



September 10, 2021

Julie Purcell
Director, US Regulatory Affairs
Cepheid
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Sunnyvale, CA 94089-1189

Device: Xpert Xpress CoV-2/Flu/RSV *plus*

EUA Number: EUA210505

Company: Cepheid

Indication: For certain authorized laboratories (see below) – Simultaneous qualitative detection and differentiation of RNA from SARS-CoV-2, influenza A, influenza B, and/or respiratory syncytial virus (RSV) in either nasopharyngeal swab, anterior nasal swab or nasal wash/aspirate specimens run on the GeneXpert Dx and GeneXpert Infinity Systems collected from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider.

For certain authorized laboratories (see below) – Simultaneous qualitative detection and differentiation of RNA from SARS-CoV-2, influenza A, influenza B, and/or respiratory syncytial virus (RSV) in nasopharyngeal or anterior nasal swab specimens run on the GeneXpert Xpress System (Tablet and Hub Configurations) collected 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: Testing of nasopharyngeal swab, anterior nasal swab or nasal wash/aspirate specimens 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 or anterior nasal swab specimens run on the GeneXpert Xpress System (Tablet and Hub Configurations) 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. Purcell:

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 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.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 “Xpert Xpress CoV-2/Flu/RSV *plus* For Use with GeneXpert Dx or GeneXpert Infinity Systems,” and the “Xpert Xpress CoV-2/Flu/RSV *plus* For Use with GeneXpert Xpress System” Instructions for Use (identified below).

There are FDA-approved/cleared tests for SARS CoV-2, influenza A virus, influenza B virus and respiratory syncytial virus (RSV), but this is not an adequate and available alternative to your product. Respiratory viral infections caused by the influenza A and B viruses, RSV and SARS-CoV-2 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, the common influenza viruses that cause seasonal epidemics of flu, and disease caused by RSV is needed.

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;

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 CoV-2/Flu/RSV *plus* used for the indication identified above.

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. 85 FR 7316 (February 7, 2020).

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 detection and differentiation of nucleic acid from SARS-CoV-2 virus, influenza A, influenza B and respiratory syncytial virus (RSV) 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 rapid, multiplexed real-time RT-PCR test intended for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV) viral RNA in either nasopharyngeal swab, anterior nasal swab or nasal wash/ aspirate specimens collected 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, influenza A, influenza B, and RSV can be similar.

Your product is intended for use with nasopharyngeal swab, anterior nasal swab or nasal wash/ aspirate specimens using the GeneXpert Dx and GeneXpert Infinity systems in laboratories certified under CLIA that meet requirements to perform high or moderate complexity tests and with nasopharyngeal and anterior nasal swab specimens using the GeneXpert Xpress System (Tablet and Hub Configurations) in POC settings, i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation. Your product is intended for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, influenza B virus and RSV nucleic acids in clinical specimens and is not intended to detect influenza C virus. RNA from SARS-CoV-2, influenza A virus, influenza B virus and RSV is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of the identified virus, but do not rule out bacterial infection or co-infection with other pathogens not detected by the test. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2, influenza A virus, influenza B virus and RSV 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.

To use your product, the respiratory specimen is transferred to the Xpert Xpress CoV-2/Flu/RSV cartridge; the cartridge is loaded onto the GeneXpert Instrument System platform (GeneXpert

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

Dx, GeneXpert Infinity or GeneXpert Xpress), which performs automated sample processing. The GeneXpert Instrument Systems automate and integrate sample preparation, nucleic acid extraction and amplification and detection of the target sequences using real-time PCR assays. The Xpert Xpress CoV-2/Flu/RSV *plus* includes the following materials or other authorized materials: Cartridges with Integrated Reaction Tubes containing freeze-dried beads (Bead 1, Bead 2 and Bead 3), lysis reagent, binding reagent, elution reagent, wash reagent, and controls and disposable transfer pipettes.

Your product requires the following control materials, or other authorized control materials (as may be requested under Condition K below), that are processed automatically with each batch of specimens tested with your product. All 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 – an positive control ensures that the sample was processed correctly; detects sample-associated inhibition, ensures that PCR reaction conditions (temperature and time) are appropriate and that PCR reagents are functional.
- Probe Check Control – a measurement of the background fluorescent signal from the probes to monitor reagent bead hydration, reaction tube filling, probe integrity, and dye stability.

You also recommend use of external controls (not provided with your product), or other authorized controls (as may be requested under Condition K below), that are commercially available and are run as outlined in the Instructions for Use:

- External Positive Control – inactivated Flu/RSV/SARS-CoV-2
- External Negative Control – inactivated Coxsackievirus

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 “Xpert Xpress CoV-2/Flu/RSV *plus* For Use with GeneXpert Dx or GeneXpert Infinity Systems,” the “Xpert Xpress CoV-2/Flu/RSV *plus* For Use with GeneXpert Xpress System,” the “Quick Reference Instructions for Xpert Xpress CoV-2/Flu/RSV *plus* and GeneXpert Xpress System (Tablet Configuration)” and the “Quick Reference Instructions for Xpert Xpress CoV-2/Flu/RSV *plus* and GeneXpert Xpress System (Hub Configuration)” (available at <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>), the Flyer insert and the following fact sheets pertaining to the emergency use, is 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: Cepheid – Xpert Xpress CoV-2/Flu/RSV *plus*
- Fact Sheet for Patients: Cepheid – Xpert Xpress CoV-2/Flu/RSV *plus*

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), 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)⁵

⁵ “Authorized Distributor(s)” are identified by you, Cepheid, in your EUA submission as an entity allowed to distribute your product.

- 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 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 physical copies of the Flyer insert, the “Quick Reference Instructions for Xpert Xpress CoV-2/Flu/RSV *plus* and GeneXpert Xpress System (Tablet Configuration)” and the “Quick Reference Instructions for Xpert Xpress CoV-2/Flu/RSV *plus* and GeneXpert Xpress System (Hub Configuration)” with each shipped product to authorized laboratories, and will make the authorized “Xpert Xpress CoV-2/Flu/RSV *plus* For Use with GeneXpert Dx or GeneXpert Infinity Systems,” and the “Xpert Xpress CoV-2/Flu/RSV *plus* For Use with GeneXpert Xpress System,” electronically available with the opportunity to request a copy in paper form, and after such request, you must promptly provide the requested information without additional cost.
- 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 they distribute.
- G. You and authorized distributor(s) must collect information on the performance of your product. You will report to 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) 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.
- 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 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 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 DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.
- L. You must comply with the following requirements pursuant to FDA regulations: 21 CFR 820 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 evaluate the analytical limit of detection and assess traceability⁶ of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA, you must 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.
- P. You must further evaluate the clinical performance of your product in an FDA agreed upon post authorization clinical evaluation study within 6 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you must update authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- Q. You will further perform an additional potential competitive interference study in an FDA agreed upon post authorization study within 30 calendar days of the date of this

⁶ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you will update your labeling to reflect the additional analysis. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- R. You must evaluate the impact of viral mutations for your 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.
- S. You must evaluate the impact of viral mutations for your 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.
- T. 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

- U. 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.
- V. 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.
- W. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- X. 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.
- Y. 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 you 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.

- Z. All operators 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

- AA. 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

- BB. All descriptive printed matter, including 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.
- CC. 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.
- DD. 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 acids from SARS-CoV-2, influenza A, influenza B, and respiratory syncytial virus (RSV), 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,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure

Technical correction September 13, 2021: correct name of device and names of authorized labeling in body of letter