

SPECIAL 510(k): Device Modification
OIR Decision Memorandum

To: BioFire Diagnostics, LLC

RE: K160462

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 de novo application number of the SUBMITTER'S previously cleared device.

Trade Name: FilmArray Meningitis/Encephalitis (ME) Panel for use with the FilmArray and FilmArray 2.0 systems
De Novo Application: DEN150013

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device, called "FilmArray® Meningitis/Encephalitis Panel for use with FilmArray systems," as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling.

Submitter states in the 510(k) Summary and in the submission that the intended use of the modified device has not changed from its predicate. The intended use of the modified device remains the same in the labeling.

3. A description of the device **MODIFICATION(S)**, including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

The modifications made to the FilmArray 2.0 system to configure the FilmArray Torch aimed to increase throughput capacity and benchtop workspace through single tower housing. Changes include:

- a reconfigured base instrument tower with optional, stacked, individual instrument modules,
- workflow altered for a manual read of the assay pouch's bar-code by the operator instead of automatic read within instrument,
- automatic edge-loading mechanism is used to load hydration reagents and clinical samples instead of a manual top-loading technique,
- automatic partial ejection of the assay pouch following conclusion of a run rather than manual removal of the pouch,
- printer is optional instead of included with the system,
- computer, barcode scanner, and touch screen interface integrated into the base of the tower configuration instead of a separate computer set-up,
- operation with kiosk-style (touch-screen) software,
- labeling appended with an additional operational procedure and with statements describing the validation/verification studies (i.e. LoD and reproducibility); these studies included an intra-laboratory precision study for the modified device.

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.

SIMILARITIES

ITEM	PREDICATE FilmArray Meningitis/Encephalitis (ME) Panel for use with FilmArray System (FilmArray 2.0) (DEN150013)	MODIFIED DEVICE FilmArray Meningitis/Encephalitis (ME) Panel for use with FilmArray Torch (K160462)
Organisms Detected	<i>Escherichia coli</i> K1, <i>Haemophilus influenzae</i> , <i>Listeria monocytogenes</i> , <i>Neisseria meningitidis</i> (encapsulated), <i>Streptococcus agalactiae</i> , <i>Streptococcus pneumoniae</i> , Cytomegalovirus, Enterovirus, Herpes simplex virus 1, Herpes simplex virus 2, Human herpesvirus 6, Human parechovirus, Varicella zoster virus, and <i>Cryptococcus neoformans/gattii</i>	SAME
Analyte	DNA/RNA	SAME
Specimen Types	Cerebrospinal fluid (CSF) from lumbar puncture	SAME
Required Accessories and Reagents	FilmArray reagent kit stored at room temperature	SAME
Sample Loading	Syringe-based loading	SAME
Sample Preparation Protocol and Processing Steps	Automated sample processing occurs in the FilmArray ME pouch	SAME
Technological Principles	Nested multiplex real-time PCR with post-amplification analysis by high resolution melting that confirms the identity of each amplified product	SAME
Instrumentation-Software Communication	Communication from multiple FilmArray Torch modules travels via Ethernet cable/port	SAME (multiple FilmArray instruments)
Instrumentation-Core Software Functions	Step-by-step on-screen instructions that guide the operator through performing a run by utilizing a kiosk-style interaction (touch-screen interface)	SAME (operator must use the computer's mouse to navigate through protocols and instructions on-screen)
Instrumentation Optics	Complimentary metal-oxide semiconductor (CMOS) camera used for capturing fluorescent images of the PCR2 reactions	SAME

Time to Result	Approximately 1 hour	SAME
Test Interpretation and Results Reporting	Automated test interpretation and results reporting; user cannot access raw data; test report can be printed at the end of the run	SAME
Controls	Two internal controls (RNA processing control and PCR2 control) are stored in each reagent pouch to ensure all steps carried out in the pouch were successful	SAME
User Complexity	Moderate/Low	SAME

DIFFERENCES

ITEM	PREDICATE FilmArray Meningitis/Encephalitis (ME) Panel for use with FilmArray System (FilmArray 2.0) (DEN150013)	MODIFIED DEVICE FilmArray Meningitis/Encephalitis (ME) Panel for use with FilmArray Torch (K160462)
Instrumentation and Set-Up	FilmArray 2.0 system that can include up to 8 separate instruments (8 pouch testing capability) connected to a single, stand-alone computer, barcode scanner, keyboard, and mouse	FilmArray Torch containing up to 12 FilmArray Torch modules (12-pouch testing capability) with a computer, barcode scanner, and touch-screen user interface incorporated in the system's base
Pouch Loading and Ejection	Manual top-loading mechanism; manual ejection after completion of run	Automated edge-loading mechanism; automatic partial ejection after completion of run
Workflow for Pouch Insertion	Pouch is automatically scanned within instrument	User must manually scan pouch prior to loading
Additional System Configuration	Printer is included with system	Printer is an optional component of the system

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

FilmArray 2.0 (K160462) Indications for use (same as DEN150013):

The FilmArray Meningitis/Encephalitis (ME) Panel is a qualitative multiplexed nucleic acid-based *in vitro* diagnostic test intended for use with FilmArray 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: *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis* (encapsulated), *Streptococcus agalactiae*, *Streptococcus pneumoniae*, Cytomegalovirus, Enterovirus, Herpes simplex virus 1,

Herpes simplex virus 2, Human herpesvirus 6, Human parechovirus, Varicella zoster virus, and *Cryptococcus neoformans/gatti*.

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.

5. A **Design Control Activities Summary** 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

A risk analysis of the modifications made to reconfigure the FilmArray 2.0 system into the integrated tower configuration of the FilmArray Torch was successfully completed in the context of 21 CFR 807.81 and the appropriate guidance. Reconfiguration of the platform did not alter the performance or capabilities of the device when run with the FilmArray ME Panel. Risk management of the FilmArray Torch Software and Firmware followed processes that were compliant with ISO 14971:2012.

- 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

In order to both validate and verify the FilmArray ME Panel for use on the FilmArray Torch, studies were completed to address risks associated with false negative, false positive, and delayed or no results. An intra-laboratory precision study was conducted between three FilmArray Torch systems (containing three Torch modules within each system for a total of 9 FilmArray Torch Modules per sample) and three sets of three FilmArray 2.0 instruments for a total of 9 FilmArray instruments. Results demonstrated that all analytes in the FilmArray ME Panel (at 1x LOD) were detected in at least 95% of the samples tested on both platforms. 100% of "Not Detected" results were observed for all analytes in the negative samples tested with the exception of *H. influenzae* that demonstrated a 98.3% agreement with the expected negative result. Additionally, melting temperature values were evaluated among the systems and results fell within the acceptance criteria of a standard deviation of $\pm 0.5^{\circ}\text{C}$ or less for each target (known system variation on the FilmArray).

Method comparison studies were conducted for the modified device (FilmArray Torch with ME Panel) and its predicate device (FilmArray 2.0 with ME Panel). These included a synthetic template method comparison study, a negative sample method comparison study, and a representative organism method comparison study. For all studies, the positive agreement was $\geq 95\%$ and the negative agreement was 100%.

An additional study was completed using the WHO International Standard for Human Cytomegalovirus (HCMV) for Nucleic Acid Amplification Techniques on the FilmArray and FilmArray 2.0 systems. The standard was tested at the previously established LoD concentration. When testing samples containing the WHO CMV standard, CMV was detected by the FilmArray ME Panel in 100% of the replicates tested at the confirmed LoD concentration on both FilmArray systems. This information was included in the revised package insert.

c) Declaration of Conformity with 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 by 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 as specified in 21 CFR 820.30 and the records are available for review.”

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.