November 7, 2024

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

Re: K242367
Trade/Device Name: BIOFIRE FILMARRAY Gastrointestinal (GI) Panel
Regulation Number: 21 CFR 866.3990
Regulation Name: Gastrointestinal Microorganism Multiplex Nucleic Acid-Based Assay
Regulatory Class: Class II
Product Code: PCH
Dated: August 8, 2024
Received: August 9, 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: 2024.11.07 14:56:19 -05'00'

Bryan Grabias
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

Indications for Use

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

510(k) Number *(if known)*
K242367

Device Name
BIOFIRE FILMARRAY Gastrointestinal (GI) Panel

Indications for Use *(Describe)*
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 GI Panel:

- Campylobacter (C. jejuni/C. coli/C. upsaliensis)
- Clostridium difficile (C. difficile) toxin A/B
- Plesiomonas shigelloides
- Salmonella
- 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 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.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel

Traditional 510(k) Summary
BioFire Diagnostics, LLC (BioFire)

Introduction:

The content of this Traditional 510(k) submission is limited to obtaining FDA clearance for the BIOFIRE FILMARRAY Gastrointestinal (GI) Panel (BIOFIRE GI Panel) (K230404) to update the instructions for use with additional clinical data obtained from a supplemental post market performance follow-up study that evaluated the Norovirus GI/GII assay compared to the most recent version of the US CDC Norovirus assay.

According to the requirements of 21 CFR 807.92, the following information 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
Telephone: 385-414-4985
Email: karli.plenert@biomerieux.com

Date Submitted:

August 08, 2024

Trade Name:

BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel (BIOFIRE GI Panel)

Classification Name:

21 CFR 866.3990 – Gastrointestinal microorganism multiplex nucleic acid-based assay

Predicate Device:

K230404 – BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel (BIOFIRE GI Panel)

Traditional 510(k) Overview:

Background

In May of 2023, an internal investigation was initiated to investigate an increase in false positive norovirus complaints from customers using the BIOFIRE GI Panel. The internal investigation of post marketing monitoring data concluded that the BIOFIRE GI Panel was performing within specification; however, a controlled Postmarket Performance Follow-up (PMPF) clinical study was initiated. This study used a more recent version of the US CDC Norovirus assay compared to the original performance evaluation. In this new study, the clinical specificity (NPA) for the Norovirus assay was found to be different from the original labeling claims.

Table 1. BIOFIRE GI Panel Norovirus GI/GII Assay Performance

Study	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	TP/(TP + FN)	%	95% CI	TN/(TN + FP)	%	95% CI
Original Clinical Study	52/55	94.5	84.9-98.9	1483/1501	98.8	98.1-99.3
PMPF (this submission)	34/35	97.1	85.1-99.9%	808/837	96.5	95.1-97.7%

As a result of the findings of the PMPF study, a recall event (FSCA 5812 – Event 93639) was initiated to inform customers of the risk of false positive norovirus results on the BIOFIRE GI Panel.

This submission, in response to FSCA 5812, consists of an update to the BIOFIRE GI Panel instructions for use (IFU) to provide the PMPF clinical study data and additional cross-reactivity identified via investigation of the PMPF study.

Updates made

Updates to the IFU include a new clinical summary section with the following two new tables:

Table 16. Demographic Summary for the BIOFIRE GI Panel Prospective Clinical Evaluation (April through July 2023)

Study Specimens	
Total Specimens	872
Sex	Number of Specimens (%)
Male	394 (45.2%)
Female	478 (54.8%)
Age Group	Number of Specimens (%)
< 1 year	70 (8.0%)
1-5 years	120 (13.8%)
6-12 years	64 (7.3%)
13-21 years	127 (14.6%)
22-64 years	283 (32.5%)
65+ years	208 (23.9%)
Status	Number of Specimens (%)
Outpatient	368 (42.2%)
Hospitalized	204 (23.4%)
Emergency	84 (9.6%)
Unknown	216 (24.8%)

Table 17. BIOFIRE GI Panel Norovirus GI/GII Performance in the Prospective Clinical Evaluation (April through July 2023)

BIOFIRE GI Panel 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. Many of the remaining false positive results appear to have been caused by cross-reactivity; refer to the Analytical Specificity (Cross-Reactivity and Exclusivity) section for cross-reactive organisms.

In addition, the following tables were updated and/or replaced in the Analytical Specificity (Cross-Reactivity and Exclusivity) section of the IFU to reflect additional testing prompted by the PMPF study (newly identified cross-reactivities noted in blue font in Table 43):

Table 43. Observed or Predicted Cross-Reactivity with Off-Panel Organisms

BIOFIRE GI Panel Test Result	Cross-Reactive Organism(s)
Entamoeba histolytica	*Entamoeba dispar*
Giardia lamblia	*Bifidobacterium spp* [a] *Ruminococcus spp* [a]
Enterotoxigenic *E.coli* (ETEC) *lt/st* [ETEC 2 assay]	*Citrobacter koseri* *Citrobacter sedlakii* *Hafnia alvei* [a] *Cedecea davisiae* [a]
Norovirus GI/GII [Noro 1 assay] [b]	*Prevotella* spp. (sequences from unculturable/uncharacterized species) [c] *Mediterraneibacter (Ruminococcus) gnavus* *Parabacteroides spp. (P. merdae, P. acidifaciens* [d]*, P. distasonis* [e]*)* *Anaerostipes hadrus (select sequences)* [f] *Enterobacter hormaechei (select sequences)* [g]
Salmonella	*E. coli* with variant type III secretion protein [h]
Vibrio (*V. parahaemolyticus/V. vulnificus/ V. cholerae*)	*Vibrio alginolyticus* *Vibrio fluvialis* [i] *Vibrio mimicus* [i] *Grimontia (*formerly *Vibrio) hollisae*
Yersinia enterocolitica	*Yersinia frederiksenii*[a,j] *Yersinia kristensenii* [j]

[a] Cross-reactivity was not observed when tested at high concentration (1.5×10^9 cells/mL). However, cross-reactivity was suspected or confirmed in clinical specimens and/or the potential for cross-reactivity is supported by *in silico* predictions.

[b] Cross-reactivity was identified by post-market investigation of suspected false positive Norovirus GI/GII results in clinical specimens. Cross-reactivity with the species listed was confirmed by analytical testing at high concentration (>$2.4x10^8$ cells/mL) and/or is supported by sequence analysis.

[c] Cross-reactive sequences are inconsistent with other *Prevotella* sequence data, suggesting non-specific interaction with atypical or uncharacterized species and/or sequences.

[d] *P. acidifaciens* was not tested but was determined by sequence analysis to have a similar risk of cross-reactivity as *P. merdae*.

[e] Norovirus GI/GII Not Detected was reported when *P. distasonis* was tested at high concentration ($3.1x10^9$ cells/mL). However, non-specific amplification products with Tm values close to the assay specific Tm range have been observed and the potential for false positive Norovirus GI/GII test results exists.

[f] The risk of false positive Norovirus GI/GII results due to cross-reactivity with *A. hadrus* is associated with only a subset of *A. hadrus* RefSeq genome sequences (<35% as of June 2024).

[g] The risk of false positive Norovirus GI/GII results due to cross-reactivity with *E. hormaechei* is associated with only a subset of *E. hormaechei* RefSeq genome sequences (<25% as of June 2024).

[h] Cross-reactivity resulting in false positive *Salmonell*a results has not been observed in analytical or clinical testing. However, non-specific amplification products with Tm values close to the assay specific Tm range have been observed and the potential for false positive *Salmonella* test results exists.

[i] Detected at concentrations near the *Vibrio* assay LoD.

[j] *Y. kristensenii* and *Y. fredericksenii* are difficult to distinguish from *Y. enterocolitica* by standard laboratory methods.

Table 44. Off-Panel Organisms Tested or Evaluated by in silico Analysis for BIOFIRE GI Panel Analytical Specificity

Species with cross-reactivity observed in analytical testing are in bold font. On-panel species were also tested at high concentration (not shown).

BACTERIA				
Tested				
Abiotrophia defectivia	*Campylobacter lari*	Diffusely adherent *E.coli*	*Lactobacillus reuteri*	*Ruminococcus flavefaciens* [b]
Acinetobacter baumannii	*Campylobacter mucosalis*	*Escherichia blattae*	*Lactococcus lactis*	*Selenomonas ruminantium*
Acinetobacter lwoffii	*Campylobacter rectus*	*Escherichia fergusonii*	*Leminorella grimontii*	*Serratia liquefaciens*
Aeromonas hydrophila	*Campylobacter showae*	*Escherichia hermannii*	*Listeria monocytogenes*	*Serratia marcescens*
Alcaligenes faecalis	*Campylobacter sputorum*	*Escherichia vulneris*	***Mediterraneibacter (Ruminococcus) gnavus***	*Shewanella algae*
Anaerococcus tetradius	*Campylobacter ureolyticus*	*Edwardsiella tarda*	*Megamonas hypermegale*	*Staphylococcus aureus*
Anaerostipes hadrus [a,d]	*Cedecea davisae* [c]	*Egglerthella lenta*	*Megasphaeara elsdenii*	*Staphylococcus epidermidis*
Arcobacter butzleri	*Chlamydia trachomatis*	*Enterobacter cloacae*	*Methanobrevibacter smithii*	*Stenotrophomonas maltophilia*
Arcobacter cryaerophilus	*Citrobacter amalonaticus*	***Enterobacter hormaechei*** [d,e]	*Morganella morganii*	*Streptococcus agalactiae*
Bacillus cereus	*Citrobacter freundii*	*Enterococcus faecalis*	*Parabacteroides distasonis* [f]	*Streptococcus intermedius*
Bacteroides fragilis	***Citrobacter koseri*** [d]	*Enterococcus faecium*	***Parabacteroides merdae*** [g]	*Streptococcus pyogenes*
Bacteroides thetaiotaomicron	***Citrobacter sedlakii***	*Eubacterium cylindroides*	*Peptoniphilus asaccharolyticus*	*Streptococcus salivarius*
Bacteroides vulgatus	*Clostridium acetobutylicum*	*Eubacterium rectale*	*Peptostreptococcus anaerobius*	*Trabulsiella guamensis*
Bifidobacterium adolescentis [b]	*Clostridium botulinum*	*Faecalibacterium prausnitzii*	*Photobacterium damselae*	*Veillonella parvula*
Bifidobacterium bifidum [b]	*Clostridium difficile* non-toxigenic [d]	*Fusobacterium varium*	*Porphyromonas asaccharolytica*	***Vibrio alginolyticus***
Bifidobacterium longum [b]	*Clostridium histolyticum*	*Gardnerella vaginalis*	*Prevotella bivia* [h]	***Vibrio fluvialis***
Bifidobacterium pseudocatenulatum	*Clostridium methylpentosum*	*Gemella morbillorum*	*Prevotella copri* [h]	***Vibrio mimicus***
Blautia (Ruminococcus) obeum	*Clostridium novyi*	***Grimontia (Vibrio) hollisae***	*Prevotella intermedia* [h]	*Yersinia bercovieri*
Blautia wexlerae	*Clostridium perfringens*	*Haemophilus influenzae*	*Prevotella histicola* [h]	*Yersinia frederiksenii* [i]
Campylobacter concisus	*Clostridium ramosum*	*Hafnia alvei* [c]	*Prevotella melaninogenica* [h]	*Yersinia intermedia*
Campylobacter curvus	*Clostridium septicum*	*Helicobacter fennelliae*	*Proteus mirabilis*	***Yersinia kristensenii***
Campylobacter fetus	*Clostridium sordellii*	*Helicobacter pylori*	*Proteus penneri*	*Yersinia mollaretii*
Campylobacter gracilis	*Clostridium tetani*	*Klebsiella* (*Enterobacter*) *aerogenes*	*Proteus vulgaris*	*Yersinia pseudotuberculosis*
Campylobacter helveticus	*Collinsella aerofaciens*	*Klebsiella oxytoca*	*Providencia alcalifaciens*	*Yersinia rohdei*
Campylobacter hominis	*Corynebacterium genitalium*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*	
Campylobacter hyointestinalis	*Desulfovibrio piger*	*Lactobacillus acidophilus*	*Ruminococcus bromii* [b]	

PROTOZOA/PARASITES				FUNGI
Tested		***In silico* Analysis Only**		**Tested**
Babesia microti	*Entamoeba gingivalis*	*Ancylostoma duodenale*	*Entamoeba hartmanni*	*Aspergillus fumigatus*
Blastocystis hominis	*Entamoeba moshkovskii*	*Ascaris lumbricoides*	*Entamoeba polecki*	*Candida albicans*
Conidiobolus lachnodes	*Giardia muris*	*Balantidium coli*	*Enterobius vermicularis*	*Candida catenulate*
Conidiobolus lobatus	*Pentatrichomonas hominis*	*Chilomastix mesnili*	*Enteromonas hominis*	*Penicillium marneffei*
Encephalitozoon hellem	*Schistosoma mansoni*	*Dientamoeba fragilis*	*Isospora belli*	*Saccharomyces boulardi*
Encephalitozoon intestinalis	*Toxoplasma gondii*	*Endolimax nana*	*Necator americanus*	*Saccharomyces cerevisiae*
Entamoeba dispar	*Trichomonas tenax*	*Entamoeba coli*		

VIRUSES				
Tested				***In silico* Analysis Only**
Adenovirus A:31	Adenovirus E:4a	Coronavirus 229E	Enterovirus 68	Adenovirus G52
Adenovirus B:34	Astrovirus variant VA1	Coxsackievirus B3	Hepatitis A	Norovirus GIV
Adenovirus C:2	Astrovirus variant MLB	Cytomegalovirus (CMV)	Herpes Simplex Type 2	Rotavirus B
Adenovirus D:37	Bocavirus Type 1	Echovirus 6	Rhinovirus 1A	Rotavirus C

[a] *Anerostipes hadrus* isolates (DSM 23942 and ATCC 29173) were tested at >2.4×10^8 cells/mL. Norovirus GI/GII Detected results were only observed with DSM 23942. The ATCC 29173 isolate does not carry the cross-reactive sequence.

[b] Though not observed in analytical testing, cross-reactivity of the *Giardia lamblia* assay with one or more *Bifidobacterium* and *Ruminococcus* species was observed in the clinical evaluation (see Table 43).

[c] Though not observed in analytical testing, possible cross-reactivity of the ETEC 2 assay with *Hafnia alvei* and *Cedecea davisiae* was observed in the clinical evaluation or predicted by in silico analysis (see Table 43).

[d] Two isolates of this species were tested for analytical specificity.

[e] *Enterobacter hormaechei* isolates (ATCC BAA-2082 and ATCC 49162) were tested at >5.0×10^8 cells/mL. Norovirus GI/GII Detected results were only observed with ATCC 49162. The ATCC BAA-2082 sequence is not predicted to be cross-reactive by in silico analysis.

[f] Though not observed in analytical testing, cross-reactivity of the Noro 1 assay with a sequence identified in roughly half (~50%) of the *P. distasonis* genomes evaluated could occur at high concentration.

[g] A similar risk of cross-reactivity was identified with sequences annotated as *Parabacteroides* sp. and *P. acidifaciens*.

[h] No cross-reactivity with high concentrations of various *Prevotella* species (commensal and pathogenic) was observed in analytical testing, but the potential for weak cross-reactivity between the Noro 1 assay and unique variant sequences annotated as unculturable *Prevotella* sp. has been identified via investigation of discrepant results in clinical specimens.

[i] Though not observed in analytical testing, in silico analysis indicates that, similar to *Y. kristensenii*, cross-reactivity between the *Yersinia entercolitica* assay and *Yersinia fredericksenii* is possible at high concentrations (see Table 43).

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 GI Panel:

- *Campylobacter* (*C. jejuni/C. coli/C. upsaliensis*)
- *Clostridiodes (Clostridium) difficile* (*C. difficile*) toxin A/B
- *Plesiomonas shigelloides*
- *Salmonella*
- *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 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.

Device Description:

The BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel is designed to simultaneously identify 22 gastrointestinal pathogens from stool specimens collected in Cary Blair transport medium. The BIOFIRE GI Panel 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 GI Panel pouch module software) is used to perform BIOFIRE GI Panel testing on these systems. Results from the BIOFIRE GI Panel 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 GI 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.

Device Comparison:

Table 2 outlines the similarities and differences between the two BIOFIRE GI Panels.

Table 2 *Comparison of the BioFire FilmArray GI Panel with current BioFire GI Panel.*

Element	Modified Device: BIOFIRE FILMARRAY GI Panel	Predicate: BIOFIRE FILMARRAY GI Panel (K230404)
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.	Same
Organisms Detected	*Campylobacter (C. jejuni/C. coli/C. upsaliensis)* *· Clostridium difficile (C. difficile) toxin A/B* *· Plesiomonas shigelloides* *· Salmonella* *· 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)*	Same
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	Single instrument BIOFIRE 2.0 System, or BIOFIRE Torch System	Same

Element	Modified Device: BIOFIRE FILMARRAY GI Panel	Predicate: BIOFIRE FILMARRAY GI Panel (K230404)
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

Conclusion:

The change in clinical and analytical specificity to the Norovirus GI/GII result and updates to the labeling (instructions for use) do not affect the fundamental scientific technology, intended use, or inherent risk of the BIOFIRE GI Panel and supports a substantial equivalence decision.