Date: July 25, 2022

BioFire Defense, LLC
Cynthia Phillips
VP of Regulatory, Quality, and Clinical Affairs
79 W 4500 S, Suite 14
Salt Lake City, Utah 84107

Re: K221460
Trade/Device Name: BioFire COVID-19 Test 2
Regulation Number: 21 CFR 866.3981
Regulation Name: Device To Detect And Identify Nucleic Acid Targets In Respiratory Specimens From Microbial Agents That Cause The SARS-Cov-2 Respiratory Infection And Other Microbial Agents When In A Multi-Target Test
Regulatory Class: Class II
Product Code: QQX
Dated: May 18, 2022
Received: May 19, 2022

Dear Cynthia Phillips:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 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 Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

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

Sincerely,

Himani Bisht, Ph.D.
Assistant Director
Viral Respiratory and HPV Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

Device Name

Indications for Use *(Describe)*

Type of Use *(Select one or both, as applicable)*

☐ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Special 510(k) Summary

I. Submitter

BioFire Defense, LLC
79 West 4500 South, Suite 14
Salt Lake City, UT 84107
Phone: (801) 262-3592
Fax: (801) 447-6907

Contact Person: Cynthia L. Phillips, Ph.D.
Date Prepared: 2022-05-18

II. Device

Name of Device: BioFire® COVID-19 Test 2
Common or Usual Name: Same
Regulation: 21 CFR 866.3981
Classification Name: Respiratory Specimen Nucleic Acid Sars-CoV-2 Test
Product Code: QQX
Regulatory Class: Class II (Special Controls)
Panel: Microbiology

III. Predicate Device

BioFire® COVID-19 Test 2 (BioFire Defense, LLC) (K211079)
This predicate has not been subject to a design-related recall.

IV. Device Description

The BioFire COVID-19 Test 2 is a multiplexed nucleic acid-based test for the detection of SARS-CoV-2 RNA from nasopharyngeal swabs (NPS) eluted in either transport medium or saline. The test was originally described and cleared in K211079. The BioFire COVID-19 Test 2 uses BioFire FilmArray technology and is for use with BioFire FilmArray 2.0 and BioFire FilmArray Torch instruments. Once the sample is injected into the FilmArray pouch the pouch is loaded into the FilmArray instrument which performs all aspects of testing including nucleic acid extraction, reverse-transcription, and nested PCR with melt analysis. The currently cleared version of the test uses three SARS-CoV-2 assays and returns a 'SARS-CoV-2 Detected' call if one or more of the SARS-CoV-2 assays are positive.

The purpose of this submission is to display results for four additional SARS-CoV-2 assays which are currently present on the test, but for which results are masked through software. The assays are being unmasked as a mitigation against the risk of future SARS-CoV-2 variants affecting the sensitivity of the BioFire COVID-19 Test 2 due to mutations in assay primer

regions. Note that to date BioFire Defense has not identified any variants that are predicted to affect the performance of the three-assay version of BioFire COVID-19 Test 2 described in K211079. These changes are being requested preemptively. The calling scheme when using the seven total SARS-CoV-2 assays will remain unchanged: one or more positive SARS-CoV-2 assay results will return an overall 'SARS-CoV-2 Detected' result.

V. Intended Use

The BioFire® COVID-19 Test 2 is a qualitative nested multiplexed RT-PCR in vitro diagnostic test intended for use with the BioFire® FilmArray® 2.0 and BioFire® FilmArray® Torch Systems. The BioFire COVID-19 Test 2 detects nucleic acids from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in nasopharyngeal swabs (NPS) from symptomatic individuals suspected of COVID-19 by their healthcare provider.

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in NPS specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out co-infection with other pathogens.

Results are meant to be used in conjunction with other clinical, epidemiologic, and laboratory data, in accordance with the guidelines provided by the relevant public health authorities. The BioFire COVID-19 Test 2 is intended for use by trained medical and laboratory professionals in a laboratory setting or under the supervision of a trained laboratory professional.

For In Vitro Diagnostic Use.

VI. Substantial Equivalence

The modified BioFire COVID-19 Test 2 is substantially equivalent to its predicate. No changes to the chemistry or intended use of the BioFire COVID-19 Test 2 have been made. Only minor modifications to the BioFire COVID-19 Test 2 Pouch Module software have been made to include results for seven SARS-CoV-2 assays instead of three. Performance evaluation studies used to support K211079 were re-analyzed with no significant impact. **Table 1** compares elements of the modified BioFire COVID-19 Test 2 to its predicate device and outlines their similarities and differences.

Table 1. Substantial Equivalence between the subject device and predicate device

Element	Subject Device: BioFire COVID-19 Test 2	Predicate Device: BioFire COVID-19 Test 2 (K211079)
Intended Use	The BioFire® COVID-19 Test 2 is a qualitative nested multiplexed RT-PCR in vitro diagnostic test intended for use with the BioFire® FilmArray® 2.0 and BioFire® FilmArray® Torch Systems. The BioFire COVID-19 Test 2 detects nucleic acids from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in nasopharyngeal swabs (NPS) from symptomatic individuals suspected of COVID-19 by their healthcare provider. Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in NPS specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out co-infection with other pathogens. Results are meant to be used in conjunction with other clinical, epidemiologic, and laboratory data, in accordance with the guidelines provided by the relevant public health authorities. The BioFire COVID-19 Test 2 is intended for use by trained medical and laboratory professionals in a laboratory setting or under the supervision of a trained laboratory professional.	Same
Specimen Type	Nasopharyngeal swabs eluted in transport medium or saline	Same
Pathogens Detected	SARS-CoV-2	Same
Analyte	RNA	Same
Number of Assays	3	7
Technological Principles	Nested multiplex RT-PCR followed by high resolution melting analysis to confirm identity of amplified product	Same
Instrumentation	FilmArray 2.0 or FilmArray Torch systems	Same
Time to Result	~45 minutes	Same
Reagent Storage	Room temperature	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data. Software uses results from 3 assays.	Automated test interpretation and report generation. User cannot access raw data. Software uses results from 7 assays.
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis	Same
Assayed External Controls	None	Same
User Complexity	Moderate/Low	Same

VII. Summary of Performance Data

Although the FDA-cleared version of the BioFire COVID-19 Test 2 described in K211079 only uses three SARS-CoV-2 assays for result interpretation, all seven assays were present on the test during the V&V study execution. Therefore, no additional testing was performed for this submission. Instead, all study data previously submitted in K211079 were re-analyzed using the updated BioFire COVID-19 Test 2 Pouch Module (Build 2.1.1.2C) to include results for the four previously masked assays in the study reports.

Table 2 summarizes the re-analyzed studies and any changes in the performance data. Note that in some cases, studies were leveraged to support both the BioFire COVID-19 Test 2 (K211079) and the BioFire COVID-19 Test v1.1 (EUA200044). The BioFire COVID-19 Test v1.1 and BioFire COVID-19 Test 2 have identical chemistry and manufacturing processes.

Table 2. Summary of Reanalyzed Performance Data

Study Number	Study Name	Summary of Results Following Reanalysis
Bench Testing		
DF-SDY-029903	BioFire COVID-19 Test Evaluation of Specificity	No unexpected reactivity was observed with any of the organisms/viruses. Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-029904	BioFire COVID-19 Test Evaluation of Sensitivity – LoD and Contrived Testing	Sensitivity of the modified BioFire COVID-19 Test 2 when using infectious SARS-CoV-2 virus is effectively equivalent to the predicate device: 3.3E+02 GC/mL.
DF-SDY-030331	BioFire COVID-19 Test 2 Determination of Limit of Detection – Inactivated Virus	Sensitivity of the modified BioFire COVID-19 Test 2 when using inactivated SARS-CoV-2 is equivalent to the predicate device: 3.3E+02 GE/mL.
DF-SDY-030333	BioFire COVID-19 Test 2 Evaluation of Specificity (Exclusivity)	No unexpected reactivity was observed with any of the organisms/viruses. Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-030334	BioFire COVID-19 Test 2 Evaluation of Potentially Interfering Substances	None of the substances tested were determined to be inhibitory to the BioFire COVID-19 Test 2. Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-030336	BioFire COVID-19 Test 2 Evaluation of Specimen Storage and Transport	The detection rate for all evaluated samples and storage conditions was 100%. Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-030358	Sensitivity/Proficiency Testing of the BioFire COVID-19 Test 2 with FDA-Provided SARS-CoV-2 Analytes	Overall results for testing the FDA Reference Panel with the modified BioFire COVID-19 Test 2 are comparable to the predicate device.
DF-SDY-030398	BioFire COVID-19 Test 2 Multi-Site Reproducibility Evaluation	Percent agreement between observed and expected results were >95% for each sample and each site, except for negative samples at Site 2. Percent agreement at Site 2 for negative samples

Study Number	Study Name	Summary of Results Following Reanalysis
		was 93.3%. The percent agreement was the same for the predicate device. Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-030404	BioFire COVID-19 Test 2 Evaluation of Reactivity (Inclusivity)	All four strains tested were detected at near LoD concentrations. Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-030666	BioFire COVID-19 Test – Saline and PBS Validation	The detection rate for NPS in saline at 1× LoD was 20/20 (100%). Performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
DF-SDY-030316	COVID-19 Stability Study for COVID	The BioFire COVID-19 Test stability evaluation demonstrated 20 months of stability at 18-30°C.
Clinical Testing		
DF-SDY-030617	BioFire COVID-19 Test 2 Prospective Clinical Evaluation	Performance of the modified BioFire COVID-19 Test 2 was 98.6% PPA (68/69), and 99.1% NPA (450/454). Whereas performance of the predicate device was 98.6% PPA (68/69) and 99.6% NPA (452/454). The overall performance of the modified BioFire COVID-19 Test 2 is equivalent to the predicate device.
In Silico Analyses		
DF-SDY-030174	COVID-19 Test In Silico Exclusivity Analyses	Only near-neighbor non-human coronavirus genomes showed significant homology to assay-specific sets of PCR2 primers and are predicted to be detected by the BioFire COVID-19 Test 2. It is unlikely that these isolates would be found in the human respiratory samples, however little is known about their potential to infect a human host. No other significant amplification of non-target sequences is predicted.
DF-OTH-030895	BioFire COVID-19 Test In Silico Inclusivity Summary	No sequences submitted to GISAID before May 4, 2022, were identified with co-occurring mutations impacting the performance of all assays. As such, BFDf predicts all strains of SARS-CoV-2, including all current VOCs, VOIs, and VUMs, will be detected by the BioFire COVID-19 Test 2.