CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW240028

II. Parent Document Number

K243544

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

BioFire Diagnostics, LLC

V. Proprietary and Established Names

BIOFIRE SPOTFIRE Respiratory/Sore Throat Panel Mini

VI. Measurand (analyte)

The respiratory menu of the BIOFIRE SPOTFIRE Respiratory/Sore Throat (R/ST) Panel Mini detects severe acute respiratory syndrome (SARS-CoV-2), influenza A, influenza B, respiratory syncytial virus (RSV), and human rhinovirus RNA from nasopharyngeal and anterior nasal swab specimens in collection medium from patients with signs and symptoms of respiratory infection. The sore throat menu of the BIOFIRE SPOTFIRE Respiratory/Sore Throat (R/ST) Panel Mini detects RNA from SARS-CoV-2, influenza A, influenza B, respiratory syncytial virus (RSV) viruses and DNA from *Streptococcus pyogenes* (Group A *Streptococcus*) in throat swabs in collection medium.

VII. Sample Type(s)

Nasopharyngeal, anterior nasal, and throat swab specimens.

VIII. Type of Test

Multiplex nucleic acid assay for use with the BIOFIRE SPOTFIRE System for the qualitative detection and identification of viral and/or bacterial pathogens in nasopharyngeal or anterior nasal swabs from patients with signs and symptoms of respiratory tract infection (BIOFIRE SPOTFIRE R Panel) or in throat swabs from patients with signs and symptoms of pharyngitis (BIOFIRE SPOTFIRE ST Panel).

IX. Test System Description

A Overview

The BIOFIRE SPOTFIRE Respiratory/Sore Throat (R/ST) Panel Mini is a multiplexed nucleic acid-amplification-based test that is intended to detect and identify multiple respiratory viral and bacterial pathogens in nasopharyngeal swab (NPS), anterior nasal swab (ANS), and throat swabs (TS) from individuals with signs and symptoms of respiratory tract infection or pharyngitis, respectively. The BIOFIRE SPOTFIRE R/ST Panel Mini is compatible with the BIOFIRE SPOTFIRE System, an automated polymerase chain reaction (PCR)-based in vitro diagnostic system for use with reagent pouches for specific indications.

The BIOFIRE SPOTFIRE System automates nucleic acid extraction and nested multiplex PCR in unitized, closed pouches. The resulting PCR products are evaluated using assay-specific DNA melting analysis. The BIOFIRE SPOTFIRE System Software executes the BIOFIRE SPOTFIRE R/ST Panel Mini test and interprets and reports the test results in approximately 15 minutes, without user intervention.

B Test System Components

Test System Components

The SPOTFIRE System is comprised of between one and four modules that are connected to a single SPOTFIRE Control Station equipped with the SPOTFIRE System Software. The first module is placed on top of the Control Station and additional modules may be stacked on top as required. Each module can be accessed at random to perform a test, independent of the other modules attached to the same Control Station.

The BIOFIRE SPOTFIRE R/ST Panel Mini Reagent Kit includes sufficient reagents and consumables to test 30 samples or controls:

- BIOFIRE SPOTFIRE R/ST Panel Mini Pouches (30 ea.)
    - Containing freeze-dried reagents
    - Each pouch is packed under vacuum in a metal canister and outer vacuum-sealed bag.
- Sample Preparation Reagent Kit (SPRK) (32 ea.)
    - Individually packaged fixed volume transfer pipette for addition of the test sample to the Sample Injection Vial
    - Sample Buffer ampoule containing ~1 mL of Sample Buffer for addition to the Sample Injection Vial
    - Sample Injection Vial (coded red) for mixing of the test sample and Sample Buffer
    - Hydration Injection Vial (coded blue) containing ~1.5 mL Hydration Solution for pouch rehydration.

X. Specific Contents for CLIA Waiver

A Demonstrating “Simple”:

The "Simple" principle was demonstrated previously. No new information was reviewed in the CLIA-Waiver by Application. The only modification to the BIOFIRE SPOTFIRE R/ST Mini is addition of an ANS specimen type. Please refer to FDA Decision Summary for CW240014 for more details.

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

   No new information was reviewed in the CLIA-Waiver by Application. The only modification to the BIOFIRE SPOTFIRE R/ST Mini is addition of an ANS specimen type. Please refer to FDA Decision Summary for CW240014 for more details.

2. Fail-Safe and Failure Alert Mechanisms:

   No new information was reviewed in the CLIA-Waiver by Application. The only modification to the BIOFIRE SPOTFIRE R/ST Mini is addition of an ANS specimen type. Please refer to FDA Decision Summary for CW240014 for more details.

3. Flex Studies: (summarize studies and refer to previous submission)

   No new information was reviewed in the CLIA-Waiver by Application. The only modification to the BIOFIRE SPOTFIRE R/ST Mini is addition of an ANS specimen type. Please refer to FDA Decision Summary for CW240014 for more details.

C Demonstrating "Insignificant Risk of an Erroneous Result" – Accuracy

1. Comparison Study
   a. Study Design
      i. Study Sites and Duration
         Clinical performance of the BIOFIRE SPOTFIRE R/ST Panel Mini was evaluated in a multi-site prospective study during March 2024 – February 2025. Five sites throughout the US participated in the clinical study. The sites consisted of urgent care settings, and pediatric and adult emergency departments which offer or perform CLIA-waived tests directly on-site.

      ii. Operators
         There were a total of 19 operators representative of intended CLIA waived users across the five clinical testing sites, with between two and six operators at each site. The test operators who participated in the study were not trained laboratory technicians.

      iii. Instructions for Use
         Operators who participated in evaluating the clinical performance of the BIOFIRE SPOTFIRE R/ST Panel Mini did not receive any training on how to perform the assay and were instructed to refer solely to the BIOFIRE SPOTFIRE R Panel Mini Panel Quick Guide. Telephone technical support was available as intended for the commercial product.

iv. Subjects (Patients)
The subjects were enrolled according to the study protocol Inclusion or Exclusion criteria from symptomatic patients.

v. Samples
Prospective Study
The clinical performance of the BIOFIRE SPOTFIRE R/ST Panel Mini when testing ANS specimens was established during a prospective multi-center study. Five geographically distinct study sites located in the U.S. and representative of the intended use setting participated in these studies from March 2024 to February 2025. All BIOFIRE SPOTFIRE R/ST Panel Mini testing was performed according to the manufacturer's instructions by operators with training and educational backgrounds representative of those in the CLIA-Waived setting.

A total of 820 ANS specimens were initially enrolled in the prospective clinical study from consented volunteers from subjects of all ages; 23 of these were excluded from all analyses. Eleven (11) specimens were excluded because no valid BIOFIRE SPOTFIRE R/ST Panel Mini test for the ANS specimen was obtained, eight specimens were excluded due to unanticipated volume constraints, and four additional specimens were excluded due to those specimens having been determined to not meet the inclusion criteria after initial enrollment. The final data set consisted of 797 specimens. Four specimens were excluded from the evaluation of influenza A virus due to initial "Uncertain" results that were not appropriately retested by the operators at study sites. Additionally, two specimens obtained "No Subtype Detected" or "Equivocal" results for comparator testing for influenza A upon initial and repeat testing. For each analyte, the performance of the BIOFIRE SPOTFIRE R/ST Panel Mini when testing ANS specimens was evaluated by comparing the test results with those from a commercially available FDA-cleared multiplexed respiratory pathogen panel.

The BIOFIRE SPOTFIRE R/ST Panel Mini reported a total of 21 ANS specimens with discernable multiple organism detections (2.6% of all ANS specimens, 21/805; 5.5% of positive ANS specimens, 21/385). The resulting co-detection combinations as reported by the BIOFIRE SPOTFIRE R/ST Panel Mini are presented in **Table 13**. This table also indicates the number of specimens with false positive (FP) results for each co-detection combination, as well as the specific analyte(s) that were discrepant.

Table 13: Multiple Detection Combinations in ANS Specimens as Reported by the SPOTFIRE R/ST Panel Mini

Distinct Co-Detection Combinations		**Total Specimens with Co-Detections**	**Number of Specimens with False Positive Co- Detections**	**False Positive Analyte(s)**
Analyte 1	**Analyte 2**			
SARS-CoV-2	Human rhinovirus	8	1	SARS-CoV-2 (1), Human rhinovirus (1)

SARS-CoV-2	Respiratory syncytial virus	1	0	-
Human rhinovirus	Influenza A	9	2	Human rhinovirus (2)
Human rhinovirus	Respiratory syncytial virus	3	1	Human rhinovirus (1)
Total Co-Detections		**21**	**4**	**5/42[a]**

[a] Of the five discrepant analytes (out of 42 total analytes), one was confirmed as being present in the specimen during discrepancy investigation.

Retrospective Study

Due to the low prevalence of influenza B during the prospective study an evaluation of preselected archived retrospective anterior nasal swab (ANS) specimens was performed to supplement the results of the prospective clinical study. Archived clinical specimens consisted of residual leftover ANS in VTM from clinician-requested testing that were obtained from one clinical laboratory and one specimen biorepository and were chosen based solely on the analyte content reported by the source laboratory. A total of 242 (35 positive and 207 negative) frozen archived ANS specimens were obtained from two external laboratories and were retrospectively tested. All 242 ANS specimens had valid results that were included in performance analysis. Comparator testing was performed using an acceptable FDA cleared molecular assay.

b. Results and Analysis

The clinical performance of the BIOFIRE SPOTFIRE R/ST Panel Mini when used by untrained operators, testing prospectively collected ANS specimens from patients with signs and symptoms of respiratory tract infection is shown in **Table 14**.

Table 14: BIOFIRE SPOTFIRE R/ST Panel Mini Prospective Clinical Performance Summary for ANS Specimens

Analyte	Positive Percent Agreement			Negative Percent Agreement		
	TP/ (TP+FN)	%	95% CI	TN/ (TN+FP)	%	95% CI
SARS-CoV-2[a]	50/52	96.2	87.0-98.9	742/745	99.6	98.8-99.9
Human Rhinovirus[b]	222/232	95.7	92.2-97.6	537/565	95.0	92.9-96.5
Influenza A[c]	50/53	94.3	84.6-98.1	738/738	100	99.5-100.0
Influenza B	13/13	100	77.2-100.0	784/784	100	99.5-100.0
Respiratory Syncytial Virus[d]	38/40	95.0	83.5-98.6	756/757	99.9	99.3-100.0

[a] SARS-CoV-2 was detected 1/3 specimens when tested with additional molecular methods.
Human rhinovirus was detected in 1/28 FP specimens using an additional molecular method.
[c] Influenza A virus was detected in the three FN specimens using an additional molecular method.
[d] Respiratory syncytial virus was detected in the single FP specimen using an additional molecular method.

The clinical performance of the BIOFIRE SPOTFIRE R/ST Panel Mini with retrospectively collected ANS specimens from patients with signs and symptoms of respiratory tract infection is shown in **Table 15**.

Table 15: BIOFIRE SPOTFIRE R/ST Panel Mini Archived Clinical Performance Summary for ANS

Analyte	Positive Percent Agreement			Negative Percent Agreement		
	TP/ (TP+FN)	%	95% CI	TN/ (TN+FP)	%	95% CI
Influenza B virus	35/35	100	90.1-100.0	206/206	100	98.2-100.0

[a] One of the 207 negative specimens was unexpectedly identified as positive by the confirmatory molecular method and was excluded.

i. Invalid Rate for Clinical Evaluation Samples
The overall success rate for initial specimen testes was 97.0% (782/806). Nine tests (9/806; 1.1%) did not complete on the initial run, resulting in a total instrument success rate of 98.9% (797/806) for initial specimen tests. All nine specimens were able to be retested and valid results were produced on the first (eight specimens) or second (one specimen) retest.

2. Device Performance with Analytes Near the Cutoff
No new data were reviewed in the CLIA-Waiver by Application. The only modification to the BIOFIRE SPOTFIRE R/ST Mini is addition of an ANS specimen type. Please refer to FDA Decision Summary for CW240014 and to the Reproducibility Study data presented in the K232954 Decision Summary for more details.

3. Operator Questionnaire
No new information was reviewed in the CLIA-Waiver by Application. The only modification to the BIOFIRE SPOTFIRE R/ST Mini is addition of an ANS specimen type. Please refer to FDA Decision Summary for CW240014 for more details.

D Labeling for Waived Devices

The labeling consists of:
1. BIOFIRE SPOTFIRE R/ST Panel Mini Instructions for Use
2. BIOFIRE SPOTFIRE R/ST Panel Mini Quick Guide
3. BIOFIRE SPOTFIRE System Operator's Manual
4. BIOFIRE SPOTFIRE System Setup Quick Guide
5. BIOFIRE SPOTFIRE R/ST Panel Mini components and kit labels

The following elements are appropriately present:
- The BIOFIRE SPOTFIRE System Operator's Manual specifies the environmental operating conditions under which testing may be performed.
- The BIOFIRE SPOTFIRE R/ST Panel Mini Quick Guide and BIOFIRE SPOTFIRE System Setup Quick Guide are clear and easy to understand.
- The BIOFIRE SPOTFIRE R/ST Panel Mini Instructions For Use and Panel Quick Guide identify the test as CLIA Waived.
- The BIOFIRE SPOTFIRE R/ST Panel Mini Instructions For Use
    - Indicate that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test.
    - Include step-by-step instructions for performing the test.
    - Include safety considerations applicable for untrained users.

- Specify the actions to be taken if an invalid test result is obtained.
- Include a summary of the studies performed to support CLIA Waiver.
- Include appropriate warnings and/or limitations pertaining to clinical interpretation of test results.
- Include recommendations for Quality Control testing including the source of appropriate control materials and the frequency of testing.

The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10

XI. Benefit-Risk Considerations

Not applicable

XII. Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.