U.S. FOOD & DRUG ADMINISTRATION

April 20, 2021

Suzette Chance
Senior Director Regulatory Affairs
Cepheid
904 Caribbean Drive
Sunnyvale, CA 94089-1189

Device:	Xpert Omni SARS-CoV-2
EUA Number:	EUA202699
Company:	Cepheid
Indication	Qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (such as nasopharyngeal, oropharyngeal, anterior nasal, or mid-turbinate swab and/or nasal wash/aspirate) collected from individuals suspected of COVID-19 by their healthcare provider. Emergency use of this test is limited to use with the GeneXpert Omni System in authorized laboratories.
Authorized laboratories:	Testing of nasopharyngeal, oropharyngeal, anterior nasal, or mid-turbinate swab and nasal wash/aspirate specimens using the Xpert Omni SARS-CoV-2 test run on the GeneXpert Omni System is 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 or moderate complexity tests. Testing of nasopharyngeal, anterior nasal, or mid-turbinate swab specimens using the Xpert Omni SARS-CoV-2 test run on the GeneXpert Omni System is limited to laboratories certified under CLIA that meet the requirements to perform high, moderate or waived complexity tests. Testing of these specimens 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 Ms. Chance:

On November 27, 2020, based on your[1] request, the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the Xpert Omni SARS-CoV-2 pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3), for the qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (such as nasopharyngeal, oropharyngeal, nasal, or mid-turbinate swab and/or nasal wash/aspirate) collected from individuals suspected of COVID-19 by their healthcare provider. Testing was limited to use of the GeneXpert Omni System in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high or moderate complexity tests. Subsequently, on December 23, 2020, FDA granted your request to update your product labeling.[2]

On March 3, 2021, you requested to amend your Emergency Use Authorization (EUA). Based on that request and having concluded that revising the November 27, 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 November 27, 2020, letter in its entirety with the revisions incorporated.[3] 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[4] is now intended for the indication described above.

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.[5]
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).

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[1] For ease of reference, this letter will use the term "you" and related terms to refer to Cepheid.
[2] On December 23, 2020, your request was granted to update GeneXpert Omni System product labels to include the CE Mark.
[3] The revisions to the November 27, 2020, letter and authorized labeling include: (1) clarifying "nasal" as anterior nasal and testing of nasopharyngeal, anterior nasal, or mid-turbinate swab specimens using the Xpert Omni SARS-CoV-2 test run on the GeneXpert Omni System at laboratories certified under CLIA that meet the requirements to perform high, moderate or waived complexity tests - testing of these specimens 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, (2) use of eNAT as an alternate transport medium, (3) updated *in silico* inclusivity study results, (4) updates to the Healthcare Provider and Patient Fact Sheets to reflect POC use and language used in more recent authorizations, (5) addition of limitation statement regarding performance with circulating variants, and (6) addition of "Xpert Omni SARS-CoV-2 Electronic Labeling Flyer."
[4] For ease of reference, this letter will use the term "your product" to refer to the Xpert Omni SARS-CoV-2 used for the indication identified above.
[5] 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).

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 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, 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.[6]

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 qualitative test for the detection of nucleic acid from SARS-CoV-2 in upper respiratory specimens (such as nasopharyngeal, oropharyngeal, anterior nasal, or mid-turbinate swab and/or nasal wash/aspirate) collected from individuals suspected of COVID-19 by their healthcare provider. The SARS-CoV-2 nucleic acid is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 nucleic acid; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. Negative results do not preclude SARS-CoV-2 infection 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.

Testing of nasopharyngeal, oropharyngeal, anterior nasal, or mid-turbinate swab and nasal wash/aspirate specimens using your product run on the GeneXpert Omni System is limited to laboratories certified under CLIA, 42 U.S.C. § 263a, that meet the requirements to perform high

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

or moderate complexity tests. Testing of nasopharyngeal, anterior nasal, or mid-turbinate swab specimens using the Xpert Omni SARS-CoV-2 test run on the GeneXpert Omni System is limited to laboratories certified under CLIA that meet the requirements to perform high, moderate or waived complexity tests. Testing of these specimens 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 applicable authorized system, automates all aspects of nucleic acid testing including sample preparation, nucleic acid extraction, reverse transcription, amplification, and detection of the SARS-CoV-2 targeted sequences using real-time (RT) PCR assays in a single-use cartridge. The Xpert Omni SARS-CoV-2 test includes the following materials or other authorized materials: Xpert Omni SARS-CoV-2 Cartridges with Integrated Reaction Tubes and disposable transfer pipettes.

Your product also includes in the cartridge the following controls, or other authorized controls (as may be requested under Condition J. 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:

- Sample Processing Control (SPC) - controls for adequate processing of the sample and to monitor for the presence of potential inhibitor(s) in the RT-PCR reaction. The SPC also ensures that the RT-PCR reaction conditions (temperature and time) are appropriate for the amplification reaction and that the RT-PCR reagents are functional.
- Probe Check Control (PCC) - verifies reagent rehydration, PCR tube filling, and confirms that all reaction components are present in the cartridge including monitoring for probe integrity and dye stability.

For quality control, you recommend use of external positive and negative controls, or other authorized controls, to be run as outlined in the Instructions for Use, described below.

The labeling entitled "Xpert Omni SARS-CoV-2 Instructions for Use" (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), "Quick Reference Instructions for Xpert Omni SARS-CoV-2 and GeneXpert Omni System," "GeneXpert Omni System Operator Manual," "Xpert Omni SARS-CoV-2 Electronic Labeling Flyer," and "GeneXpert Omni Reference Guide," and the following fact sheets pertaining to the emergency use, which is required to be made available as set forth in the Conditions of Authorization (Section IV), are collectively referred to as the "authorized labeling:

- Fact Sheet for Healthcare Providers: Cepheid - Xpert Omni SARS-CoV-2
- Fact Sheet for Patients: Cepheid - Xpert Omni SARS-CoV-2

The above described product when accompanied by the authorized labeling 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), 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:

Cepheid (You) and Authorized Distributor(s)[7]

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).

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

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 include the "Xpert Omni SARS-CoV-2 Electronic Labeling Flyer" and "Quick Reference Instructions for Xpert Omni SARS-CoV-2 and GeneXpert Omni System" with each shipped product to authorized laboratories and will make the "Xpert Omni SARS-CoV-2 Instructions for Use," "GeneXpert Omni System Operator Manual," and the "GeneXpert Omni Reference Guide" electronically available, with the opportunity to request a copy in paper form, and promptly provide the requested information without additional cost.

D. 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.

E. 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.

F. You and authorized distributor(s) must collect information on the performance of your product. You will report to FDA any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the product of which you become aware.

G. 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.

Cepheid (You)

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

I. 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).

J. 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 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) and require appropriate authorization from FDA prior to implementation.

K. You must comply with the following requirements pursuant to FDA regulations: 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).

L. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must ensure that your product 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 must evaluate the analytical limit of detection and assess traceability[8] of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA, you will update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

O. You must have a process in place to track adverse events, including any occurrence of false results with your product and report to FDA pursuant to 21 CFR Part 803.

Authorized Laboratories

P. 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.

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 must collect information on the performance of your product and

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

report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and you (via phone: +1 888.838.3222 or via email: techsupport@cepheid.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.

U. 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.

Cepheid (You), Authorized Distributors and Authorized Laboratories

V. 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

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 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 detection of nucleic acid from SARS-CoV-2, 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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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure