

March 20, 2020

Ronald D. Dunn
Vice President Global Regulatory Affairs
Cepheid
904 Caribbean Drive,
Sunnyvale, CA 94089-1189 US

Device: Xpert Xpress SARS-CoV-2 test
Company: Cepheid
Indications: 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. Emergency use of this test is limited to use of 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. Emergency use of this test is authorized to be distributed and used in patient care settings using the GeneXpert Xpress System (Tablet and Hub Configurations).

Authorized Laboratories and Other Authorized Testing Locations:

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

Dear Mr. Dunn:

This letter is in response to your¹ 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, 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

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

² For ease of reference, this letter will use the term “your product” to refer to the Xpert Xpress SARS-CoV-2 used for the indications identified above.

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-19.³ 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.⁴

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 Section of this letter (Section II), subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

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

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your product may be effective in diagnosing COVID-19, 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.⁵

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 nasopharyngeal swab and/or nasal wash/aspirate specimens collected from individuals suspected of COVID-19 by their healthcare provider. The SARS-CoV-2 RNA is generally detectable in nasopharyngeal swab specimens and/or nasal wash/aspirate 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

³ On February 11, 2020, the virus tentatively named 2019-nCoV was formally designated as Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Also on February 11, 2020, the disease caused by SARS-CoV-2 was formally designated as Coronavirus Disease 2019 (COVID-19). This document uses the updated names.

⁴ 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.

⁵ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

infection status. Positive results do not rule out bacterial infection or co-infection with other viruses.

Testing of nasopharyngeal 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 SARS-CoV-2 Instructions for Use - For Use with GeneXpert Dx or GeneXpert Infinity systems”, is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high and moderate complexity tests.

Testing of nasopharyngeal 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” and the associated Quick Reference Instructions for the Tablet and Hub Configurations, is authorized to be distributed and used in patient care settings outside of the clinical laboratory environment.

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 Test 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 controls, 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, when labeled consistently with the labeling authorized by FDA, entitled “Xpert Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Dx or GeneXpert Infinity systems” (available at <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>), which may be revised in consultation

with, and with concurrence of, the Division of Microbiology Devices (DMD)/Office of Health Technology 7 Office of In Vitro Diagnostics and Radiological Health (OHT7-OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH), 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.

The above described product, when labeled consistently with the labeling authorized by FDA, entitled “Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Xpress 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/emergency-situations-medical-devices/emergency-use-authorizations>), which may be revised in consultation with, and with concurrence of, the Division of Microbiology Devices (DMD)/Office of Health Technology 7 Office of In Vitro Diagnostics and Radiological Health (OHT7-OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH), is authorized to be distributed to and used in patient care settings using the point of care GeneXpert Xpress System (Tablet and Hub Configurations) despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

Your product is authorized to be accompanied by 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: Xpert Xpress SARS-CoV-2
- Fact Sheet for Patients: Xpert Xpress SARS-CoV-2

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your authorized product, when used for the qualitative detection of SARS-CoV-2 and used consistently 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 for the indications above, when used consistently 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) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1),

your product is authorized for the indications above.

This EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under Section 564(b)(2) of the Act or when the EUA is revoked under Section 564(g) of the Act.

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:

Cepheid (You) and Authorized Distributor(s)⁶

- 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)); any 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) will make your product available with the authorized labeling to authorized laboratories and patient care settings. You may request changes to the authorized labeling. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- C. You and authorized distributor(s) will provide to authorized laboratories and patient care settings the Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients. You may request changes to the authorized Fact Sheets. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- D. You and authorized distributor(s) will make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.

⁶ “Authorized Distributor(s)” are identified by you, Cepheid, in your EUA submission as an entity allowed to distribute your device to authorized laboratories, and to patient care settings that use the point of care GeneXpert Xpress System (Tablet and Hub Configurations).

- E. You and authorized distributor(s) will inform relevant public health authorities, authorized laboratories and patient care settings of this EUA, including the terms and conditions herein, and any updates made to your product, authorized labeling and authorized Fact Sheets.
- F. Through a process of inventory control, you and authorized distributor(s) will maintain records of the authorized laboratories and patient care settings to which they distribute the test and number of tests they distribute.
- G. You and authorized distributor(s) will 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.
- 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.

Cepheid (You)

- I. You will notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).
- J. You will provide its authorized distributor(s) with a copy of this EUA and communicate to authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).
- K. You may request changes to the Scope of Authorization (Section II in this letter) of your product. Such requests will be made in consultation with DMD/OHT7-OIR/OPEQ/CDRH, and require concurrence of, Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and DMD/OHT7-OIR/OPEQ/CDRH.
- L. You may request the addition of other instruments and associated software within the GeneXpert Dx, GeneXpert Infinity, or point of care GeneXpert Xpress Systems for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- M. You may request the addition of other specimen types for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- N. You may request the addition and/or substitution of primers or probes for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- O. You may request the addition and/or substitution of control materials for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- P. You may request the addition and/or substitution of other ancillary reagents and materials for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- Q. You will evaluate the analytical limit of detection and assess traceability⁷ of your product with any FDA-recommended reference material(s). After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, You will update its labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- R. You will complete the agreed upon analytical sensitivity study by assessing the limit of detection using virus with your product within 15 days of the date of this letter. After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, you will update its labeling to reflect the additional study. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- S. You will track adverse events, including any occurrence of false results and report to FDA under 21 CFR Part 803.

Authorized Laboratories and Patient Care Settings

- T. Authorized laboratories and patient care settings using your product will include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- U. Authorized laboratories using your product will use your product as outlined in the Xpert Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Dx or GeneXpert Infinity systems. 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.
- V. Patient Care Settings using your product will use your product as outlined in the point of care Xpress SARS-CoV-2 Instructions for Use - For Use with GeneXpert Xpress System and associated 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).

⁷ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

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.

- W. Authorized laboratories and patient care settings that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- X. Authorized laboratories and patient care settings using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Y. Authorized laboratories and patient care settings will collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and You (+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.
- Z. 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 Distributors and Authorized Laboratories and Patient Care Settings

- AA. You, authorized distributors, and authorized laboratories and patient care settings using your product will 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

- BB. All advertising and promotional descriptive printed matter relating to the use of your product shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.
- CC. All advertising and promotional descriptive printed matter relating to the use of your product shall clearly and conspicuously state that:
 - This test has not been FDA cleared or approved;
 - This test has been authorized by FDA under an EUA for use by authorized laboratories;

- This test has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

No advertising or promotional descriptive printed matter 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.

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 diagnostic tests 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

Enclosures