BioFire Defense, LLC
David Rabiger
Associate Director of Regulatory, Quality, and Clinical Affairs
79 W 4500 S, Suite 14
Salt Lake City, Utah 84107

Re: K220870
Trade/Device Name: BioFire Global Fever Panel, BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel
Regulation Number: 21 CFR 866.3966
Regulation Name: Device To Detect And Identify Selected Microbial Agents That Cause Acute Febrile Illness
Regulatory Class: Class II
Product Code: QMV, PMN
Dated: March 24, 2022
Received: March 25, 2022

Dear David Rabiger:

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,

for

Noel Gerald
Branch Chief
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)*
K220870

Device Name
BioFire® Global Fever Panel

Indications for Use *(Describe)*
The BioFire® Global Fever Panel is a qualitative, multiplexed, nucleic acid-based in vitro diagnostic test intended for use with BioFire® FilmArray® 2.0 and BioFire® FilmArray® Torch Systems. The BioFire Global Fever Panel detects and identifies selected bacterial, viral, and protozoan nucleic acids directly from EDTA whole blood collected from individuals with signs and/or symptoms of acute febrile illness or recent acute febrile illness and known or suspected exposure to the following target pathogens: chikungunya virus, dengue virus (serotypes 1, 2, 3 and 4), Leptospira spp., and Plasmodium spp. (including species differentiation of Plasmodium falciparum and Plasmodium vivax/ovale). Evaluation for more common causes of acute febrile illness (e.g., infections of the upper and lower respiratory tract or gastroenteritis, as well as non-infectious causes) should be considered prior to evaluation with this panel. Results are meant to be used in conjunction with other clinical, epidemiologic, and laboratory data, in accordance with the guidelines provided by the relevant public health authorities.

Positive results do not rule out co-infections with pathogens not included on the BioFire Global Fever Panel. Not all pathogens that cause acute febrile illness are detected by this test, and negative results do not rule out the presence of other infections. In the United States, patient travel history and consultation of the CDC Yellow Book should be considered prior to use of the BioFire Global Fever Panel as some pathogens are more common in certain geographical locations.

For In Vitro Diagnostic Use.

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.

510(k) Summary

I. Submitter

BioFire Defense, LLC
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Phone: (801) 262-3592
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Contact Person: David Rabiger, Ph.D.
Date Prepared: 2022-03-24

II. Device

Name of Device: BioFire® Global Fever Panel
Common or Usual Name: Same
Regulation: 21 CFR 866.3966
Classification Name: Device to detect and identify selected microbial agents that cause acute febrile illness
Product Code: QMV
Regulatory Class: Class II (Special Controls)
Panel: Microbiology – 83

Name of Device: BioFire® SHIELD™ Control Kit for the BioFire® Global Fever Panel
Common or Usual Name: Same
Regulation: 21 CFR 866.3920
Classification Name: Assayed quality control material for clinical microbiology assays
Product Code: PMN
Regulatory Class: Class II (Special Controls)
Panel: Microbiology – 83

III. Predicate Devices

BioFire® Global Fever Panel (BioFire Defense, LLC) [DEN200043]
This predicate has not been subject to a design-related recall.

BioFire® SHIELD™ Control Kit for the BioFire® Global Fever Panel (BioFire Defense, LLC) [K202382]
This predicate has not been subject to a design-related recall.

IV. Device Description

The BioFire Global Fever Panel is a multiplexed nucleic acid-based test for the detection and identification of six pathogens which cause acute febrile illness (AFI) from whole blood specimens on BioFire FilmArray systems. The BioFire Global Fever Panel detects and identifies the following pathogens: chikungunya virus, dengue virus, *Leptospira* spp., and *Plasmodium* spp., including species differentiation between *P. falciparum* and *P. vivax/ovale*. The BioFire Global Fever Panel was originally described and was granted De Novo classification in DEN200043.

The BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel is an assayed quality control intended for monitoring the diagnostic performance of the BioFire Global Fever Panel. The Control Kit consists of Positive and Negative External Controls in a FilmArray Control Injection Vial format. The Positive External Control contains external assayed quality control material consisting of a set of non-infectious DNA segments dried on the filter of a FilmArray Control Injection Vial and detected by the Global Fever Panel. The Negative External Control contains no DNA and is also provided in the Control Injection Vial format. Analysis of the controls is carried out by specific pouch modules that are included in the BioFire Global Fever Panel Pouch Module Package. The BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel was fully described and cleared in K202382.

The purpose of this submission is to add BioFire FilmArray Torch as an additional instrument system for use with the BioFire Global Fever Panel and BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel, which were previously marketed for use with BioFire FilmArray 2.0 Systems. The FilmArray Torch is a modular configuration of the FilmArray 2.0 that minimizes instrument footprint by stacking up to twelve individual FilmArray Torch Modules on top of a single FilmArray Torch System Base. This 510(k) request describes modifications to the BioFire Global Fever Panel Pouch Module Package software and validation efforts to support adding FilmArray Torch Systems to the intended use of both the BioFire Global Fever Panel and associated BIOFIRE SHIELD Control Kit.

V. Intended Use

BioFire Global Fever Panel Intended Use:

The BioFire® Global Fever Panel is a qualitative, multiplexed, nucleic acid-based in vitro diagnostic test intended for use with BioFire® FilmArray® 2.0 and BioFire® FilmArray® Torch Systems. The BioFire Global Fever Panel detects and identifies selected bacterial, viral, and protozoan nucleic acids directly from EDTA whole blood collected from individuals with signs and/or symptoms of acute febrile illness or recent acute febrile illness and known or suspected exposure to the following target pathogens: chikungunya virus, dengue virus (serotypes 1, 2, 3 and 4), *Leptospira* spp., and *Plasmodium* spp. (including species differentiation of *Plasmodium falciparum* and *Plasmodium vivax/ovale*). Evaluation for more common causes of acute febrile illness (e.g., infections of the upper and lower respiratory tract or gastroenteritis, as well as non-infectious causes) should be considered prior to evaluation with this panel. Results are meant to be used in conjunction with other clinical, epidemiologic, and laboratory data, in accordance with the guidelines provided by the relevant public health authorities.

Positive results do not rule out co-infections with pathogens not included on the BioFire Global Fever Panel. Not all pathogens that cause acute febrile illness are detected by this test, and negative results do not rule out the presence of other infections. In the United States, patient travel history and consultation of the CDC Yellow Book should be considered prior to use of the BioFire Global Fever Panel as some pathogens are more common in certain geographical locations.

For In Vitro Diagnostic Use.

BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel Intended Use:

The BIOFIRE® SHIELD™ Control Kit for the BioFire® Global Fever Panel contains Positive and Negative External Controls intended for use as assayed quality controls to monitor the performance of in vitro diagnostic laboratory nucleic acid testing procedures for the qualitative detection of chikungunya virus, dengue virus (serotypes 1, 2, 3, and 4), *Leptospira* spp., and *Plasmodium* spp. (including species differentiation of *Plasmodium falciparum* and *Plasmodium vivax/ovale*) when using the BioFire® Global Fever Panel on BioFire® FilmArray® 2.0 and BioFire® FilmArray® Torch Systems. The BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel is designed for and intended to be used solely with the BioFire Global Fever Panel. This product does not replace manufacturer internal controls provided as part of the BioFire Global Fever Panel device.

Both the Positive and Negative External Controls are provided in a FilmArray Control Injection Vial format. The Positive Control Injection Vial contains dried synthetic DNA segments in buffer and stabilizer to assess the presence of each individual assay on the BioFire Global Fever Panel. The Negative Control Injection Vial contains no DNA and is non-reactive with the BioFire Global Fever Panel assays.

VI. Substantial Equivalence

The purpose of this 510(k) submission is to add BioFire FilmArray Torch systems to the intended use of both the BioFire Global Fever Panel and the BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel. No changes have been made to the BioFire Global Fever Panel or BIOFIRE SHIELD Control Kit themselves. Only minor modifications to the BioFire Global Fever Panel Pouch Module Package have been made to add compatibility with BioFire FilmArray Torch systems.

The BioFire Global Fever Panel for use with BioFire FilmArray Torch (BioFire Global Fever Panel v2.1) is substantially equivalent to the BioFire Global Fever Panel v2.0. Table 1 compares the BioFire Global Fever Panel v2.1 to the previously granted BioFire Global Fever Panel v2.0.

Table 1. BioFire Global Fever Panel Predicate Comparison

Element	Subject Device: BioFire Global Fever Panel	Predicate: BioFire Global Fever Panel [DEN200043]
Specimen Type	Whole blood (collected in EDTA tube)	Same as subject device
Intended Use	Individuals with signs and/or symptoms of acute febrile illness and known or suspected exposure to pathogens on the panel	Same as subject device
Pathogens Detected	Chikungunya virus, dengue virus (serotypes 1, 2, 3, and 4), *Leptospira* spp., *Plasmodium* spp. (including species differentiation of *P. falciparum* and *P. vivax/ovale*.	Same as subject device
Analyte	RNA/DNA	Same as subject device
Technological Principles	Highly multiplexed, nested, nucleic acid amplification test with melt analysis	Same as subject device
Instrumentation	BioFire FilmArray 2.0 or BioFire FilmArray Torch systems	BioFire FilmArray 2.0 systems
Time to Result	~1 hour	Same as subject device
Reagent Storage	Room temperature	Same as subject device
Test Interpretation	Automated test interpretation and report generation; user cannot access raw data	Same as subject device
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis	Same as subject device
Assayed External Controls	BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel (Part No. DFA2-ASY-0006)	Same as subject device
User Complexity	Moderate	Same as subject device

The BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel for use with BioFire FilmArray Torch is substantially equivalent to the previously cleared BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel. Table 2 outlines the similarities and differences between the two control kits.

Table 2. BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel Predicate Comparison

Element	Subject Device: BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel	Predicate: BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel [K202382]
Intended Use	Positive and negative external assayed quality controls to monitor assay performance in the BioFire Global Fever Panel	Same as subject device
Physical Format	External control material dried on Control Injection Vial filter	Same as subject device
Composition	Tm-shifted synthetic DNA (positive control only)	Same as subject device
Targets Monitored	Chikungunya virus, dengue virus (serotypes 1, 2, 3, and 4), *Leptospira* spp., and *Plasmodium* spp. (including species differentiation of *P. falciparum* and *P. vivax/ovale*.	Same as subject device
Instrumentation	BioFire Global Fever Panel run on BioFire FilmArray 2.0 or BioFire FilmArray Torch systems	BioFire Global Fever Panel run on BioFire FilmArray 2.0 systems
Test Interpretation	Automated test interpretation and report generation; user cannot access raw data	Same as subject device
Reagent Storage	Room temperature	Same as subject device

VII. Summary of Performance Data

Performance of the BioFire Global Fever Panel on BioFire FilmArray Torch Systems

Negative samples containing no analyte and contrived samples containing representative pathogens on the BioFire Global Fever Panel at concentrations near the limit of detection (LoD) were tested in parallel on three BioFire FilmArray 2.0 systems and three BioFire FilmArray Torch systems. Testing was performed over five days by two operators per system for a total of 90 replicates per sample per platform. The performance of the BioFire Global Fever Panel on the BioFire FilmArray Torch platform was similar to performance on the BioFire FilmArray 2.0 platform. Overall agreement with expected results for the BioFire Global Fever Panel on the BioFire FilmArray Torch platform was 98.9% as compared to 99.4% on the BioFire FilmArray 2.0 platform. Detection rates and percent agreement between observed and expected test results are shown in Table 3.

Table 3. Reproducibility of the BioFire Global Fever Panel on BioFire FilmArray Platforms

Analyte (Source / ID)		Concentration Tested (copies/mL)	Expected Result	Detection Rate (n/N) % Agreement with Expected Result							
				FilmArray 2.0 Platform				FilmArray Torch Platform			
				System 1	System 2	System 3	All FA 2.0 Systems [95% CI]	System 1	System 2	System 3	All FA Torch Systems [95% CI]
Leptospira interrogans* serovar *icterohaemorrhagiae (ATTC / 23581)		Moderate Positive 3×LoD (1.0E+03)	Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
		Low Positive 1×LoD (3.4E+02)	Detected	29/30 96.7%	29/30 96.7%	28/30 93.3%	**86/90 95.6%** [89.1-98.3%]	29/30 96.7%	28/30 93.3%	28/30 93.3%	**85/90 94.4%** [87.6-97.6%]
		Negative (No Analyte)	Not Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
Dengue virus DENV-2 New Guinea C (Zeptometrix / 0810089CF)		Moderate Positive 3×LoD (1.0E+03)	Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
		Low Positive 1×LoD (3.4E+02)	Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	29/30 96.7%	30/30 100%	**89/90 98.9%** [94.0-99.8%]
		Negative (No Analyte)	Not Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	29/30 96.7%	**89/90 98.9%** [94.0-99.8%]
Plasmodium falciparum IPC 4884 (BEI / MRA-1238)	***Plasmodium* spp. Detection Results**	Moderate Positive 3×LoD (5.4E+02)	Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
		Low Positive 1×LoD (1.8E+02)	Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
		Negative (No Analyte)	Not Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
	***Plasmodium falciparum* Detection Results**	Moderate Positive 3×LoD (5.4E+02)	Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	29/30 96.7%	30/30 100%	**89/90 98.9%** [94.0-99.8%]
		Low Positive 1×LoD (1.8E+02)	Detected	30/30 100%	28/30 93.3%	29/30 96.7%	**87/90 96.7%** [90.7-98.9%]	30/30 100%	28/30 93.3%	28/30 93.3%	**86/90 95.6%** [89.1-98.3%]
		Negative (No Analyte)	Not Detected	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]	30/30 100%	30/30 100%	30/30 100%	**90/90 100%** [95.9-100%]
Overall Agreement with Expected Result		**All Concentrations**	**All Results**	**1073/1080 99.4%** [98.7-99.7%]				**1068/1080 98.9%** [98.1-99.4%]			

Abbreviations: FA – FilmArray; 95% CI – 95% Confidence Interval

Performance of the BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel on BioFire FilmArray Torch Systems

Reproducibility of the BIOFIRE SHIELD Control Kit on the BioFire FilmArray Torch platform was evaluated by testing Positive External Controls and Negative External Controls on three BioFire FilmArray Torch systems over five days by two users per system for a total of 135 replicates for each control type. Overall agreement with the expected results was 99.6%. Results are summarized in Table 4.

Table 4. Reproducibility of the BIOFIRE SHIELD Control Kit on the BioFire FilmArray Torch Platform

SHIELD Control Type	Expected Result	Observed/Expected (Percent Agreement)			
		Torch System 1	Torch System 2	Torch System 3	Overall [95% Confidence Interval]
Positive	Passed	45/45 (100%)	45/45 (100%)	45/45 (100%)	**135/135 (100%)** [97.2-100%]
Negative	Passed	44/45 (97.8%)	45/45 (100%)	45/45 (100%)	**134/135 (99.3%)** [95.9-99.9%]
Overall Agreement with Expected Result		**269/270 (99.6%)** [97.9-99.9%]			