DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

BioFire Diagnostics, LLC
C/O Kristen Kanack, Ph.D
Vice President of Regulated Products and Clinical Affairs
390 Wakara Way
Salt Lake City, UT 84108

October 8, 2015

Re: DEN150013
FilmArray® Meningitis/Encephalitis (ME) Panel
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 866.3970
Regulation Name: Device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid.
Regulatory Classification: Class II
Product Code: PLO, OOI, NSU
Dated: April 8, 2015
Received: April 9, 2015

Dear Dr. Kanack:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your *de novo* request for classification of the FilmArray Meningitis/Encephalitis (ME) Panel, a prescription device. The intended use of the FilmArray Meningitis/Encephalitis (ME) Panel is:

> The FilmArray Meningitis/Encephalitis (ME) Panel is a qualitative multiplexed nucleic acid-based *in vitro* diagnostic test intended for use with FilmArray and FilmArray 2.0 systems. The FilmArray ME Panel is capable of simultaneous detection and identification of multiple bacterial, viral, and yeast nucleic acids directly from cerebrospinal fluid (CSF) specimens obtained via lumbar puncture from individuals with signs and/or symptoms of meningitis and/or encephalitis. The following organisms are identified using the FilmArray ME Panel:
>
> Bacteria:
>
> *Escherichia coli* K1
> *Haemophilus influenzae*
> *Listeria monocytogenes*
> *Neisseria meningitidis* (encapsulated)
> *Streptococcus agalactiae*
> *Streptococcus pneumoniae*
>
> Viruses:
> Cytomegalovirus

Enterovirus
Herpes simplex virus 1
Herpes simplex virus 2
Human herpesvirus 6
Human parechovirus
Varicella zoster virus

Yeast:
Cryptococcus neoformans/gattii

The FilmArray ME Panel is indicated as an aid in the diagnosis of specific agents of meningitis and/or encephalitis and results are meant to be used in conjunction with other clinical, epidemiological, and laboratory data.

Results from the FilmArray ME Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out co-infection with organisms not included in the FilmArray ME Panel. The agent detected may not be the definite cause of the disease. Negative results do not preclude central nervous system (CNS) infection. Not all agents of CNS infection are detected by this test and sensitivity in clinical use may differ from that described in the package insert.

The FilmArray ME Panel is not intended for testing of specimens collected from indwelling CNS medical devices.

The FilmArray ME Panel is intended to be used in conjunction with standard of care culture for organism recovery, serotyping, and antimicrobial susceptibility testing.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the FilmArray Meningitis/Encephalitis (ME) Panel, and substantially equivalent devices of this generic type, into class II under the generic name, "Device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid."

FDA identifies this generic type of device as: Device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid.

A device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid is identified as a qualitative *in vitro* device intended for the detection and identification of microbial-associated nucleic acid sequences from patients suspected of meningitis or encephalitis. A device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid is intended to aid in the diagnosis of meningitis or encephalitis when used in conjunction with clinical signs and symptoms and other clinical and laboratory findings.

Section 513(f)(2) of the Food, Drug & Cosmetic Act (FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for *de novo* classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the FD&C Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the FD&C Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk- based classification of the device under section 513(a)(1) of the FD&C Act without first submitting a

510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On April 9, 2015, FDA received your *de novo* request for classification of the FilmArray Meningitis/Encephalitis Panel. The petition was submitted under section 513(f)(2) of the FD&C Act. In order to classify the FilmArray Meningitis/Encephalitis Panel into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the *de novo* request, FDA has determined that the FilmArray Meningitis/Encephalitis (ME) Panel intended for use as follows

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> Enterovirus
> Herpes simplex virus 1
> Herpes simplex virus 2
> Human herpesvirus 6
> Human parechovirus
> Varicella zoster virus
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> Yeast:
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> Results from the FilmArray ME Panel are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results do not rule out co-infection with organisms not included in the FilmArray ME Panel. The agent detected may not be the definite cause of the disease. Negative results do not preclude central nervous system

(CNS) infection. Not all agents of CNS infection are detected by this test and sensitivity in clinical use may differ from that described in the package insert.

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can be classified in class II with the establishment of special controls for this type of device. FDA believes that the class II special controls identified later in this order, along with the applicable general controls, including the design controls under 21 CFR part 820, provide reasonable assurance of the safety and effectiveness of the device type.

Table – Identified Risks and Required Mitigations

Identified Risks to Health	**Required Mitigations**
Incorrect identification or lack of identification of a pathogenic microorganism by the device can lead to improper patient management	Special Controls (1), (2), (3), (4), and (5)
Failure to correctly interpret test results	Special Controls (6), (7), (8), and (9)
Failure to correctly operate the instrument	Special Control (10)

In combination with the general controls of the FD&C Act, a device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid is subject to the following special controls:

1) Premarket notification submissions must include detailed device description documentation, including the device components, ancillary reagents required but not provided, and a detailed explanation of the methodology including primer/probe sequence, design, and rationale for sequence selection.
2) Premarket notification submissions must include detailed documentation from the following analytical studies: Analytical sensitivity (Limit of Detection), inclusivity, reproducibility, interference, cross reactivity, and specimen stability.
3) Premarket notification submissions must include detailed documentation from a clinical study. The study, performed on a study population consistent with the intended use population, must compare the device performance to results obtained from well-accepted comparator methods.
4) Premarket notification submissions must include detailed documentation for device software, including, but not limited to, software applications and hardware-based devices that incorporate software.
5) The Intended Use statement in the device labeling must include a statement that the device is intended to be used in conjunction with standard of care culture.
6) A detailed explanation of the interpretation of results and acceptance criteria must be included in the device's 21 CFR 809.10(b)(9) compliant labeling.
7) The device labeling must include a limitation that negative results do not preclude the possibility of central nervous system infection.
8) The device labeling must include a limitation that device results are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions.

9) The device labeling must include a limitation stating that positive results do not mean that the organism detected is infectious or is the causative agent for clinical symptoms.
10) As part of the risk management activities performed as part of your 21 CFR 820.30 design controls, you must document an appropriate end user device training program that will be offered as part of your efforts to mitigate the risk of failure to correctly operate the instrument.

In addition, this is a prescription device. Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the device to detect and identify microbial pathogen nucleic acids in cerebrospinal fluid they intend to market prior to marketing the device and receive clearance to market from FDA.

Please be advised that FDA's decision to grant this *de novo* request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and 809); medical device reporting (reporting of medical device- related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD&C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the *de novo* request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Kimberly Sconce at 301-796-6679.

Sincerely yours,

Uwe Scherf -S

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