

**SPECIAL 510(k): Device Modification
OIR Decision Memorandum**

To: BioFire Diagnostics, LLC

RE: K160457

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II device requiring 510(k). The following items are present and acceptable:

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.

Trade Name: FilmArray Blood Culture Identification (BCID) Panel for use with Multi-Instrument FilmArray System (2.0)
510(k) Number: K143171

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device, called "FilmArray® Blood Culture Identification (BCID) Panel for use with FilmArray Torch", as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, and package labeling.

Submitter states in the submission that the intended use of the modified device has not changed from its predicate. The intended use in the labeling is the same.

3. A description of the device **MODIFICATION(S)**, including clearly labeled diagrams, engineering drawings, photographs, assay instruction and instrument operations manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

The modifications of the FilmArray Torch comprise a reconfigured instrument to increase throughput and reduce workspace. Changes include:

1. The computer, barcode scanner, and a touch screen user interface are integrated into the FilmArray Torch System Base instead of being a separate stand-alone computer with monitor, barcode scanner, keyboard, and mouse.
2. The modified FilmArray 2.0 instruments are now called FilmArray Torch Modules. Two FilmArray Torch Modules are included as part of the FilmArray Torch System Base and up to five additional Duplexes, each containing two FilmArray Torch Modules, can be stacked onto the FilmArray Torch System Base to create a system with a 12-pouch testing capability.
3. In order for the FilmArray Torch Modules to be stacked, a new edge-load mechanism for introducing the pouches into the FilmArray Torch Modules was created to replace the previous top-load mechanism. The edge load mechanism automatically pulls the pouch into the FilmArray Torch Module; the pouch is automatically ejected at the end of the run.
4. The workflow for inserting a pouch and starting a run is slightly modified by requiring the user to scan the pouch before loading into the FilmArray Torch Module instead of scanning the pouch after top-loading. This is required due to the barcode being inaccessible once pulled into the FilmArray Torch Module by the edge-load mechanism. Labeling was appended in the instruction manual to address this change.
5. Non-significant changes were made to the FilmArray 2.0 Software in order to control testing of 12 FilmArray Torch Modules from the single computer base.
6. A printer is optional for the FilmArray Torch.

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including, labeling, intended use, physical characteristics, and software is shown in the table below.

Element	Modified Device: FilmArray BCID Panel for use with the FilmArray Torch	Predicate: FilmArray BCID Panel (K143171)
Organisms Detected	<i>Enterococci</i> , <i>Listeria monocytogenes</i> , <i>Staphylococci</i> (including specific differentiation of <i>Staphylococcus aureus</i>), <i>Streptococci</i> (with specific differentiation of <i>Streptococcus agalactiae</i> , <i>Streptococcus pneumoniae</i> , and <i>Streptococcus pyogenes</i>), <i>Acinetobacter baumannii</i> , <i>Enterobacteriaceae</i> (including specific differentiation of the <i>Enterobacter cloacae</i> complex, <i>Escherichia coli</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus</i> , and <i>Serratia marcescens</i>), <i>Haemophilus influenzae</i> , <i>Neisseria meningitidis</i> (encapsulated), <i>Pseudomonas aeruginosa</i> , <i>Candida albicans</i> , <i>Candida glabrata</i> , <i>Candida krusei</i> , <i>Candida parapsilosis</i> , <i>Candida tropicalis</i> , and resistance markers <i>mecA</i> , <i>vanA</i> , <i>vanB</i> , and <i>bla_{KPC}</i> (KPC)	Same
Analyte	DNA	Same
Specimen Types	Positive blood culture samples containing gram-positive or gram-negative bacteria and/or yeast.	Same
Technological Principles	Nested multiplex PCR followed by high resolution melting analysis to confirm identity of amplified product.	Same
Instrumentation	Single instrument FilmArray System, FilmArray 2.0 System, or FilmArray Torch System	Single instrument FilmArray System or FilmArray 2.0 System
Instrument-Software Communication	Communication for multiple FilmArray Torch Modules travels via Ethernet cable/port.	Same (multiple instruments)
Time to result	About 1 hour	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same
Reagent Hydration and Sample Loading	FilmArray Injection Vial-based loading procedure	Same
Sample Preparation Method	Sample Processing is automated in the FilmArray BCID pouch.	Same
Reagent Storage	Reagents are stored at room temperature.	Same

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	Moderate/Low	Same

The indications for use provided below are identical for both devices.

FilmArray 2.0 (K143171) Indications for use (same as K160457):

The FilmArray Blood Culture Identification (BCID) Panel is a qualitative multiplexed nucleic acid-based *in vitro* diagnostic test intended for use with FilmArray systems. The FilmArray BCID Panel is capable of simultaneous detection and identification of multiple bacterial and yeast nucleic acids and select genetic determinants of antimicrobial resistance. The BCID assay is performed directly on blood culture samples identified as positive by a continuous monitoring blood culture system that demonstrate the presence of organisms as determined by Gram stain.

The following gram-positive bacteria, gram-negative bacteria, and yeast are identified using the FilmArray BCID Panel: *Enterococci*, *Listeria monocytogenes*, *Staphylococci* (including specific differentiation of *Staphylococcus aureus*), *Streptococci* (with specific differentiation of *Streptococcus agalactiae*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*), *Acinetobacter baumannii*, *Enterobacteriaceae* (including specific differentiation of the *Enterobacter cloacae* complex, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus*, and *Serratia marcescens*), *Haemophilus influenzae*, *Neisseria meningitidis* (encapsulated), *Pseudomonas aeruginosa*, *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, and *Candida tropicalis*.

The FilmArray BCID Panel also contains assays for the detection of genetic determinants of resistance to methicillin (*mecA*), vancomycin (*vanA* and *vanB*), and carbapenems (*blaKPC*) to aid in the identification of potentially antimicrobial resistant organisms in positive blood culture samples. The antimicrobial resistance gene 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 carbapenems exist.

FilmArray BCID is indicated as an aid in the diagnosis of specific agents of bacteremia and fungemia and results should be used in conjunction with other clinical and laboratory findings. Positive FilmArray results do not rule out co-infection with organisms not included in the FilmArray BCID Panel. FilmArray BCID is not intended to monitor treatment for bacteremia or fungemia.

Subculturing of positive blood cultures is necessary to recover organisms for susceptibility testing and epidemiological typing, to identify organisms in the blood culture that are not detected by the FilmArray BCID Panel, and for species determination of some *Staphylococci*, *Enterococci*, *Streptococci*, and *Enterobacteriaceae* that are not specifically identified by the FilmArray BCID Panel assays.

5. A **Design Control Activities Summary** was present which includes:
- a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.
 - b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied.

Risk analysis was performed to identify risks, their possible causes, and appropriate control mechanisms. All risks were evaluated in the context of 21 CFR 807.81(a)(3) and FDA's guidance document '501(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device.' Upon analysis, the following risks were found: 1. False negatives caused by minor changes in the FilmArray Torch Module design; 2. False positives caused by pouch ruptures and contamination caused by edge-load ejection mechanism; 3. Delayed or no results caused by user error/confusion with new User Interface or pouches stuck due to new edge-load mechanism. No user injury risks were found. To assess the risks relating to false negatives/positives and delayed/no results, verification and validation studies were performed.

To validate the modified device, precision testing was performed in samples containing the analytes in concentrations that were consistent with what has been previously measured in positive blood cultures. Results of the precision testing indicated that all analytes in the device intended use were detected in 100% of the samples tested. "Not detected" results were obtained in 100% of the negative samples for all analytes except *C. krusei*, which was obtained in 98% of the negative samples.

In addition to analyte detection, the precision of T_m (melting temperature) on FilmArray Torch was evaluated. The standard deviation in T_m for each assay on each of the 3 FilmArray Torch systems and modules met the acceptance criteria of $\pm 0.5^{\circ}\text{C}$ or less.

Method comparison studies were performed on the modified and predicate devices with different types of samples in order to determine agreement. Analyte detection and T_m values from reproducibility testing of 4 organisms were equivalent (i.e., 100% agreement) between the 2 systems. Greater than 95% agreement was also obtained between the two systems when comparing negative samples, synthetic templates, and representative organisms.

- c) Declaration of Conformity to Design Controls

A "Declaration of Conformity" statement was submitted for the BioFire Diagnostics, LLC manufacturing facility. It was signed by the Vice President, Regulated Products and Clinical Affairs, and the Director of Quality Assurance. The statements indicate that:

- i. "To the best of my knowledge, the verification activities, as required for the risk analysis, for the modification were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met."
- ii. "The manufacturing facility, BioFire Diagnostics, LLC, is in conformance with the design control requirements

6. Conclusion

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared device