August 30, 2021

Kevin Bourzac Ph.D.
VP, Regulatory and Clinical Affairs
BioFire Diagnostics, LLC
515 Colorow Drive
Salt Lake City, UT 84108

Device:	BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ)
EUA:	EUA202392
Company:	BioFire Diagnostics, LLC
Indication:	A multiplexed polymerase chain reaction (PCR) test intended for the simultaneous qualitative detection and differentiation of nucleic acids from multiple viral and bacterial respiratory organisms,[1] including nucleic acid from the SARS-CoV-2 virus, in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory infection consistent with COVID-19 by their healthcare provider. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high, moderate, or waived complexity tests. The BioFire RP2.1-EZ is authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Dear Dr. Bourzac:

On October 2, 2020, based on your[2] request the Food and Drug Administration (FDA) issued a letter authorizing use of the BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) for the simultaneous qualitative detection and differentiation of nucleic acids from multiple viral and bacterial

[1] The BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) is intended for the detection and differentiation of nucleic acid from SARS-CoV-2 and the following organism types and subtypes: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza A, including subtypes H1, H3 and H1-2009, Influenza B, Parainfluenza Virus, Respiratory Syncytial Virus*, Bordetella parapertussis, Bordetella pertussis, Chlamydia pneumoniae,* and *Mycoplasma pneumoniae*. Four types of Parainfluenza Virus (PIV1, PIV2, PIV3 and PIV4) can be detected and will be reported as Parainfluenza Virus Detected (type information is not reported).

[2] For ease of reference, this letter will use the term "you" and related terms to refer to BioFire Diagnostics, LLC.

respiratory organisms (refer to Footnote 1), including nucleic acid from the SARS-CoV-2 virus, in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory infection consistent with COVID-19 by their healthcare providerpursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). Testing was limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high, moderate, or waived complexity tests. The BioFire RP2.1-EZ was authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation. Based on your requests, FDA granted updates to the authorized labeling on December 22, 2020[3] and April 27, 2021.[4]

On August 16, 2021, you requested to revise your Emergency Use Authorization (EUA). Based on that request, and having concluded that revising the October 2, 2020, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the October 2, 2020, letter in its entirety with the revisions incorporated.[5] Accordingly, your product[6] is hereby authorized pursuant to section 564 of the Act when used pursuant to the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.[7]

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[3] On December 22, 2020, your request was granted to update the Instructions for Use (IFU) of the BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) to include the results of the FDA SARS-CoV-2 Reference Panel testing and fix some errors in the BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) Quick Guide. Some minor updates were also made to the Fact Sheet for Healthcare Providers and Fact Sheet for Patients. FDA made minor updates to the BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) IFU and Quick Guide to reflect language used in more recent authorizations.

[4] On April 27, 2021, your request was granted to update the IFU of the BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) to; (1) align with the IFU of the de novo for the BioFire Respiratory Panel 2.1 (RP2.1) including performance data, (2) addition of saline (up to 3 mL) as an acceptable transport medium for collection of nasopharyngeal swabs, and (3) update the in silico inclusivity analysis. FDA also made minor updates to the IFU, Quick Guide, Fact Sheet for Healthcare Providers and Fact Sheet for Patients to reflect language used in more recent authorizations.

[5] The revisions to the October 2, 2020, letter and authorized labeling include: (1) updates to the inclusivity *in silico* analysis in the performance section and some minor updates to the IFU for clarity; (2) updates to the Conditions of Authorization to add new Conditions related to circulating variants (Conditions P. and Q. below); and (3) updates to the IFU, Conditions of Authorization, Fact Sheets for Healthcare Providers and Patients to reflect language used in more recent authorizations.

[6] For ease of reference, this EUA will use the term "your product" to refer to the BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) used for the indication identified above.

[7] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. 85 FR 7316 (February 7, 2020).

There is an FDA-approved/cleared test for the qualitative detection and identification of SARS-CoV-2, influenza A virus and influenza B virus, along with the other organism types and subtypes targeted by this test, but this is not an adequate and available alternative to your product. Respiratory infections caused by the respiratory pathogens targeted by your product and SARS-CoV-2 can have similar clinical presentation and diagnostic considerations. Thus, to differentially detect SARS-CoV-2, information from a test that detects and differentiates the virus that causes COVID-19 and other common respiratory pathogens, including the influenza viruses that causes the flu, is needed. FDA considered the totality of scientific information available in authorizing the emergency use of your product for the indication above. A summary of the performance information FDA relied upon is contained in the Instructions for Use (identified below).

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of your product, described in the Scope of Authorization Section of this letter (Section II), subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of your product meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your product may be effective in diagnosing COVID-19, through the simultaneous detection and differentiation of nucleic acid from SARS-CoV-2 virus and multiple other respiratory viral and bacterial organisms[8] and that the known and potential benefits of your product when used for diagnosing COVID-19, outweigh the known and potential risks of your product; and

3. There is no adequate, approved, and available alternative to the emergency use of your product.[9]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to the indication above.

Authorized Product Details

Your product is a multiplexed nucleic acid test intended for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory viral and bacterial

[8] Refer to footnote 1.

[9] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

organisms, including nucleic acid from the SARS-CoV-2 virus, in nasopharyngeal swabs (NPS) obtained from individuals suspected of COVID-19 by their healthcare provider.

The BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) is intended for the detection and differentiation of nucleic acid from SARS-CoV-2 and the following organism types and subtypes: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza A, including subtypes H1, H3 and H1-2009, Influenza B, Parainfluenza Virus, Respiratory Syncytial Virus, *Bordetella parapertussis, Bordetella pertussis, Chlamydia pneumoniae,* and *Mycoplasma pneumoniae.* Four types of Parainfluenza Virus (PIV1, PIV2, PIV3 and PIV4) can be detected and will be reported as Parainfluenza Virus Detected (type information is not reported).

SARS-CoV-2 ribonucleic acid (RNA) and nucleic acids from the other respiratory viral and bacterial organisms identified by this test are generally detectable in NPS during the acute phase of infection. Positive results from individuals exhibiting signs and/or symptoms of respiratory infection are indicative of the presence of the identified microorganism(s); clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Positive results are indicative of the presence of the identified organism, do not rule out co-infection with other organisms. The agent detected may not be the definite cause of disease. Negative results in the setting of a respiratory illness may be due to infection with pathogens not detected by this test, or lower respiratory tract infection that may not be detected by an NPS specimen. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for treatment or other patient management decisions. Negative SARS-CoV-2 results must be combined with clinical observations, patient history, and epidemiological information. Negative results for other organisms identified by the test may require additional laboratory testing (e.g., bacterial and viral culture, immunofluorescence and radiography) when evaluating a patient with possible respiratory tract infection.

Your product is authorized to test NPS specimens using the BioFire FilmArray 2.0 EZ Configuration (BioFire 2.0 EZ) System, as outlined in the "BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ)" Instructions for Use. Testing is limited to laboratories certified under CLIA, 42 U.S.C. §263a, that meet the requirements to perform high, moderate, or waived complexity tests. Your product is authorized for use at the POC, i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Your product, when used with the BioFire 2.0 EZ, automates all aspects of nucleic acid testing including sample preparation, nucleic acid extraction and PCR amplification using nested multiplex PCR, and detection and differentiation of nucleic acids from multiple respiratory viral and bacterial organisms, including the SARS-CoV-2 virus, in a single-use cartridge. The BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) includes the following materials or other authorized materials: BioFire RP2.1 pouches, Single-use Sample Buffer ampoules, Single-use pre-filled Hydration Injection Vials, Single-use Sample Injection Vials, and individually packaged Transfer Pipettes.

Your product also includes in the cartridge the following controls, or other authorized controls (as may be requested under Condition K. below), that are processed along with the patient

samples when tested with your product. The controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- RNA Process Control - targets an RNA transcript from the yeast *Schizosaccharomyces pombe*. The yeast is present in the pouch in a freeze-dried form and becomes rehydrated when sample is loaded. The control material is carried through all stages of the test process, including lysis, nucleic acid purification, reverse transcription, PCR1, dilution, PCR2, and DNA melting. A positive control result indicates that all steps were carried out successfully.
- PCR2 Control - detects a DNA target that is dried into wells of the array along with the corresponding primers. A positive result indicates that PCR2 was successful.

You also recommend use of the external positive and negative controls, to be run regularly as outlined in the Instructions for Use, described below. Your product also requires the use of additional authorized materials and authorized ancillary reagents that are not included with your product and are described in the Instructions for Use, described below.

The labeling entitled "BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ)" Instructions for Use and the "BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) Quick Guide" (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), and the following fact sheets pertaining to the emergency use, is required to be made available as set forth in the Conditions of Authorization (Section IV), and are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: BioFire Diagnostics, LLC - BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ)
- Fact Sheet for Patients: BioFire Diagnostics, LLC - BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ)

The above described product, with the authorized labeling provided as set forth in the Conditions (Section IV), is authorized to be distributed to and used by authorized laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your authorized product, when used for the qualitative detection and differentiation of SARS-CoV-2 and multiple other respiratory viral and bacterial organisms[10] and used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your product.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that your product may be effective in diagnosing COVID-19, through the simultaneous detection and differentiation of SARS-CoV-2 and multiple other respiratory viral and bacterial organisms[11], when used consistent with the

[10] Refer to footnote 1.
[11] Refer to footnote 1.

Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that your product (as described in the Scope of Authorization of this letter (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) of the Act described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1) of the Act, your product is authorized for the indication above.

III. Waiver of Certain Requirements

I am waiving the following requirements for your product during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of your product, but excluding Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

IV. Conditions of Authorization

Pursuant to Section 564(e) of the Act, I am establishing the following conditions on this authorization:

BioFire Diagnostics, LLC (You) and Authorized Distributor(s)[12]

A. Your product must comply with the following labeling requirements under FDA regulations: the intended use statement (21 CFR 809.10(a)(2), (b)(2)); adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)); appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4); and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

B. You and authorized distributor(s) must include a physical copy of the authorized BioFire Respiratory Panel 2.1-EZ (RP2.1-EZ) Quick Guide with each shipped kit, to authorized laboratories, and must make the authorized Instructions for Use electronically available with the opportunity to request a copy in paper form, and after

[12] "Authorized Distributor(s)" are identified by you, BioFire Diagnostics, LLC, in your EUA submission as an entity allowed to distribute your product.

such request, promptly provide the requested information without additional cost.

C. You and authorized distributor(s) must make your product available with the authorized labeling to authorized laboratories.

D. You and authorized distributor(s) must make available on your website(s) the authorized labeling.

E. You and authorized distributor(s) must inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

F. Through a process of inventory control, you and authorized distributor(s) must maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.

G. You and authorized distributor(s) must collect information on the performance of your product. You will report to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) any suspected occurrence of false positive and false negative results and significant deviations from the established performance characteristics of the product of which you become aware.

H. You and authorized distributor(s) are authorized to make available additional information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.

BioFire Diagnostics, LLC (You)

I. You must notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).

J. You must provide authorized distributor(s) with a copy of this EUA and communicate to authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).

K. You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling, including requests to make available additional authorized labeling specific to an authorized distributor. Such additional labeling may use another name for the product but otherwise must be consistent with the authorized labeling, and not exceed the terms of authorization of this letter. Any request for changes to this EUA should be submitted to DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.

L. You must comply with the following requirements pursuant to FDA regulations: 21 CFR 820 Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

M. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must ensure that the tests released for distribution have the clinical and analytical performance claimed in the authorized labeling.

N. If requested by FDA, you must submit lot release procedures to FDA, including sampling protocols, testing protocols, and acceptance criteria, that you use to release lots of your product for distribution in the U.S. If such lot release procedures are requested by FDA, you must provide it within 48 hours of the request.

O. You must evaluate the analytical limit of detection and assess traceability[13] of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA, you will update labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

P. You must evaluate the impact of viral mutations for your target analytes on your product's performance. Such evaluations must occur on an ongoing basis and must include any additional data analysis that is requested by FDA in response to any performance concerns you or FDA identify during routine evaluation. Additionally, if requested by FDA, you must submit records of these evaluations for FDA review within 48 hours of the request. If your evaluation identifies viral mutations that affect the stated expected performance of your device, you must notify FDA immediately.

Q. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA, such as those related to the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

R. You will have a process in place to track adverse events, including any occurrence of false results, and report to FDA pursuant to 21 CFR Part 803.

Authorized Laboratories

S. Authorized laboratories using your product must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

T. Authorized laboratories using your product must use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the

[13] Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.

U. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.

V. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

W. Authorized laboratories must collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and you (support@BioFireDX.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.

X. All laboratory personnel using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

BioFire Diagnostics, LLC (You), Authorized Distributors and Authorized Laboratories

Y. You, authorized distributors, and authorized laboratories using your product must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Printed Materials, Advertising and Promotion

Z. All descriptive printed matter, advertising and promotional materials relating to the use of your product shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and meet the requirements set forth in section 502(a), (q)(1), and (r) of the Act, as applicable, and FDA implementing regulations.

AA. No descriptive printed matter, advertising or promotional materials relating to the use of your product may represent or suggest that this test is safe or effective for the detection of SARS-CoV-2.

BB. All descriptive printed matter, advertising and promotional materials relating to the use of your product shall clearly and conspicuously state that:

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms; and,

- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

The emergency use of your product as described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure