



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

April 29, 2022

Re: DEN200066

Trade/Device Name: BioFire Joint Infection (JI) Panel

Regulation Number: 21 CFR 866.3988

Regulation Name: Device to detect and identify microorganism nucleic acids and resistance markers from patients with suspected orthopedic infection

Regulatory Class: Class II

Product Code: QSN

Dated: October 23, 2020

Received: October 27, 2020

Dear Kevin Bourzac:

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 BioFire Joint Infection (JI) Panel, a prescription device with the following indications for use:

The BioFire Joint Infection (JI) Panel is a multiplexed nucleic-acid-based, in vitro diagnostic test intended for use with BioFire FilmArray 2.0 and BioFire FilmArray Torch Systems for the simultaneous qualitative detection and identification of multiple bacterial and yeast nucleic acids and select antimicrobial resistance genes from synovial fluid obtained from individuals suspected to have a joint infection.

The following organisms are identified using the BioFire JI Panel: *Anaerococcus prevotii/vaginalis*, *Bacteroides fragilis*, *Candida* spp., *Candida albicans*, *Citrobacter*, *Clostridium perfringens*, *Cutibacterium avidum/granulosum*, *Enterobacter cloacae* complex, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Fingoldia magna*, *Haemophilus influenzae*, *Kingella kingae*, *Klebsiella aerogenes*, *Klebsiella pneumoniae* group, *Morganella morganii*, *Neisseria gonorrhoeae*, *Parvimonas micra*, *Peptoniphilus*, *Peptostreptococcus anaerobius*, *Proteus* spp., *Pseudomonas aeruginosa*, *Salmonella* spp., *Serratia marcescens*, *Staphylococcus aureus*, *Staphylococcus lugdunensis*, *Streptococcus* spp., *Streptococcus agalactiae*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*.

The BioFire JI Panel contains assays for the detection of genetic determinants associated with *S. aureus* resistance to methicillin (mecA/C) in conjunction with the SCCmec right extremity junction (MREJ)), enterococcal resistance to vancomycin (vanA and vanB), and some mechanisms of gram-

negative bacterial resistance β -lactams including penicillins, cephalosporins, monobactams, and carbapenems (blaCTX-M, blaIMP, blaKPC, blaNDM, blaOXA-48-like, blaVIM). Detection of these genetic determinants can aid in the identification of potentially antimicrobial-resistant organisms in synovial fluid samples. The antimicrobial resistance gene or marker detected may or may not be associated with the agent responsible for disease. Negative results for these select antimicrobial resistance gene assays do not indicate susceptibility, as multiple mechanisms of resistance to methicillin, vancomycin, and β -lactams exist.

The BioFire JI Panel is indicated as an aid in the diagnosis of specific agents of joint infection and results should be used in conjunction with other clinical and laboratory findings. Negative results may be due to infection with pathogens that are not detected by this test, pathogens present below the limit of detection of the assay, or infection that may not be detected in a synovial fluid specimen. Positive results do not rule out co-infection with other organisms. The BioFire JI Panel is not intended to monitor treatment for joint infections.

Culture of synovial fluid is necessary to recover organisms for susceptibility testing and epidemiological typing, to identify organisms in the synovial fluid that are not detected by the BioFire JI Panel, and to further identify species in the genus, complex or group results.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the BioFire Joint Infection (JI) Panel, and substantially equivalent devices of this generic type, into Class II under the generic name a device to detect and identify microorganism nucleic acids and resistance markers from patients with suspected orthopedic infection.

FDA identifies this generic type of device as:

Device to detect and identify microorganism nucleic acids and resistance markers from patients with suspected orthopedic infection. A device to detect and identify microorganism nucleic acids and resistance markers from patients with suspected orthopedic infection is a qualitative in vitro device intended to simultaneously detect and identify microorganism nucleic acids from human clinical specimens collected from patients with suspected orthopedic infection. The device detects specific nucleic acid sequences for microorganism identification as well as markers for antimicrobial resistance. This device is intended to aid in the diagnosis of orthopedic infections when used in conjunction with other clinical signs and symptoms and other laboratory findings. However, the device does not replace traditional methods for culture and susceptibility testing.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This 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 Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. 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 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 announcing the classification.

On October 27, 2020, FDA received your De Novo requesting classification of the BioFire Joint Infection (JI) Panel. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the BioFire Joint Infection (JI) 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, for the previously stated indications for use, the BioFire Joint Infection (JI) Panel can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks to health are the risk of false test results, failure to correctly interpret test results, and failure to correctly operate the device. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health	Mitigation Measures
Risk of false test results leading to improper patient management	Use of certain specimen collection devices identified in special control (1). Certain labeling information identified in special control (2), including limitations, warnings, device descriptions, explanation of procedures, and performance information identified in special controls (3)(iii) and (3)(iv). Certain design verification and validation identified in special control (3), including documentation of certain analytical studies and clinical studies and device descriptions.
Failure to correctly interpret test results leading to misdiagnosis and associated risk of false test results	Certain labeling information identified in special control (2), including limitations, warnings, device descriptions, explanation of procedures, and performance information identified in special controls (3)(iii) and (3)(iv). Certain design verification and validation identified in special control (3), including documentation of certain analytical studies and clinical studies and device descriptions.
Failure to correctly operate the device leading to false test results or incorrect interpretation of test results	Use of certain specimen collection devices identified in special control (1). Certain labeling information identified in special control (2), including limitations, warnings, device descriptions, explanation of procedures, and performance information

Identified Risks to Health	Mitigation Measures
	identified in special controls (3)(iii) and (3)(iv). Certain design verification and validation identified in special control (3), including documentation of certain analytical studies and clinical studies and device descriptions.

In combination with the general controls of the FD&C Act, the device to detect and identify microorganism nucleic acids and resistance markers from patients with suspected orthopedic infection is subject to the following special controls:

1. Any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt (standalone or as part of a test system) for the collection of specimen types claimed by this device; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.
2. The labeling required under 21 CFR 809.10(b) must include:
 - i. An intended use that includes a detailed description of targets the device detects and measures, the results provided to the user, the clinical indications appropriate for test use, and the specific population(s) for which the device is intended.
 - ii. Limiting statements, when applicable, indicating:
 - (A) The device is intended to be used in conjunction with clinical history, signs and symptoms, and results of other diagnostic tests, including culture and anti-microbial susceptibility testing;
 - (B) Detection of resistance markers cannot be definitively linked to specific microorganisms and that the source of a detected resistance marker may be an organism not detected by the assay; and
 - (C) Antimicrobial resistance can occur via multiple mechanisms. A not detected result for the antimicrobial resistance gene assays does not indicate antimicrobial susceptibility. Culturing and susceptibility testing of isolates is needed to determine antimicrobial susceptibility.
 - iii. A detailed device description, including reagents, instruments, ancillary materials, all control elements, and a detailed explanation of the methodology, including all pre-analytical methods for processing of specimens.

iv. Detailed descriptions of the performance characteristics of the device for all claimed specimen types as shown by the analytical and clinical studies required under paragraphs (3)(iii) and (3)(iv) except specimen stability performance characteristics.

3. Design verification and validation must include:

- i. A detailed device description, including all device parts, control elements incorporated into the test procedure, reagents required but not provided, the principle of device operation and test methodology, and the computational path from collected raw data to reported result (e.g., how collected raw signals are converted into a reported result).
- ii. A detailed description of the impact of any software, including software applications and hardware-based devices that incorporate software, on the device's functions.
- iii. Detailed documentation of analytical studies, including those demonstrating Limit of Detection (LoD), inclusivity, cross-reactivity, microbial interference, interfering substances, competitive inhibition, carryover/cross contamination, specimen stability, within lab precision, and reproducibility, as appropriate.
- iv. Detailed documentation and performance results from a clinical study that includes prospective (sequentially collected) samples for each claimed specimen type and, when determined to be appropriate by FDA, additional characterized clinical samples. The study must be performed on a study population consistent with the intended use population and compare the device performance to results obtained using a comparator method that FDA has determined to be appropriate. Detailed documentation must include the clinical study protocol (including a predefined statistical analysis plan), study report, testing results, and results of all statistical analyses.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

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 A device to detect and identify microorganism nucleic acids and resistance markers from patients with suspected orthopedic infection they intend to market prior to marketing the device.

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 Parts 801 and 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 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.

For comprehensive regulatory information about medical devices and radiation-emitting products, 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).

If you have any questions concerning the contents of the letter, please contact Bryan Grabias at 240-402-9563.

Sincerely,

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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