

January 7, 2021

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

Device: Xpert Xpress SARS-CoV-2

Company: Cepheid

Indications: Qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (i.e., nasopharyngeal, oropharyngeal, nasal, or mid-turbinate swab or nasal wash/aspirate) collected from individuals suspected of COVID-19 by their healthcare provider.

Emergency use of this test is limited to authorized laboratories.

Authorized Laboratories: Testing of nasopharyngeal, oropharyngeal, nasal, or mid-turbinate swab or nasal wash/aspirate specimens using the Xpert Xpress SARS-CoV-2 test run on the GeneXpert Dx and GeneXpert Infinity Systems is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high or moderate complexity tests.

Testing of nasopharyngeal, nasal, or mid-turbinate swab specimens using the Xpert Xpress SARS-CoV-2 test run on the GeneXpert Xpress System (Tablet and Hub Configurations) is limited to laboratories certified under CLIA that meet 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 March 20, 2020, based on your¹ request, the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the Xpert Xpress SARS-CoV-2 test pursuant to Section 564 of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3) for the

¹ For ease of reference, this letter will use the term “you” and related terms to refer to Cepheid.

qualitative detection of nucleic acid from the SARS-CoV-2 in: (1) nasopharyngeal swab and nasal wash/aspirate specimens collected from individuals suspected of COVID-19 by their healthcare provider, to be used with the GeneXpert Dx and GeneXpert Infinity Systems in authorized laboratories; and (2) nasopharyngeal swab specimens collected from individuals suspected of COVID-19 by their healthcare provider, for distribution and use in patient care settings using the GeneXpert Xpress System (Tablet and Hub Configurations).² Based on your requests, FDA has granted updates to the Instructions for Use (IFU) on April 28, 2020³ and August 8, 2020.⁴

On November 13, 2020, you requested to further revise your Emergency Use Authorization (EUA). Based on this request, and having concluded that revising the March 20, 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 March 20, 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 product⁶ is now authorized for use consistent with 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.⁷

² The March 20, 2020, letter defined “Authorized Laboratories and Other Authorized Testing Locations” as : Authorized laboratories - laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high and moderate complexity tests. Other Authorized Testing Locations - Patient care settings.

³ On April 28, 2020, your request was granted to (1) add an Early Assay Termination (EAT) feature to the Assay Definition File (ADF), (2) add saline as an alternative swab transport media, (3) add oropharyngeal swab specimen to the Intended Use for the moderate or high complexity assays, (4) include labeling changes to accommodate co-labeling with CE mark, (5) make additional minor edits, and (6) make associated updates to the Healthcare Provider Fact Sheet.

⁴ On August 8, 2020, your request was granted to (1) update the Limit of Detection and Clinical data in the Performance Characteristics section to reflect a change in one of the cartridge reagent sources, (2) update the number of transfer pipettes supplied with the kit, (3) update the in silico inclusivity information, (4) update the limitations section to remove reference to symptomatic population testing with nasal and mid-turbinate swabs, (5) add assay cutoff information, and (6) make some additional minor clarifications and edits, including to the Healthcare Provider and Patient Fact Sheets.

⁵ The revisions to the March 20, 2020, letter include: (1) updating the IFU for the Xpert Xpress SARS-CoV-2 to include recent in silico inclusivity study results; (2) updating the Intended Use to include more recent language used to describe authorized laboratories; and (3) minor edits and clarifications, including to update and consolidate conditions of authorization to reflect language used in more recent authorizations.

⁶ For ease of reference, this letter will use the term “your product” to refer to the Xpert Xpress SARS-CoV-2 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).

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 included in both 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 II) of this letter, 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.⁸

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 indications above.

Authorized Product Details

Your product is for the qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (i.e., nasopharyngeal, oropharyngeal, nasal, or mid-turbinate swab or nasal wash/aspirate) collected from individuals suspected of COVID-19 by their healthcare provider. The SARS-CoV-2 RNA is generally detectable in upper respiratory specimens during the acute phase of infection. Positive results are indicative of active infection with SARS-CoV-2; 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 treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

Testing of nasopharyngeal, oropharyngeal, nasal, or mid-turbinate swab and nasal wash/aspirate specimens using your product run on the GeneXpert Dx and GeneXpert Infinity systems, and using authorized instruments and software within the System as outlined in the “Xpert Xpress

⁸ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

SARS-CoV-2 Instructions for Use -For Use with GeneXpert Dx or GeneXpert Infinity Systems,” is limited to laboratories certified under the CLIA to perform high and moderate complexity tests.

Testing of nasopharyngeal, nasal, or mid-turbinate swab specimens using your product run on the point of care GeneXpert Xpress System (Tablet and Hub Configurations), using authorized instruments and software within the System as outlined in the point of care “Xpert Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Xpress System (point of care system),” and the associated Quick Reference Instructions for the Tablet and Hub Configurations, is limited to laboratories certified under CLIA that meet 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 systems automates all aspects of nucleic acid testing including sample preparation, nucleic acid extraction and amplification, and detection of the SARS-CoV-2 targeted sequences using real-time (RT) PCR assays in a single-use cartridge. The Xpert Xpress SARS-CoV-2 includes the following materials or other authorized materials: Xpert Xpress SARS-CoV-2 Cartridges with Integrated Reaction Tubes, disposable transfer pipettes, CD – containing assay definition file.

Your product also includes in the cartridge the following controls, or other authorized control materials (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

You also recommend use of external positive and negative controls, or other authorized controls, to be run as outlined in both sets of 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 both sets of Instructions for Use, described below.

The above described product is authorized to be accompanied with labeling entitled “Xpert Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Dx or GeneXpert Infinity Systems,” “Xpert Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Xpress System (point of care system),” “Quick Reference Instructions for Xpert Xpress SARS-CoV-2 and GeneXpert Xpress System (Hub configuration),” and “Quick Reference Instructions for Xpert Xpress SARS-CoV-2 and GeneXpert Xpress System (Tablet configuration),” (all available at <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use->

[authorizations-medical-devices/vitro-diagnostics-euas](#)), and the following product-specific information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

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

The above described product, when accompanied by the two Instructions for Use, two Quick Reference Instructions (identified above) and the two Fact Sheets (collectively referenced as “authorized labeling”) 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 for the qualitative detection of SARS-CoV-2 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, 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 indications 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)⁹

- 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 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 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/or 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 and 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).

⁹ “Authorized Distributor(s)” are identified by you, Cepheid, in your EUA submission as an entity allowed to distribute your product.

- 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, 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 (OHT 7) - 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 evaluate the analytical limit of detection and assess traceability¹⁰ of your product with any FDA-recommended reference material(s). After submission to and review and concurrence with the data by FDA, you must update labeling to reflect the additional testing. Such labeling updates must be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- L. You will 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).
- 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 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

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

Cepheid (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 will be made available to FDA for inspection upon request.

Conditions Related to 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 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
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- 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,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure