April 6, 2023

BioFire Diagnostics, LLC
Kevin Bourzac
Vice President, Regulatory and Clinical Affairs
515 Colorow Drive
Salt Lake City, Utah 84108

Re: K230404
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

Dear Kevin Bourzac:

The Food and Drug Administration (FDA) is sending this letter to notify you of an administrative change related to your previous substantial equivalence (SE) determination letter dated March 16, 2023. Specifically, FDA is updating this SE Letter to correct a typo in the trade name (i.e., missing the last "A" in FILMARRAY) as an administrative correction.

Please note that the 510(k) submission was not re-reviewed. For questions regarding this letter please contact Noel Gerald OHT7: Office of In Vitro Diagnostics, by email (Noel.Gerald@fda.hhs.gov) or phone (301-796-4695).

Sincerely,

Noel J. Gerald -S

Noel J. Gerald, Ph.D.
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

BioFire Diagnostics, LLC
Kevin Bourzac
Vice President, Regulatory and Clinical Affairs
515 Colorow Drive
Salt Lake City, Utah 84108

March 16, 2023

Re: K230404
Trade/Device Name: BIOFIRE FILMARRY 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: February 14, 2023
Received: February 15, 2023

Dear Kevin Bourzac:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 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,

Noel J. Gerald -S

Noel J. Gerald, Ph.D.
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K230404

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)
- 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.

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

BIOFIRE FILMARRAY Gastrointestinal (GI) Panel

Introduction:

Purpose

The content of this Special 510(k) submission is limited to obtaining FDA clearance for the BIOFIRE FILMARRAY Gastrointestinal (GI) Panel (BIOFIRE GI Panel) (K160459) with a software update to mitigate the erroneous interpretation of a non-specific Crypt 2 assay product.

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.

Background

An increased number of reports of false positive *Cryptosporidium* results were received from customers using the BIOFIRE GI Panel. The BIOFIRE GI Panel contains two assays for the detection of *Cryptosporidium*: Crypt 1 and Crypt 2. The organism is reported as "Detected" if one or both of the assays are positive.

An internal investigation was initiated and revealed that a subset of the false positive *Cryptosporidium* results appeared to be caused by a previously unknown non-specific product that was being generated by the Crypt 2 assay.

This amplification product was being incorrectly interpreted as "positive" by the software, leading to a *Cryptosporidium* Detected result. As of the date of this submission, this rare, non-specific product has been primarily observed in a small fraction of patient samples and there has been no correlation to specific reagent lots, instruments, or Cary Blair media.

Software Update

A software update was developed to mitigate the erroneous interpretation of the non-specific Crypt 2 assay product.

This software change does not modify any performance claims.

The software change requires a minor IFU update to remove one row from the "*Cryptosporidium* Inclusivity Results" table (Table 31), which currently indicates a *Cryptosporidium canis* detection below Limit of Detection (note: *Cryptosporidium canis* will still be detected, but not below the claimed Limit of Detection), in addition to updated footnotes.

This change does not affect the intended use, design, manufacture, or labeling of the BIOFIRE GI Panel reagent pouch, reagent kit, or the Quick Guide. Only the BIOFIRE GI Panel pouch module software and instructions for use (IFU) would be updated. The pouch module version number is considered a minor revision update from version 2.0.1 to version 2.0.3.

Submitted by:
BioFire Diagnostics, LLC (BioFire)
515 Colorow Drive
Salt Lake City, UT 84108

Contact:
Kevin Bourzac, Ph.D.
Telephone: 801-736-6354, ext. 1358
Fax: 801-588-0507
Email: kevin.bourzac@biomerieux.com

Date Submitted:
February 14, 2023

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:
K160459 – FilmArray Gastrointestinal (GI) Panel

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 1 outlines the similarities and differences between the two BIOFIRE GI Panels.

Element	Modified Device: BIOFIRE FILMARRAY GI Panel (with software update)	Predicate: BIOFIRE FILMARRAY GI Panel (K160459)
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 (minor branding update)

Element	Modified Device: BIOFIRE FILMARRAY GI Panel (with software update)	Predicate: BIOFIRE FILMARRAY GI Panel (K160459)
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
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

Element	Modified Device: BIOFIRE FILMARRAY GI Panel (with software update)	Predicate: BIOFIRE FILMARRAY GI Panel (K160459)
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	Low/Moderate	Same

Conclusion:
The minor software modification and update to the labeling (instructions for use) do not affect the fundamental scientific technology, performance claims, or risk of the BIOFIRE GI Panel. Therefore, the modified BIOFIRE GI Panel performs as well as the predicate device.