November 20, 2020

BioFire Defense, LLC
Cynthia Phillips
VP of Regulatory, Quality, and Clinical Affairs
79 West 4500 South, Suite 14
Salt Lake City, Utah 84107

Re: K202382
Trade/Device Name: FilmArray Global Fever Panel External Control Kit
Regulation Number: 21 CFR 866.3920
Regulation Name: Assayed quality control material for clinical microbiology assays
Regulatory Class: Class II
Product Code: PMN
Dated: August 19, 2020
Received: August 20, 2020

Dear Cynthia Phillips:

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,

Kristian Roth, Ph.D.
Branch Chief
Bacterial Respiratory and Medical Counter Measures
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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)*
K202382

Device Name
FilmArray Global Fever Panel External Control Kit

Indications for Use *(Describe)*
The FilmArray® Global Fever Panel External Control Kit 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 FilmArray® Global Fever Panel targets on FilmArray® 2.0 systems. The Global Fever Panel External Control Kit is designed for and intended to be used solely with the FilmArray Global Fever Panel. This product does not replace manufacturer internal controls provided as part of the 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 FilmArray Global Fever Panel. The Negative Control Injection Vial contains no DNA, and is non-reactive with the Global Fever Panel assays.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary

510(k) Number:

Purpose for submission: New product

Applicant Information:

Applicant:	BioFire Defense, LLC
Address:	79 West 4500 South, Suite 14 Salt Lake City, Utah 84107
Contact Person:	Cynthia Phillips, VP of Regulatory, Quality, and Clinical Affairs
Phone:	801-262-3592 extension 1370
Fax:	801-447-6907
Email Address:	cynthia.phillips@biofiredefense.com

Preparation Date: August 19, 2020

Device

Device Trade Name:	FilmArray® Global Fever Panel External Control Kit
Device Common Name:	Quality Control Material for Microbiology Assays
Device Type:	Assayed quality control material for clinical microbiology assays
Class:	Class II (Special Controls)
Regulation:	21 CFR 866.3920
Panel:	Microbiology - 83
Product code:	PMN

Predicate Device

FilmArray Warrior Control Panel M290 (K163522)

Device Description

The FilmArray Global Fever Panel External Control Kit contains Positive and Negative External Controls. The Positive External Control has been optimized to be detected by all pathogen assays contained in the Global Fever Panel (Table 1). The Negative External Control contains no nucleic acid and a successful run will be negative for all assays on the panel. These controls are not intended to replace the internal FilmArray Global Fever Panel pouch controls (RNA process control and second stage PCR array control). The Global Fever Panel External Control Kit contains no biological hazards and is 100% non-infectious.

Table 1. Pathogens Detected by the FilmArray Global Fever Panel

Disease	Pathogen Assay Result	Type
Leptospirosis	*Leptospira* spp.	Bacterial
Malaria	*Plasmodium* spp. *Plasmodium falciparum* *Plasmodium vivax/ovale*	Protozoan
Chikungunya fever	Chikungunya virus	Viral
Dengue fever	Dengue virus	

The External Controls are referenced in the Quick Guide and product literature as Control Injection Vials. The use of room-temperature stable External Controls contained within an injection vial simplifies the workflow and allows for use of the External Controls in settings where access to refrigeration may be limited. Each individually packaged, ready-to-use FilmArray Global Fever External Control is processed separately according to the Instructions for Use, and follows the procedure as outlined in the Quick Guide for the FilmArray Global Fever External Control Kit. Each External Control Injection Vial is intended for a single use.

The Global Fever Panel External Control Kit is designed to mitigate the risk of control contamination and misuse when evaluating clinical samples on the FilmArray 2.0 System.

- Negative External Controls are tested using the Negative External Control protocol, which monitors for contamination from both external control material and target pathogens; it will fail if either is detected.
- The Positive External Control contains DNA sequences that produce signature amplicon melting temperature (Tm) values distinct from the amplicon Tm values produced by each of the pathogens detected by the Global Fever Panel. By design, the Positive ECM will not be detected when using the Global Fever Panel Whole Blood Protocol, and reciprocally, amplified pathogen-specific nucleic acid will not be detected when using the Positive External Control Protocol. Through modification of the sequence between the inner primers for each ECM target, the Tm value of the amplicon is shifted to higher or

lower Tm values relative to the expected Global Fever Panel target amplicon while running the same Global Fever Panel pouches with the same physical pouch manipulation in the FilmArray 2.0 Instrument. Positive External Control-specific pouch module software detects the expected shifted Tm values as being from ECM amplicon, thereby evaluating the performance of the FilmArray 2.0 System. Also, the modification of the ECM sequence mitigates possible contamination events and does not cause false positives in clinical samples. In the unlikely event that Positive ECM or ECM amplicon is introduced into a patient sample, the resulting amplification Tm value(s) is not detected within the pathogen(s) Tm window in the Global Fever Panel Whole Blood Protocol, where different Tm windows are used to detect amplified pathogen sequence.

Device Intended Use

The FilmArray® Global Fever Panel External Control Kit 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 FilmArray® Global Fever Panel targets on FilmArray® 2.0 systems. The Global Fever Panel External Control Kit is designed for and intended to be used solely with the FilmArray Global Fever Panel. This product does not replace manufacturer internal controls provided as part of the 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 FilmArray Global Fever Panel. The Negative Control Injection Vial contains no DNA, and is non-reactive with the Global Fever Panel assays.

Substantial Equivalence

Element	**New Device:** **FilmArray Global Fever Panel External Control Kit**	**Predicate:** **FilmArray Warrior Control Panel M290 (K163522)**
Indications for Use	Positive and Negative External assayed quality controls to monitor multiple targets in an *in vitro* lab nucleic acid diagnostic test	Same
Technological Principles	Nested multiplex RT-PCR followed by melting analysis to confirm identity of amplified product.	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same
Sample Preparation Method	Process like patient sample.	Same
Composition	Tm-shifted Synthetic DNA	Synthetic DNA
Physical format	External Control Material dried on Control Injection Vial filter	Ready-to-use liquid

Element	New Device: FilmArray Global Fever Panel External Control Kit	Predicate: FilmArray Warrior Control Panel M290 (K163522)
Reagent Storage	Reagents are stored at room temperature (18° to 30°C).	Reagents are stored refrigerated (2°C to 8°C).
Pouch Module Software	External Control-specific protocols providing overall passed or failed results.	Sample specific protocols providing pathogen-specific results.

Summary Performance Data

Clinical Testing

During the prospective clinical evaluation of the FilmArray Global Fever Panel, six sites were required to perform one valid Global Fever Panel External Control test at the start of each day of specimen testing or contamination monitoring. A valid External Control run was one that exactly matched the expected results for each analyte in the mix (i.e., Positive or Negative). Results are shown in Table 2.

Table 2. FilmArray Global Fever Panel External Control Performance as Compared to the Expected ('Passed') Result

External Control Type	Completed with Expected Result	Total Completed	%
Positive	159[a]	160	99.4%
Negative	155[a]	157	98.7%
Overall	**314**	**317**	**99.1%**

[a] Appeared that user accidentally swapped Positive and Negative External Control-loaded pouches on instrument load.

Between July 2019 and January 2020, a total of 317 External Control tests (160 positive and 157 negative) were completed and had internal pouch controls that passed. Two Positive External Controls (2/160; 1.3%) and two Negative External Controls (2/157; 1.3%) had unexpected (Failed) results, for an overall External Control 'Passed' rate of 98.7% (313/317). Negative External Control testing identified one instance of pathogen contamination out of 157 tests, but no instances of External Control amplicon contamination. In all cases of a 'Failed' External Control test, the site immediately tested a new External Control and obtained the expected result.

Repeatability / Multi-Site Reproducibility

Repeatability was evaluated by having one operator testing one kit lot of External Controls using one reagent kit lot on one FilmArray 2.0 Instrument over 14 days. Table 3 shows the results for the Repeatability evaluation.

Table 3. Summary of Global Fever Panel External Control Repeatability Test Results

Global Fever Panel External Control Type	Expected Result	Observed/Expected (Percent Agreement)
Positive	Passed [1]	45/45 (100%)
Negative	Passed [2]	45/45 (100%)

[1] All Global Fever Panel assays have a positive amplicon melt in the External Control melt range.
[2] All Global Fever Panel assays have no melt in both the External Control melt range and in the pathogen melt range.

All 45 Positive and 45 Negative External Controls passed with no failures and therefore no additional testing was performed. For Positive External Controls, all target assays had Tm standard deviations between 0.1-0.2°C, with coefficient of variation (CV) between 0.1-0.3%. Combined with the pass rate, these results demonstrate repeatability for both the Negative and Positive External Controls.

The reproducibility of External Control test results was evaluated in a multi-site study using three External Control kits and three reagent pouch lots. Testing was performed at three sites, with two operators and three FilmArray 2.0 instruments at each site.

The percent agreement between the observed and expected test results for the Positive and Negative External Controls per test site and overall are shown in Table 4.

Table 4. Multi-Site Reproducibility Test Results of the Global Fever Panel Positive and Negative External Controls

Global Fever Panel External Control Type	Expected Result	Observed/Expected (Percent Agreement) [95% Confidence Interval]			
		Site 1	Site 2	Site 3	All Sites
Positive	Passed [1]	42/45 (93.3%)	45/45 (100%)	45/45 (100%)	**132/135 (97.8%)** [93.7-99.2%]
Negative	Passed [2]	45/45 (100%)	44/45 [3] (97.8%)	44/45 [4] (97.8%)	**133/135 (98.5%)** [94.8-99.6%]
Overall Agreement with Expected Result		**265/270 (98.1%)** [95.7-99.2%]			

[1] All Global Fever Panel assays have a positive amplicon melt in the External Control melt range.
[2] All Global Fever Panel assays have no melt in both the External Control melt range and in the pathogen melt range.
[3] Unexpected detection of pathogen amplicon for an off-panel assay, suspected laboratory contamination.
[4] Unexpected detection of pathogen amplicon for DENV 2_1 assay, suspected laboratory contamination.

The expected 'Passed' results for Positive External Controls were observed in 132 out of 135 (97.8%) tests, meeting the required pass rate of ≥95%. Three Positive External Controls failed; one failed due a single assay being called negative, and the other two showed no amplification of

External Control Material for any of the Global Fever Panel assays. For Negative External Controls, 133 out of 135 (98.5%) tests passed. The two Negative External Control failures were caused by detection of pathogen and not due to contamination with Positive External Control material.