August 01, 2023

Marcia Eisenberg, PhD
Chief Scientific Officer & Senior Vice President
Laboratory Corporation of America
1912 Alexander Dr.
Research Triangle Park, NC 27709

Device:	Clear Dx SARS-CoV-2 WGS v3.0 Test
EUA Number:	EUA230011
Company:	Laboratory Corporation of America (Labcorp)
Indication:	This test is indicated for the identification and differentiation of SARS-CoV-2 Phylogenetic Assignment of Named Global Outbreak (PANGO) lineages, when clinically indicated, from individuals with a positive SARS-CoV-2-diagnostic test result. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Testing is limited to laboratories designated by Labcorp that are certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet requirements to perform high complexity tests.

Dear Dr. Eisenberg:

This letter is in response to your[1] request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of your product,[2] pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

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

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Laboratory Corporation of America ("Labcorp").
[2] For ease of reference, this letter will use the term "your product" to refer to the Clear Dx SARS-CoV-2 WGS v3.0 Test used for the indication identified above.

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.[3]

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 EUA Summary (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 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 identification and differentiation of SARS-CoV-2 Phylogenetic Assignment of Named Global Outbreak (PANGO) lineages, 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.[4]

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 next generation sequencing (NGS) test on the MinION sequencer from Oxford Nanopore Technologies (ONT) intended for the identification and differentiation of SARS-CoV-2 Phylogenetic Assignment of Named Global Outbreak (PANGO) lineages, when clinically indicated, from individuals with a positive SARS-CoV-2-diagnostic test result. Testing is limited

[3] 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").

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

to laboratories designated by Labcorp that are certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet requirements to perform high complexity tests.

Your product is intended to be used in conjunction with patient history and other diagnostic information, when clinically indicated, i.e., in situations where results may aid in determining appropriate clinical management. Results of this test are intended to be interpreted by the ordering health care professional. The test is not intended for use as an aid in the primary diagnosis of infection with SARS-CoV-2 or to confirm the presence of SARS-CoV-2 infection, and it is not intended for identification of specific SARS-CoV-2 genomic mutations. Results should not be used as the sole basis for treatment or other patient management decisions.

To use your product, extracted SARS-CoV-2 nucleic acid from SARS-CoV-2 positive specimens is reverse transcribed into cDNA, followed by PCR amplification steps, and whole genome sequencing using a MinION sequencing instrument as described in the authorized labeling (described below).

Your product uses all commercially sourced materials or other authorized materials and authorized ancillary reagents commonly used in clinical laboratories as described in the authorized labeling (described below).

Your product requires controls, as outlined in the authorized labeling (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 authorized labeling (described below).

The labeling entitled EUA Summary (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), the Labcorp standard operating procedures (SOPs) *i.e.*, SARS-CoV-2 Variant Identification SOP, Clear Dx WGS SARS-CoV-2 Analysis Pipeline SOP, and Clear Dx WGS SARS-CoV-2 v3.0 IFU, and the two fact sheets (listed below) pertaining to the emergency use, is required to be made available as set forth in the Conditions of Authorization (Section IV), and together are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: Labcorp – Clear Dx SARS-CoV-2 WGS v3.0 Test
- Fact Sheet for Patients: Labcorp – Clear Dx SARS-CoV-2 WGS v3.0 Test

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, through the identification and differentiation of SARS-CoV-2 Phylogenetic Assignment of Named Global Outbreak (PANGO) lineages, 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.

IV. Conditions of Authorization

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

Labcorp (You)

A. Your product must comply with the following labeling requirements pursuant to 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 must make available on your website(s), the authorized Fact Sheet for Healthcare Providers and Fact Sheet for Patients.

C. You 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.

D. You must make your product available with the authorized labeling to authorized laboratories and communicate any subsequent updates that might be made to this EUA and its authorized accompanying materials.

E. You must maintain records of the laboratories you designate as authorized laboratories and you must also maintain records of test usage by all such authorized laboratories.

F. You must inform relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

G. You must ensure that the authorized laboratories using your product have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

H. 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. Any request for changes to this EUA should be submitted to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) and require appropriate authorization from FDA prior to implementation.

I. You must collect information on the performance of your product. You must report to FDA any significant deviations from the established performance characteristics of your product of which you become aware.

J. You must have a process in place to track adverse events, including any occurrence of inaccurate results with your product and report to FDA pursuant to 21 CFR Part 803. Serious adverse events should immediately be reported to DMD/OHT7/OPEQ/CDRH (via email: CDRH-EUAReporting@fda.hhs.gov).

K. You must submit to FDA an SOP for the *in silico* analysis to assess the likelihood that probes fail to bind to variant regions, within 1 month of the date of this letter (unless otherwise agreed to with DMD/OHT7/OPEQ/CDRH). After submission to and concurrence with the SOP by FDA, you must update authorized labeling to reflect the additional SOP. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7/OPEQ/CDRH.

L. You must provide to FDA a software change protocol for PANGO software updates that may impact performance of your device, within 1 month of the date of this letter (unless otherwise agreed to with DMD/OHT7/OPEQ/CDRH). After submission to and concurrence with the change protocol by FDA, you must update authorized labeling to reflect the additional information. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7/OPEQ/CDRH, prior to implementation.

M. You must complete the additional software validation for your product in an FDA agreed upon post authorization study within 3 months of the date of this letter (unless otherwise agreed to with DMD/OHT7/OPEQ/CDRH) and submit the validation results for review and concurrence by DMD/OHT7/OPEQ/CDRH.

N. You must evaluate the impact of SARS-CoV-2 viral mutations 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).

O. 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

P. Authorized laboratories 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.

Q. 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.

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

S. 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.

T. Authorized laboratories using your product must collect information on the performance of your product and report to DMD/OHT7/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and you (via email: covid19requests@labcorp.com) any significant deviations from the established performance characteristics of your product of which they become aware.

U. All laboratory personnel using your product must be appropriately trained in the operation of the Clear Dx system, the MinION sequencer, and next generation sequencing workflows, as well as in vitro diagnostic procedures and use appropriate

laboratory and personal protective equipment when handling this kit and use your product in accordance with the authorized labeling.

Labcorp (You), Authorized Distributor(s) and Authorized Laboratories

V. 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

W. 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.

X. 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.

Y. 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 identification of SARS-CoV-2 PANGO Lineages, not for any other viruses or pathogens; 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