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Device: SARS-CoV-2 real time RT-PCR test

Sponsor: University of Louisville Infectious Diseases Laboratory

Indication: The SARS-CoV-2 assay is a real-time RT PCR (RT-PCR) test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal (NP) swabs specimens from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to the University of Louisville Infectious Diseases Laboratory that is a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high complexity laboratory.

Results are for the detection of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; 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. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

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.

The assay is intended for use under the Food and Drug Administration's (FDA) Emergency Use Authorization.

Dear Dr. Wolf:

This letter is in response to your request that the U.S. Department of Health and Human Services (HHS) issue an Emergency Use Authorization (EUA) for emergency use of the University of Louisville Infectious Diseases Laboratory SARS-CoV-2 real time RT-PCR test for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal (NP) swabs specimens from individuals suspected of COVID-19 by their healthcare provider,

pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). Testing is limited to applying laboratory and, in the United States, certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity tests.¹

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of 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 2019-nCoV. 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 novel coronavirus (2019-nCoV) subject to the terms of any authorization issued under Section 564(a) of the Act.²

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 SARS-CoV-2 real time RT-PCR test (as described in the scope Section of this letter (Section II)) in individuals who meet University of Louisville Infectious Diseases Laboratory criteria for 2019-nCoV testing for the presumptive detection of 2019-nCoV by the authorized laboratory, subject to the terms of this authorization, including additional evaluation of clinical samples. Please increase the total number of samples in the method comparison to include at least 30 positives and 30 negatives (specifically an additional 5 positive and 5 negatives). Additional samples can be actual clinical samples added to the previous study. Please report the performance of the additional samples including performance estimates for positive percent agreement and negative percent agreement for the entire study within 30 days of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the SARS-CoV-2 real time RT-PCR test in individuals who meet University of Louisville Infectious Diseases Laboratory criteria for 2019-nCoV testing meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

1. The 2019-nCoV 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 HHS, it is reasonable to believe that the University of Louisville Infectious Diseases Laboratory SARS-CoV-2 real time RT-PCR test may be effective in diagnosing 2019-nCoV infection, and that the known and potential benefits of the SARS-CoV-2 real time RT-PCR test, when used for diagnosing 2019-nCoV infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the SARS-CoV-2 real time RT-PCR test for diagnosing 2019-nCoV infection.³

¹ For ease of reference, this letter will refer to “qualified laboratories designated by CDC and, in the United States, certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high complexity tests” as “authorized laboratory.”

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.

³ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

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 use of the authorized SARS-CoV-2 real time RT-PCR test by the authorized laboratory for the presumptive detection of 2019-nCoV in individuals who meet University of Louisville Infectious Diseases Laboratory criteria for 2019-nCoV testing.

The Authorized SARS-CoV-2 real time RT-PCR test

The SARS-CoV-2 real time RT-PCR test is for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal (NP) swabs specimens from individuals suspected of COVID-19 by their healthcare provider. The University of Louisville SARS-CoV-2 assay is performed on the Food and Drug Administration's (FDA) cleared Luminex ARIES Instrument. The instrument has also been authorized with an assay developed and distributed by Luminex. The Luminex ARIES Instrument is capable of automated extraction and purification of nucleic acids from multiple sample types. The University of Louisville uses the same reagents that Luminex provides for their system except the primers and probes. University of Louisville chose to use two primers and probes sequences (N1 and N3) originally identified and used by the CDC in its assay.

The above described SARS-CoV-2 real time RT-PCR test, when labeled consistently with the labeling authorized by HHS, entitled "SARS-CoV-2 real time RT-PCR test Instructions for Use" (available at <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>), which may be revised by University of Louisville Infectious Diseases Laboratory 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 used by the authorized laboratory under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

The above-described SARS-CoV-2 real time RT-PCR test is authorized to be accompanied by the following information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: SARS-CoV-2 real time RT-PCR test
- Fact Sheet for Patients: SARS-CoV-2 real time RT-PCR 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 SARS-CoV-2 real time RT-PCR test when used for the presumptive detection of 2019-nCoV and used consistently with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of such a product.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to HHS, that it is reasonable to believe that the authorized SARS-CoV-2 real time RT-PCR test may be effective in the presumptive detection of 2019-nCoV, when used consistently with the Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

HHS has reviewed the scientific information available to HHS, including the information supporting the conclusions described in Section I above, and concludes that the authorized SARS-CoV-2 real time RT-PCR test, when used for detection of the 2019-nCoV in the specified population (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 the authorized SARS-CoV-2 real time RT-PCR test 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 SARS-CoV-2 real time RT-PCR test described above is authorized to detect 2019-nCoV in individuals who meet University of Louisville Infectious Diseases Laboratory criteria for 2019-nCoV testing.

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 SARS-CoV-2 real time RT-PCR test 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, and storage of the SARS-CoV-2 real time RT-PCR test
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 21 CFR 809.30, except for 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)

IV. Conditions of Authorization

Pursuant to Section 564(e) of the Act, I am establishing the following conditions on this authorization:

University of Louisville Infectious Diseases Laboratory

- A. University of Louisville Infectious Diseases Laboratory will notify DMD/OHT7-OIR/OPEQ/CDRH in advance of any changes to the University of Louisville Infectious Diseases Laboratory criteria for 2019-nCoV testing.
- B. University of Louisville Infectious Diseases Laboratory will make available the authorized SARS-CoV-2 real time RT-PCR test with the authorized labeling only to authorized laboratories. University of Louisville Infectious Diseases Laboratory may request changes to the authorized labeling. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- C. The authorized laboratory will produce the authorized SARS-CoV-2 real time RT-PCR test Fact Sheet for Healthcare Providers and the authorized SARS-CoV-2 real time RT-PCR test Fact Sheet for Patients. University of Louisville Infectious Diseases Laboratory may request changes to the authorized SARS-CoV-2 real time RT-PCR test Fact Sheet for Healthcare Providers and the authorized SARS-CoV-2 real time RT-PCR test Fact Sheet for Patients. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- D. University of Louisville Infectious Diseases Laboratory will make available on its website the authorized SARS-CoV-2 real time RT-PCR test Fact Sheet for Healthcare Providers and the authorized SARS-CoV-2 real time RT-PCR test Fact Sheet for Patients.
- E. University of Louisville Infectious Diseases Laboratory will inform relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to the SARS-CoV-2 real time RT-PCR test, authorized labeling and authorized Fact Sheets.
- F. University of Louisville Infectious Diseases Laboratory will ensure that the authorized laboratory using the authorized SARS-CoV-2 real time RT-PCR test have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- G. Through a process of inventory control, University of Louisville Infectious Diseases Laboratory will maintain records of test usage.
- H. University of Louisville Infectious Diseases Laboratory will collect information on the performance of the test. University of Louisville Infectious Diseases Laboratory will report to FDA any suspected occurrence of false positive and false negative results and significant deviations from the established performance characteristics of the test of which University of Louisville Infectious Diseases Laboratory becomes aware.
- I. University of Louisville Infectious Diseases Laboratory is authorized to make available additional information relating to the emergency use of the authorized SARS-CoV-2 real time RT-PCR test that is consistent with, and does not exceed, the terms of this letter of authorization.
- J. University of Louisville Infectious Diseases Laboratory may request new Fact Sheets for the SARS-CoV-2 real time RT-PCR test, if appropriate, and may request changes to such Fact Sheets. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, 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. University of Louisville Infectious Diseases Laboratory may request the addition of other instruments and associated software for use with the authorized SARS-CoV-2 real time RT-PCR test. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- L. University of Louisville Infectious Diseases Laboratory may request the addition of other extraction methods for use with the authorized SARS-CoV-2 real time RT-PCR test. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- M. University of Louisville Infectious Diseases Laboratory may request the addition of other specimen types for use with the authorized SARS-CoV-2 real time RT-PCR test. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- N. University of Louisville Infectious Diseases Laboratory may request the addition and/or substitution of other control materials for use with the authorized SARS-CoV-2 real time RT-PCR test. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- O. University of Louisville Infectious Diseases Laboratory may request the addition and/or substitution of other ancillary reagents and materials for use with the authorized SARS-CoV-2 real time RT-PCR test. Such requests will be made by University of Louisville Infectious Diseases Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- P. University of Louisville Infectious Diseases Laboratory will evaluate the analytical limit of detection and assess traceability⁴ of the SARS-CoV-2 real time RT-PCR test with any FDA-recommended reference material(s). After submission and review of and concurrence with the data, University of Louisville Infectious Diseases Laboratory 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.
- Q. University of Louisville Infectious Diseases Laboratory will track adverse events and report to FDA under 21 CFR Part 803.

Authorized Laboratory

- R. The authorized laboratory will include with reports of the results of the SARS-CoV-2 real time RT-PCR test, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- S. The authorized laboratory will perform the SARS-CoV-2 real time RT-PCR test according to the Instructions for Use. Deviations from the authorized procedures, including the authorized RT-PCR instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to perform the SARS-CoV-2 real time RT-PCR test are not permitted.
- T. The authorized laboratory will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- U. The authorized laboratory will collect information on the performance of the test and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and CDC (respvirus@cdc.gov) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the test of which they become aware.
- V. All laboratory personnel using the test must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.

⁴Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

University of Louisville Infectious Diseases Laboratory

- W. University of Louisville Infectious Diseases Laboratory will ensure that any records associated with this EUA are maintained until otherwise notified by the EUA issuing authority. Such records will be made available to FDA for inspection upon request.

Conditions Related to Advertising and Promotion

- X. All advertising and promotional descriptive printed matter relating to the use of the authorized SARS-CoV-2 real time RT-PCR 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.
- Y. All advertising and promotional descriptive printed matter relating to the use of the authorized SARS-CoV-2 real time RT-PCR test shall clearly and conspicuously state that:
- This test has not been FDA cleared or approved;
 - This test has been authorized by HHS under an EUA for use by authorized laboratories;
 - This test has been authorized only for the detection of nucleic acid from 2019-nCoV, 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 2019-nCoV 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 the authorized SARS-CoV-2 real time RT-PCR test may represent or suggest that this test is safe or effective for the detection of 2019-nCoV.

The emergency use of the authorized SARS-CoV-2 real time RT-PCR test 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 2019-nCoV is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely yours,

Brett P. Giroir, M.D.
ADM, USPHS