April 4, 2024

Beth Stofka
Director, Regulatory Affairs
GenMark Diagnostics, Inc.
5964 La Place Court
Carlsbad, CA 92008

Device:	cobas eplex respiratory pathogen panel 2 (RP2 Panel)
EUA Number	EUA201822
Company:	GenMark Diagnostics, Inc.
Indication:	This test is authorized for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory viral and bacterial organisms[1], including nucleic acid from Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), in nasopharyngeal swab (NPS) specimens eluted in viral transport media obtained from individuals suspected of respiratory viral 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 requirements to perform moderate or high complexity tests.

Dear Beth Stofka:

On October 7, 2020, based on your request, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the ePlex Respiratory Pathogen Panel 2 (ePlex RP2 Panel) pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) for the indication stated in the letter[2]. In addition, FDA established

[1] The cobas eplex respiratory pathogen panel 2 (RP2 Panel) is intended for the detection and differentiation of nucleic acid from SARS-CoV-2 and the following virus types, subtypes, and bacteria: adenovirus, coronavirus (229E, HKU1, NL63, OC43), SARS-CoV-2, human metapneumovirus, human rhinovirus/enterovirus, influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3, parainfluenza virus 4, respiratory syncytial virus (RSV) A, respiratory syncytial virus (RSV) B, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*.

[2] The October 7, 2020, letter authorized the ePlex Respiratory Pathogen Panel 2 (ePlex RP2 Panel) for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory viral and bacterial organisms, including nucleic acid from Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), in nasopharyngeal swabs (NPS) eluted in viral transport media obtained from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. Emergency use of this test is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests. The ePlex RP2 Panel is intended for the

additional Conditions of Authorization in response to the continued emergence of new variants of SARS-CoV-2 on September 23, 2021[3].

On February 16, 2024, you[4] requested to revise your Emergency Use Authorization. Based on this request, and having concluded that revising the October 7, 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 7, 2020, letter in its entirety with the revisions incorporated.[5] Pursuant to section 564 of the Act and the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter, your product[6] is now authorized for use consistent with the indication described above.

On February 4, 2020, as amended on March 15, 2023, 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, or a significant potential for a public health emergency, that affects, or 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]

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). There are a few FDA-approved/cleared tests for simultaneous qualitative detection and differentiation of nucleic acids from SARS-CoV-2 and other respiratory pathogens, along in some cases with some other

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detection and differentiation of nucleic acid from SARS-CoV-2 and the following virus types, subtypes, and bacteria: adenovirus, coronavirus (229E, HKU1, NL63, OC43), SARS-CoV-2, human metapneumovirus, human rhinovirus/enterovirus, influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3, parainfluenza virus 4, respiratory syncytial virus (RSV) A, respiratory syncytial virus (RSV) B, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*.

[3] The Viral Mutation Revision Letter – September 23, 2021, can be accessed at: https://www.fda.gov/media/152406/download.

[4] For ease of reference, this letter will use the term "you" and related terms to refer to GenMark Diagnostics, Inc. GenMark Diagnostics, Inc. is a member of the Roche Group.

[5] The revisions to the October 7, 2020, letter and authorized labeling include: (1) updating the name of the EUA device from "ePlex Respiratory Pathogen Panel 2 (ePlex RP2 Panel)" to "cobas eplex respiratory pathogen panel 2 (RP2 Panel)," (2) adding a novel shelf-life claim of 30 days when stored at 25°C, based on the results of real-time shelf-life stability data, (3) updating the IFU, Fact Sheet for Healthcare Providers, Fact Sheet for Patients and the Letter of Authorization to reflect the updates made and for consistency with language used in more recent authorizations, (4) updating the results summary for the in silico inclusivity study in the IFU, (5) updating contact information in the IFU, and (6) providing minor edits to the IFU.

[6] For ease of reference, this letter will use the term "your product" to refer to the cobas eplex respiratory pathogen panel 2 (RP2 Panel) 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*. February 4, 2020. 85 FR 7316 (February 7, 2020). U.S. Department of Health and Human Services, Amended Determination of a Public Health Emergency or Significant Potential for a Public Health Emergency Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b). March 15, 2023. 88 FR 16644 (March 20, 2023) ("Amended Determination").

organism types and subtypes not targeted by your product, but they are not adequate and available alternatives to your product. Respiratory viral infections caused by SARS-CoV-2 and the other targeted respiratory pathogens 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 respiratory pathogens is needed. For example, the common influenza viruses that cause seasonal epidemics of flu, influenza A and B, is needed during the flu season that coincides with the COVID-19 pandemic. FDA has granted a De Novo classification request and cleared tests for the qualitative detection of nucleic acid from SARS-CoV-2, but these are not adequate and available alternatives to your product.[8]

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 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 qualitative detection and differentiation of nucleic acids from SARS-CoV-2 and other respiratory viral and bacterial organisms[9], and that the known and potential benefits of your product when used for such a use, 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.[10]

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.

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[8] To date, the FDA granted a De Novo classification request for the BioFire Respiratory Panel 2.1 (RP2.1) (Product Code: QOF; DEN200031) and cleared various tests (Search FDAs 510(k) Premarket Notification database; https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm; Product codes: QOF, QWR, QQX) for the qualitative detection of nucleic acid from SARS-CoV-2 in respiratory clinical specimens. Available information indicates that these are not adequate and available alternatives to your product.

[9] Refer to footnote 1.

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

Authorized Product Details

Your product is a multiplexed nucleic acid *in vitro* diagnostic test intended for use on the ePlex Instrument for the simultaneous qualitative detection and differentiation of nucleic acids from multiple respiratory viral and bacterial organisms, including nucleic acid from Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), in nasopharyngeal swab (NPS) specimens eluted in viral transport media (VTM) obtained from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and the targeted respiratory viral and bacterial organisms can be similar. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet requirements to perform moderate or high complexity tests.

You product is intended for the detection and differentiation of nucleic acid from SARS-CoV-2 and the following virus types, subtypes, and bacteria: adenovirus, coronavirus (229E, HKU1, NL63, OC43), SARS-CoV-2, human metapneumovirus, human rhinovirus/enterovirus, influenza A, influenza A H1, influenza A H1-2009, influenza A H3, influenza B, parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3, parainfluenza virus 4, respiratory syncytial virus (RSV) A, respiratory syncytial virus (RSV) B, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*.

SARS-CoV-2 RNA and nucleic acids from the other respiratory viral and bacterial organisms identified by this test are generally detectable in NPS specimens during the acute phase of infection. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and/or symptoms of respiratory infection aids in the diagnosis of respiratory infection when used in conjunction with other clinical and epidemiological information. 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 active infection with the identified respiratory pathogen but do not rule out infection or co-infection with non-panel organisms. The agent detected by the cobas eplex RP2 panel may not be the definitive cause of disease.

Negative results for SARS-CoV-2 and other organisms on the cobas eplex RP2 panel may be due to infection with pathogens that are not detected by this test, or lower respiratory tract infection that may not be detected by a nasopharyngeal swab specimen. Negative results do not preclude infection with SARS-CoV-2 or other organisms on the cobas eplex RP2 panel and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

Negative results for other organisms detected 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, when used with the ePlex instrument, or other authorized instruments, automates all aspects of nucleic acid testing including extraction, amplification, and detection, combining electrowetting and GenMark's eSensor technology in a single-use cartridge, for simultaneous detection and differentiation of nucleic acids from SARS-CoV-2 and other respiratory pathogens targeted by the panel from NPS specimens eluted in VTM. The cobas eplex respiratory pathogen panel 2 (RP2 Panel) includes the materials (or other authorized materials as may be requested under Condition N. below) described in the Instructions for Use.

Your product requires control materials (or other authorized control materials as may be requested under Condition N. below) that are described in the Instructions for Use.

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.

The labeling entitled "cobas eplex respiratory pathogen panel 2 package insert" Instructions for Use (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas), and the following fact sheets pertaining to the emergency use, are 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: GenMark Diagnostics, Inc. - cobas eplex respiratory pathogen panel 2 (RP2 Panel)
- Fact Sheet for Patients: GenMark Diagnostics, Inc. - cobas eplex respiratory pathogen panel 2 (RP2 Panel)

The above described product, when accompanied by the authorized labeling provided as set forth in the Conditions of Authorization (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 product, when 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, when used consistent with the 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), Subpart O (Statistical Techniques, 21 CFR 820.250), and Subpart M (Complaint Files, 21 CFR 820.198).

IV. Conditions of Authorization

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

GenMark Diagnostics, Inc. (You) and Authorized Distributor(s)[11]

A. Your product must comply with the following labeling requirements: 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 make your product available with the authorized labeling to authorized laboratories.

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

D. You and authorized distributor(s) must include a physical copy of the "cobas eplex respiratory pathogen panel 2 package insert" Instructions for Use with each shipped product to authorized laboratories.

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 your product and number of your product they distribute.

G. You and authorized distributor(s) must collect information on the performance of your product. You must report any significant deviations from the established performance

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

characteristics of your product of which you become aware to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) (via email: CDRH-EUAReporting@fda.hhs.gov).

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.

GenMark Diagnostics, Inc. (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 must comply with the following requirements: 21 CFR 820 Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), Subpart O (Statistical Techniques, 21 CFR 820.250), and Subpart M (Complaint Files, 21 CFR 820.198).

L. 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.

M. 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.

N. 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 must not exceed the terms of authorization of this letter. Any request for changes to this EUA should be submitted to DMD/OHT7/OPEQ/CDRH and requires appropriate authorization from FDA prior to implementation.

O. You must evaluate the analytical limit of detection and assess traceability[12] of your product with any FDA-recommended reference material(s) if requested by FDA. After submission to and concurrence with the data by FDA, you must update labeling to reflect the additional testing, if requested by FDA. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7/OPEQ/CDRH.

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

P. You must have a process in place to track adverse events and report to FDA pursuant to 21 CFR Part 803.

Q. You must evaluate the impact of SARS-CoV-2 viral mutations **and** all other 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 (via email: CDRH-EUA-Reporting@fda.hhs.gov).

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

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 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 must report any significant deviations from the established performance characteristics of your product of which they become aware to DMD/OHT7/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and you (via email: cad.technical_support_us@roche.com).

X. All laboratory personnel using your product must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

GenMark Diagnostics, Inc. (You), Authorized Distributor(s) and Authorized Laboratories

Y. You, authorized distributor(s) and authorized laboratories using your product must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records must 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 from SARS-CoV-2 and 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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Jeffrey E. Shuren, M.D., J.D.
Director
Center for Devices and Radiological Health
Food and Drug Administration

Enclosure