILMARRAY® Systems. The BIOFIRE FILMARRAY GI Panel Mid is capable of the simultaneous detection and identification of nucleic acids from multiple bacteria, viruses, and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following bacteria, parasites, and viruses are identified using the BIOFIRE FILMARRAY GI Panel Mid:

Bacteria	Viruses
Campylobacter (*C. jejuni/C. coli/ C. upsaliensis*)	Norovirus GI/GII
Clostridioides (Clostridium) difficile (toxin A/B)	
Salmonella	
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*	**Parasites**
*Shigella/*Enteroinvasive *E. coli* (EIEC)	*Cryptosporidium*
Vibrio (V. parahaemolyticus/V. vulnificus/ V. cholerae)	*Cyclospora cayetanensis*
Yersinia enterocolitica	*Giardia lamblia*

The BIOFIRE FILMARRAY GI Panel Mid is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness and results are meant to be used in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not included in the BIOFIRE FILMARRAY GI Panel Mid. The agent detected may not be the definite cause of the disease.

Concomitant culture is necessary for organism recovery and further typing of bacterial agents.

This device is not intended to monitor or guide treatment for *C. difficile* infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Yersinia enterocolitica* were established primarily with retrospective clinical specimens.

Performance characteristics for *Vibrio* (*V. parahaemolyticus, V. vulnificus,* and *Vibrio cholerae*) was established primarily using contrived clinical specimens.

Negative BIOFIRE FILMARRAY GI Panel Mid results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.

A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute gastroenteritis in the context of outbreaks.

Device Description:

The BIOFIRE® FILMARRAY® Gastrointestinal Panel Mid is designed to simultaneously identify 11 gastrointestinal pathogens from stool specimens collected in Cary Blair transport medium. The BIOFIRE FILMARRAY GI Panel Mid is compatible with BioFire's PCR-based in vitro diagnostic BIOFIRE® FILMARRAY® 2.0 and BIOFIRE® FILMARRAY® TORCH Systems for infectious disease testing. A panel-specific software module (i.e., BIOFIRE FILMARRAY GI Panel Mid pouch module software) is used to perform BIOFIRE FILMARRAY GI Panel Mid testing on these systems. Results from the BIOFIRE FILMARRAY GI Panel Mid test are available within about one hour.

A test is initiated by loading Hydration Solution into one port of the BIOFIRE pouch and a stool sample (in Cary Blair transport medium) mixed with the provided Sample Buffer into the other port of the BIOFIRE FILMARRAY GI Panel Mid pouch and placing it in a BIOFIRE System. The pouch contains all the reagents required for specimen testing and analysis in a freeze-dried format; the addition of Hydration Solution and Sample/Buffer Mix rehydrates the reagents. After the pouch is prepared, the BIOFIRE Software guides the user though the steps of placing the pouch into the instrument, scanning the pouch barcode, entering the sample identification, and initiating the run.

The BIOFIRE System contains a coordinated system of inflatable bladders and seal points, which act on the pouch to control the movement of liquid between the pouch blisters. When a bladder is inflated over a reagent blister, it forces liquid from the blister into connecting channels. Alternatively, when a seal is placed over a connecting channel it acts as a valve to open or close a channel. In addition, electronically-controlled pneumatic pistons are positioned over multiple plungers in order to deliver the rehydrated reagents into the blisters at the appropriate times. Two Peltier devices control heating and cooling of the pouch to drive the PCR reactions and the melt curve analysis.

Nucleic acid extraction occurs within the BIOFIRE pouch using mechanical and chemical lysis followed by purification using standard magnetic bead technology. After extracting and purifying nucleic acids from the unprocessed sample, the BIOFIRE system performs a nested multiplex PCR that is executed in two stages. During the first stage, the BIOFIRE System performs a single, large volume, highly multiplexed reverse transcription PCR (rt-PCR) reaction. The products from first stage PCR are then diluted and combined with a fresh, primer-free master mix and a fluorescent double stranded DNA binding dye (LC Green Plus®, BioFire Diagnostics). The solution is then distributed to each well of the array. Array wells contain sets of primers designed specifically to amplify sequences internal to the PCR products generated during the first stage PCR reaction. The 2nd stage PCR, or nested PCR, is performed in single plex fashion in each well of the array. At the end of the 2nd stage PCR, the array is interrogated by melt curve analysis for the detection of signature amplicons denoting the presence of specific targets. A digital camera placed in front of the 2nd stage PCR captures fluorescent images of the PCR reactions and software interprets the data.

The BIOFIRE Software automatically interprets the results of each DNA melt curve analysis and combines the data with the results of the internal pouch controls to provide a test result for each organism on the panel.

The BIOFIRE FILMARRAY GI Panel Mid is intended for use by trained medical and laboratory professionals in a laboratory setting or under the supervision of a trained laboratory professional.

Substantial Equivalence:

The BIOFIRE FILMARRAY GI Panel Mid is substantially equivalent to the BIOFIRE GI Panel (K242367), which was cleared on November 7, 2024, and determined to be a Class II device.

A comparison of the BIOFIRE FILMARRAY GI Panel Mid to the BIOFIRE GI Panel is provided in Table 1, differences are shown in blue text.

Table 1. Similarities and differences between the BIOFIRE FILMARRAY GI Panel Mid and the BIOFIRE GI Panel

Element	Predicate: BIOFIRE FILMARRAY GI Panel (K242367)	New Device: BIOFIRE FILMARRAY GI Panel Mid
Intended Use	The BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel is a qualitative multiplexed nucleic acid-based *in vitro* diagnostic test intended for use with BIOFIRE® FILMARRAY® Systems. The BIOFIRE GI Panel is capable of the simultaneous detection and identification of nucleic acids from multiple bacteria, viruses, and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following bacteria (including several diarrheagenic *E. coli/Shigella* pathotypes), parasites, and viruses are identified using the BIOFIRE FILMARRAY GI Panel Mid: · *Campylobacter (C. jejuni/C. coli/C. upsaliensis)* · *Clostridium difficile (C. difficile) toxin A/B* · *Plesiomonas shigelloides* · *Salmonella*	The BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel Mid is an automated qualitative multiplexed nucleic acid-based in vitro diagnostic test intended for use with BIOFIRE® FILMARRAY® Systems. The BIOFIRE FILMARRAY GI Panel Mid is capable of the simultaneous detection and identification of nucleic acids from multiple bacteria, viruses, and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following bacteria, parasites, and viruses are identified using the BIOFIRE FILMARRAY GI Panel Mid: ·*Campylobacter (C. jejuni/C. coli/C. upsaliensis)* · *Clostridioides (Clostridium) difficile (toxin A/B)* · *Vibrio* (*V. parahaemolyticus/V. vulnificus/ V. cholerae*)

Element	Predicate: BIOFIRE FILMARRAY GI Panel (K242367)	New Device: BIOFIRE FILMARRAY GI Panel Mid
	· *Vibrio* (*V. parahaemolyticus/V. vulnificus/ V. cholerae*), including specific identification of *Vibrio cholerae* · *Yersinia enterocolitica* · Enteroaggregative Escherichia coli (EAEC) · Enteropathogenic Escherichia coli (EPEC) · Enterotoxigenic Escherichia coli (ETEC) lt/st · Shiga-like toxin-producing *Escherichia coli* (STEC) stx1/stx2 (including specific identification of the E. coli O157 serogroup within STEC) · Shigella/ Enteroinvasive *Escherichia coli* (EIEC) · *Cryptosporidium* · *Cyclospora cayetanensis* · *Entamoeba histolytica* · *Giardia lamblia* (also known as G. intestinalis and G. duodenalis) · Adenovirus F 40/41 · Astrovirus · Norovirus GI/GII · Rotavirus A · Sapovirus (Genogroups I, II, IV, and V) The BIOFIRE GI Panel is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness and results are meant to be used in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not included in the BIOFIRE GI Panel. The agent detected may not be the definite cause of the disease. Concomitant culture is necessary for organism recovery and further typing of bacterial agents. This device is not intended to monitor or guide treatment for *C. difficile* infection. Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *E. coli* O157, *Plesiomonas shigelloides*, *Yersinia enterocolitica,* Astrovirus, and Rotavirus A were established primarily with retrospective clinical specimens. Performance characteristics for *Entamoeba histolytica,* and *Vibrio* (*V. parahaemolyticus, V. vulnificus,* and *Vibrio cholerae*) were	· *Yersinia enterocolitica* · Shiga-like toxin-producing *Escherichia coli* (STEC) stx1/stx2 · Shigella/ Enteroinvasive *Escherichia coli* (EIEC) · *Cryptosporidium* · *Cyclospora cayetanensis* · *Giardia lamblia* (also known as G. intestinalis and G. duodenalis) · Norovirus GI/GII The BIOFIRE FILMARRAY GI Panel Mid is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness and results are meant to be used in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not included in the BIOFIRE FILMARRAY GI Panel Mid. The agent detected may not be the definite cause of the disease. Concomitant culture is necessary for organism recovery and further typing of bacterial agents. This device is not intended to monitor or guide treatment for *C. difficile* infection. Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Yersinia enterocolitica* were established primarily with retrospective clinical specimens. Performance characteristics for *Vibrio* (*V. parahaemolyticus, V. vulnificus,* and *Vibrio cholerae*) was established primarily using contrived clinical specimens. Negative BIOFIRE FILMARRAY GI Panel Mid results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease. A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute gastroenteritis in the context of outbreaks.

Element	Predicate: BIOFIRE FILMARRAY GI Panel (K242367)	New Device: BIOFIRE FILMARRAY GI Panel Mid
	established primarily using contrived clinical specimens. Negative BIOFIRE GI Panel results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease. A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute gastroenteritis in the context of outbreaks.	
Analyte	DNA/RNA	Same
Specimen Types	Human stool sample collected in Cary Blair transport media.	Same
Technological Principles	Nested multiplex PCR followed by high resolution melting analysis to confirm the identity of amplified product.	Same
Instrumentation	BIOFIRE FILMARRAY 2.0 System or BIOFIRE FILMARRAY TORCH System	Same
Time to result	About 1 hour	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same
Sample Preparation Method	Sample Processing is automated in the BIOFIRE System.	Same
Reagent Storage	Reagents are stored at room temperature.	Same
Shelf-Life	12 months from Date of Manufacture	Same
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis.	Same
User Complexity	Moderate	Same

Summary of Performance Data:

The BIOFIRE FILMARRAY GI Panel Mid has an abbreviated panel menu compared to the original BIOFIRE FILMARRAY GI Panel, reporting only 11 of the original 22 analytes. The performance presented here was established during the original clinical and analytical evaluations for the BIOFIRE FILMARRAY GI Panel.

The performance data for the BIOFIRE FILMARRAY GI Panel Mid is summarized in the *BIOFIRE FILMARRAY GI Panel Mid Instructions for Use*. A summary of the BIOFIRE FILMARRAY GI Panel Mid performance data is also provided below.

Clinical Performance

Table 2 provides a summary of the performance of each analyte from the Prospective Clinical Evaluation performed for the BIOFIRE FILMARRAY GI Panel Mid.

Table 2. BIOFIRE FILMARRAY GI Panel Mid Performance in the Prospective Clinical Evaluation (May through September 2013)

BIOFIRE FILMARRAY GI Panel Mid Analyte	Sensitivity/PPA[a]			Specificity/NPA[a]		
	TP/(TP + FN)	%	95% CI	TN/(TN + FP)	%	95% CI
Bacteria						
Campylobacter (*C. jejuni/C. coli/C. upsaliensis*)	34/35[b]	97.1	85.1-99.9%	1497/1521[b]	98.4	97.7-99.0%
Clostridioides (Clostridium) difficile toxin A/B[a]	163/165[c]	98.8	95.7-99.9%	1350/1391[c]	97.1	96.0-97.9%
Salmonella	31/31	100	88.8-100%	1519/1525[d]	99.6	99.1-99.9%
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*	33/33	100	89.4-100%	1518/1523[e]	99.7	99.2-99.9%
Shigella/Enteroinvasive *E. coli* (EIEC)	47/49	95.9	86.0-99.5%	1505/1507	99.9	99.5-100%
Vibrio (*V. parahaemolyticus*/*V. vulnificus*/*V. cholerae*)	0/0	-	-	1554/1556[f]	99.9	99.5-100%
Yersinia enterocolitica	1/1	100	-	1555/1555	100	99.8-100%
Parasites						
Cryptosporidium	18/18	100	81.5-100%	1532/1538[g]	99.6	99.2-99.9%
Cyclospora cayetanensis	19/19	100	82.4-100%	1537/1537	100	99.8-100%
Giardia lamblia	20/20	100	83.2-100%	1529/1536[h]	99.5	99.1-99.8%
Viruses						
Norovirus GI/GII	52/55[q]	94.5	84.9-98.9%	1483/1501[i]	98.8	98.1-99.3%

[a] *C. difficile* performance is reported as positive percent agreement/negative percent agreement in contrast to the table headings. The performance measures of sensitivity and specificity only refer to those analytes for which the gold-standard bacterial culture was used as the reference method; *Campylobacter*, *Salmonella*, *Vibrio*, and *Yersinia enterocolitica*. Performance measures of positive percent agreement (PPA) and negative percent agreement (NPA) refer to all other analytes, for which PCR/sequencing assays were used as comparator methods.
[b] *Campylobacter jejuni* subsp. *doylei* was identified in the single false negative specimen using bi-directional sequence analysis. *Campylobacter* was detected in 19/24 false positive specimens using bi-directional sequence analysis.
[c] *C. difficile* was detected in 1/2 false negative specimens and 41/41 false positive specimens using bi-directional sequence analysis.
[d] *Salmonella* was detected in 6/6 false positive specimens using bi-directional sequence analysis.
[e] STEC was detected in 5/5 false positive specimens using bi-directional sequence analysis.
[f] *Vibrio* was detected in 2/2 false positive specimens using bi-directional sequence analysis.
[g] *Cryptosporidium* was detected in 6/6 false positive specimens using bi-directional sequence analysis.
[h] *G. lamblia* was detected in 4/7 false positive specimens using bi-directional sequence analysis. Two false positive results appear to be caused by cross-reactivity with *Bifidobacterium longum* and *Ruminococcus callidus*.
[i] The BIOFIRE FILMARRAY GI Panel Mid detected Norovirus in 1/3 false negative specimens when retested. Norovirus was detected in 1/2 remaining false negative specimens and 8/18 false positive specimens using bi-directional sequence analysis. Refer to Table 3 below for additional Norovirus GI/GII performance results.

Table 3. BIOFIRE FILMARRAY GI Panel Mid Norovirus GI/GII Performance in the Prospective Clinical Evaluation (April through July 2023)

BIOFIRE FILMARRAY GI Panel Mid Result	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	TP/(TP + FN)	%	95% CI	TN/(TN + FP)	%	95% CI
Norovirus GI/GII	34/35[a]	97.1	85.1-99.9%	808/837[a]	96.5	95.1-97.7%

[a] Norovirus was detected in the single FN specimen using bi-directional sequencing analysis. Norovirus was detected in 3/29 false positive specimens using bi-directional sequencing analysis. Twenty (20) of the remaining false positive results appear to have been caused by cross-reactivity; refer to the **Error! Reference source not found.** section in the Instructions for Use for the cross-reactive organisms.

Analytical Performance Characteristics

Bench performance (analytical) testing for the BIOFIRE FILMARRAY GI Panel Mid was designed to validate the performance of all analytes. Table 4 provides an overall summary of the analytical studies, their results, and conclusions.

Table 4. Summary of Bench Performance (Analytical) Testing for the BIOFIRE FILMARRAY GI Panel Mid

Study	Purpose	Results & Conclusions
Limit of Detection	The purpose of the LoD studies was to determine the limit of detection (LoD; lowest concentration of analyte that can be detected in at least 95% of replicates tested) for each of the	Confirmed LoD concentrations for bacteria range from 1.0E+02 CFU/mL up to 8.0E+04 cells/mL and for parasites range from 5.0E+01 to 5.0E+03 units/mL. For Norovirus GI/GII, the confirmed LoD

Study	Purpose	Results & Conclusions
	organisms detected by the BIOFIRE FILMARRAY GI Panel Mid. LoD was initially estimated and confirmed on the first generation BIOFIRE FILMARRAY system, with subsequent studies to verify that ≥95% detection could be achieved at the same LoD concentration on the next generation BIOFIRE 2.0 and BIOFIRE TORCH systems.	concentration is 1.0E+04 RNA copies/mL. LoD testing demonstrated that detection at the LoD concentration is equivalent between the BIOFIRE FILMARRAY (no longer in production), BIOFIRE 2.0, and BIOFIRE TORCH systems. The clinical data demonstrates that the analytically determined detection limit of the BIOFIRE FILMARRAY GI Panel Mid assays is appropriate for the levels of pathogens in clinical specimens (including co-infections or polymicrobial specimens).
Analytical Reactivity (Inclusivity)	The purpose of this study was to evaluate and define the analytical reactivity of BIOFIRE FILMARRAY GI Panel Mid. The study describes the diversity of panel analytes that are efficiently amplified and accurately detected, and also identifies known limitations on assay reactivity with specific subspecies, types, or variant sequences.	The reactivity of each of the panel assays was found to be consistent with the intent of the design and the assays will accurately identify the expected diversity of the analytes, with limitations noted in the Instructions for Use.
Reproducibility	Studies were performed to evaluate the within-lab (intermediate precision/repeatability) and between-lab (reproducibility) precision of analyte detection by the BIOFIRE FILMARRAY GI Panel Mid on the BIOFIRE FILMARRAY (no longer in production), BIOFIRE 2.0 and/or BIOFIRE TORCH systems. Each study evaluated multiple within-lab and between-lab operational variables including day, site, operator, instrument/system, and reagent lot. Precision for a qualitative test without an underlying numerical value is measured as percent (%) agreement between runs or % agreement with the expected result (Detected, Not Detected or N/A). The run-to-run precision was evaluated for negative samples as well as positive samples. The product design inputs require a minimum run-to-run agreement of 85%, with a desired run-to-run agreement of 95%.	For negative samples, the expected Not Detected (or N/A) results were reported for >95% of replicates tested on each system. For positive samples, detection agreement between runs was >95% at the 1× and/or 3×LoD concentrations for each analyte evaluated, with the exception of *Giardia lamblia* (84.3% and 91.7% at 1× LoD on the BIOFIRE FILMARRAY and TORCH Systems respectively; not tested on BIOFIRE 2.0). Subsequent investigation determined that the lower % agreement for *G. lamblia* was an artifact of instability of the analyte stock (experimental error) rather than imprecision of the test. Testing of *G. lamblia* was later repeated on the BIOFIRE FILMARRAY, BIOFIRE 2.0 and BIOFIRE TORCH Systems with samples prepared from a stable culture stock and run-to-run agreement for *G. lamblia* was 100% at the 1× LoD concentration. The combination of studies demonstrate that the precision of analyte detection by the BIOFIRE FILMARRAY GI Panel Mid is high; repeatable within-day and within-lab and reproducible within and between labs on BIOFIRE FILMARRAY, BIOFIRE 2.0, and BIOFIRE TORCH

Study	Purpose	Results & Conclusions
		systems. High reproducibility is achieved when samples are tested on multiple reagent lots by different operators, on different instruments/modules, at different sites, and on different days.
Exclusivity/Cross-Reactivity	The purpose of the study was to identify on-panel or off-panel organisms that might lead to inaccurate test results due to non-specific amplification or cross-reactivity with assay primers. On-panel organisms were tested to assess the potential for intra-panel cross-reactivity while off-panel organisms (those not intended to be detected by the panel) were tested to assess the potential for non-specific amplification of normal flora or other pathogens that may be present in stool samples.	Testing and sequence analysis identified a subset of BIOFIRE FILMARRAY GI Panel Mid assays that may non-specifically interact with and amplify homologous sequences in a few closely related or near-neighbor species as well as with a few unrelated organisms that might be found in stool samples. In most cases, the non-specific interaction is inefficient and very high levels of the cross-reacting organism must be present in the sample to obtain a false positive result. The product literature describes all known or predicted cross-reactivities.
Interference	The purpose of this study was to evaluate the potential for substances that may be present in a sample to interfere with the function of the pouch and/or the accuracy of test results. Testing also evaluated the potential for competitive inhibition or microbial interference on analyte detection near LoD.	Testing established that the BIOFIRE FILMARRAY GI Panel Mid is a highly robust multi-pathogen detection device that is resistant to interference from a variety of substances that could be present in stool samples, including blood and other biological substances, oral and topical treatments, and high levels of potentially competing microorganisms. Warnings and recommendations against the testing of stool prepared in off-label fixative-containing media is indicated in the Instructions for Use (fixative can negatively impact analyte detection) as well as risks associated with damage to nucleic acids that can be caused by bleach.

Conclusion:

The fundamental scientific technology, performance, and risk of the BIOFIRE FILMARRAY GI Panel Mid remain unchanged from the legally marketed BIOFIRE GI Panel. There is no change to the product itself, except for modified software that has been verified and validated to show no change in safety and effectiveness. Therefore, the BIOFIRE FILMARRAY GI Panel Mid performs as well as the predicate device.