

March 31, 2020

To: Laboratories Who Have Developed a Molecular-Based Test (LDTs) for Coronavirus Disease 2019 (COVID-19)¹

Authorized Tests: Molecular-based Laboratory Developed Tests for Detection of Nucleic Acid from SARS-CoV-2 (Molecular LDT COVID-19).

Indication: Qualitative detection of nucleic acid from SARS-CoV-2 in respiratory specimens collected from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to the authorized laboratories.

Authorized Laboratories: Testing is limited to the single laboratory that developed the authorized test and that is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a to perform high complexity tests.

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.²

On March 31, 2020, in response to this evolving public health emergency and continued concerns from clinical laboratories about the availability of sufficient in vitro diagnostic tests, FDA has concluded based on the totality of scientific evidence available that molecular-based laboratory developed tests that are authorized for use by the singular developing laboratory are appropriate to protect the public health or safety (as described under the Scope of Authorization (Section II)) under section 564 of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. § 360bbb-3). Under this EUA, authorized tests are authorized for use in the single laboratory that

¹ 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.

² 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.

developed the authorized test and that is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests.

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 the authorized tests,³ as described in the Scope of Authorization (Section II) and pursuant to the Conditions of Authorization (Section IV) of this letter for use in the single laboratory that developed the authorized test to detect SARS-CoV-2 in specimens from individuals suspected of COVID-19 by their healthcare provider. Authorized tests will be added to this letter of authorization in Appendix A which will be maintained on FDA's webpage.⁴

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the authorized tests 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 the authorized tests may be effective in diagnosing COVID-19, and that the known and potential benefits of the authorized tests when used for diagnosing COVID-19, outweigh the known and potential risks of the authorized tests; and
3. There is no adequate, approved, and available alternative to the emergency use of the authorized tests.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 indication above.

Tests Eligible for Authorization

Tests are eligible for authorization under this EUA if:

1. The test is the subject of an EUA request⁶ that includes submission of a completed "Accelerated" Template for Laboratories Certified to Perform High-

³ For ease of reference, this letter will refer to "authorized tests" as Molecular-based Laboratory Developed Tests for Detection of Nucleic Acid from SARS-CoV-2 (Molecular LDT COVID-19) that meet the criteria for issuance under this EUA and are listed in Appendix A for the identified intended use.

⁴ CDRH EUA webpage <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>.

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

⁶ Please also refer to the "Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff: Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency": <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-diagnostic-tests-coronavirus-disease-2019-during-public-health-emergency>

Complexity Testing Under CLIA: EUA Template or equivalent data and the laboratory developed test procedure for performing the authorized test;⁴

2. The test is a molecular-based test for the qualitative detection of nucleic acid from SARS-CoV-2 in respiratory specimens collected from individuals suspected of COVID-19 by their healthcare provider;
3. Testing is limited to the single laboratory that developed the test, and that is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests;
4. The test is either new and not covered at the time of the EUA request by an existing commercially distributed EUA-authorized test, or the test represents a significant deviation from an existing commercially distributed EUA-authorized test and is not otherwise currently marketed in the U.S.;
5. The test is a typical real-time reverse transcription PCR test in which SARS-CoV-2 nucleic acid is first extracted, isolated and purified from human respiratory specimens, using authorized extraction methods. The purified nucleic acid is then reverse transcribed into cDNA followed by nucleic acid amplification and detection using an authorized detection instrument;
6. The test uses test material components that are either designed and manufactured by the laboratory or represent commercially sourced materials, such as research use only (RUO) components from third party manufacturers in addition to other authorized materials and authorized ancillary reagents commonly used in clinical laboratories as described in the authorized test procedures submitted as part of the EUA request, and;
7. The test uses some combination of the following control materials, or other authorized control materials, that are to be run as outlined in the authorized procedures submitted as part of the EUA request. The controls when used in combination must evaluate all aspects of the authorized test procedure. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the authorized test procedures submitted as part of the EUA request:
 - Internal Process Control (IPC) – included in each clinical sample and controls for specimen quality and demonstrates that nucleic acid was generated by the extraction process. Examples include endogenous RNA control such as RNase P (RP) control and exogenous RNA, such as MS2 bacteriophage.
 - Extraction Control (EC) – serves both as a negative extraction control to monitor for any cross-contamination that occurs during the extraction process, and can validate extraction reagents and successful RNA extraction when used in combination with certain IPC. Example includes a previously characterized negative patient sample.
 - External Positive Control or Positive Template Control (PTC) - contains SARS-CoV-2 genomic regions targeted by the test. The positive control is used to monitor for failures of rRT-PCR reagents and reaction conditions.

Examples include in vitro transcript SARS-CoV-2 RNA, pseudo SARS-CoV-2 virus, previously characterized positive patient specimen.

- No Template (Negative) Control (NTC) - used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents. Examples include nuclease-free, molecular-grade water or buffer.

Authorized Tests

The above described eligible tests, when labeled consistently with the authorized test procedures submitted as part of the EUA request, and as described in the EUA summary (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), are authorized to be used by the laboratory that developed the authorized test, despite the fact that they do not meet certain requirements otherwise required by applicable federal law.

Authorized tests are authorized to be accompanied by the following product information pertaining to their emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Molecular LDT COVID-19 Authorized Test
- Fact Sheet for Patients: Molecular LDT COVID-19 Authorized Test

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 the authorized tests outweigh the known and potential risks of such authorized tests.

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 the authorized tests may be effective for the indication 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 the authorized tests (as described in the Scope of Authorization of this letter (Section II)) meet the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized tests 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), the product is authorized for the indication 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 the 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:

Authorized Laboratories

- A. Your authorized test 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 will inform relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your authorized test, authorized labeling and authorized Fact Sheets.
- C. You will notify the relevant public health authorities of your intent to run your authorized test.
- D. You will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- E. You will include with result reports of your authorized test, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- F. You will make available on your website(s), if applicable, the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.
- G. You are authorized to make available additional information relating to the emergency use of your authorized test that is consistent with, and does not exceed, the terms of this

letter of authorization.

- H. You will use your authorized test as outlined in the authorized test procedures submitted as part of the EUA request. Deviations from the authorized test procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and/or authorized materials required to use your product are not permitted.
- I. You will collect information on the performance of your authorized test. You will report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your authorized test of which you become aware.
- J. You may request changes to the Scope of Authorization (Section II in this letter) of your authorized test. 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.
- K. 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.
- L. 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.
- M. You may request the addition of other instruments and associated software for use with your authorized test. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- N. You may request the addition of other extraction methods for use with your authorized test. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- O. You may request the addition of other specimen types for use with your authorized test. 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 primers or probes for use with your authorized test. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- Q. You may request the addition and/or substitution of control materials for use with your authorized test. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- R. You may request the addition and/or substitution of other ancillary reagents and materials for use with your authorized test. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- S. You will evaluate the analytical limit of detection and assess traceability of your authorized test with any FDA-recommended reference material(s), if requested by FDA⁷. After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, FDA will update the EUA summary to reflect the additional testing. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- T. You will track adverse events, including any occurrence of false results with your authorized test and report any such events to FDA under 21 CFR Part 803.
- U. All laboratory personnel using your authorized test must be appropriately trained in molecular techniques and use appropriate laboratory and personal protective equipment when handling this product, and use your authorized test in accordance with the authorized test procedure.
- V. You 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

- W. All advertising and promotional descriptive printed matter relating to the use of your authorized test 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.
- X. All advertising and promotional descriptive printed matter relating to the use of your authorized test 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

⁷ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material. FDA may request, for example, that you perform this study in the event that we receive reports of adverse events concerning your authorized test.

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 authorized test 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