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Device: PMSF-INNO SARS-CoV-2 RT-PCR Test

Sponsor: INNO Diagnostics Reference Laboratory, Ponce Medical School

Indication: The SARS-CoV-2 assay is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 obtained from samples collected in upper respiratory specimens (nasopharyngeal swabs) from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to INNO Diagnostics Reference Laboratory at Ponce Medical School Foundation, Inc. in Ponce, Puerto Rico, which is a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratories.

The test is for the detection and identification 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 active infection with SARS-CoV-2 but 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 by CLIA certified high-complexity laboratories with experience in developing molecular diagnostics and is only for use under the Food and Drug Administration's (FDA) Emergency Use Authorization.

Dear Vanessa Rivera-Amill:

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 INNO Diagnostics

Reference Laboratory, Ponce Medical School SARS-CoV-2 RT-PCR for the qualitative detection of nucleic acid from the SARS-CoV-2 obtained from samples collected in upper respiratory specimens (nasopharyngeal swabs) 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 INNO Diagnostics Reference Laboratory at Ponce Medical School Foundation, Inc. in Ponce, Puerto Rico, which is a Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratories.[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 RT-PCR Test (as described in the scope Section of this letter (Section II)) in individuals who meet INNO Diagnostics Reference 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 the completion of a limit of detection (LOD) with the FDA reference panel within 30 days of the issuance of this letter.**

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the SARS-CoV-2 RT-PCR Test in individuals who meet INNO Diagnostics Reference 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 INNO Diagnostics Reference Laboratory SARS-CoV-2 RT-PCR Test may be effective in diagnosing 2019-nCoV infection, and that the known and potential benefits of the SARS-CoV-2 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 RT-PCR Test for diagnosing 2019-nCoV infection.[3]

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1 For ease of reference, this letter will refer to "qualified laboratory 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 RT-PCR Test by the authorized laboratory for the presumptive detection of 2019-nCoV in individuals who meet INNO Diagnostics Reference Laboratory criteria for 2019-nCoV testing.

The Authorized SARS-CoV-2 RT-PCR Test

The SARS-CoV-2 RT-PCR Test is for the qualitative detection of nucleic acid from the SARS-CoV-2 obtained from samples collected in upper respiratory specimens (nasopharyngeal swabs) from individuals suspected of COVID-19 by their healthcare provider. The INNO SARS-CoV-2 RT-PCR assay is performed on the Roche LightCycler 480 II instrument and uses primers and probes previously implemented by CDC that target the N gene. The oligonucleotides (primers and a dual labeled hydrolysis probe) are designed to detect two regions in the viral nucleocapsid gene (N gene, specifically N1 and N2) and an additional set of primers/probe are used to identify the internal control (extraction control gene: RNase P). Viral RNA is extracted from nasopharyngeal samples (swab collection) by using QIAamp Viral RNA kit (Qiagen) according to the manufacturer's instructions. The viral RNA is reverse transcribed to cDNA and amplified (reverse transcription polymerase chain reaction) by using real-time PCR procedure with the qScript XLT 1-Step RT-qPCR kit (Quantabio) and the Roche Lightcycler 480 II instrument.

The above described SARS-CoV-2 RT-PCR Test, when labeled consistently with the labeling authorized by HHS, entitled " SARS-CoV-2 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 INNO Diagnostics Reference 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 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 RT-PCR Test
- Fact Sheet for Patients: SARS-CoV-2 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 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 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 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 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 RT-PCR Test described above is authorized to detect 2019-nCoV in individuals who meet INNO Diagnostics Reference 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 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 RT-PCR Test l

- 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:

INNO Diagnostics Reference Laboratory

A. INNO Diagnostics Reference Laboratory will notify DMD/OHT7-OIR/OPEQ/CDRH in advance of any changes to the INNO Diagnostics Reference Laboratory criteria for 2019-nCoV testing.

B. INNO Diagnostics Reference Laboratory will make available the authorized SARS-CoV-2 RT-PCR Test with the authorized labeling only to authorized laboratories. INNO Diagnostics Reference Laboratory may request changes to the authorized labeling. Such requests will be made by INNO Diagnostics Reference Laboratory in consultation with, and require

concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

C. The authorized laboratory will produce the authorized SARS-CoV-2 RT-PCR Test Fact Sheet for Healthcare Providers and the authorized SARS-CoV-2 RT-PCR Test Fact Sheet for Patients. INNO Diagnostics Reference Laboratory may request changes to the authorized SARS-CoV-2 RT-PCR Test Fact Sheet for Healthcare Providers and the authorized SARS-CoV-2 RT-PCR Test Fact Sheet for Patients. Such requests will be made by INNO Diagnostics Reference Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

D. INNO Diagnostics Reference Laboratory will make available on its website the authorized SARS-CoV-2 RT-PCR Test Fact Sheet for Healthcare Providers and the authorized SARS-CoV-2 RT-PCR Test Fact Sheet for Patients.

E. INNO Diagnostics Reference 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 RT-PCR Test, authorized labeling and authorized Fact Sheets.

F. INNO Diagnostics Reference Laboratory will ensure that the authorized laboratory using the authorized SARS-CoV-2 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, INNO Diagnostics Reference Laboratory will maintain records of test usage.

H. INNO Diagnostics Reference Laboratory will collect information on the performance of the test. INNO Diagnostics Reference 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 INNO Diagnostics Reference Laboratory becomes aware.

I. INNO Diagnostics Reference Laboratory is authorized to make available additional information relating to the emergency use of the authorized SARS-CoV-2 RT-PCR Test that is consistent with, and does not exceed, the terms of this letter of authorization.

J. INNO Diagnostics Reference Laboratory may request new Fact Sheets for the SARS-CoV-2 RT-PCR Test, if appropriate, and may request changes to such Fact Sheets. Such requests will be made by INNO Diagnostics Reference 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. INNO Diagnostics Reference Laboratory may request the addition of other instruments and associated software for use with the authorized SARS-CoV-2 RT-PCR Test. Such requests will be made by INNO Diagnostics Reference Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

L. INNO Diagnostics Reference Laboratory may request the addition of other extraction methods for use with the authorized SARS-CoV-2 RT-PCR Test. Such requests will be made by INNO

Diagnostics Reference Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

M. INNO Diagnostics Reference Laboratory may request the addition of other specimen types for use with the authorized SARS-CoV-2 RT-PCR Test. Such requests will be made by INNO Diagnostics Reference Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

N. INNO Diagnostics Reference Laboratory may request the addition and/or substitution of other control materials for use with the authorized SARS-CoV-2 RT-PCR Test. Such requests will be made by INNO Diagnostics Reference Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

O. INNO Diagnostics Reference Laboratory may request the addition and/or substitution of other ancillary reagents and materials for use with the authorized SARS-CoV-2 RT-PCR Test. Such requests will be made by INNO Diagnostics Reference Laboratory in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

P. INNO Diagnostics Reference Laboratory will evaluate the analytical limit of detection and assess traceability[4] of the SARS-CoV-2 RT-PCR Test with any FDA-recommended reference material(s). After submission and review of and concurrence with the data, INNO Diagnostics Reference 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. INNO Diagnostics Reference 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 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 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 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

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

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.

INNO Diagnostics Reference Laboratory

W. INNO Diagnostics Reference 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 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 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.

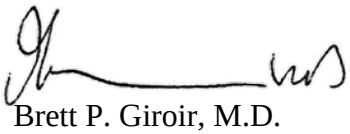
No advertising or promotional descriptive printed matter relating to the use of the authorized SARS-CoV-2 RT-PCR Test may represent or suggest that this test is safe or effective for the detection of 2019-nCoV.

The emergency use of the authorized SARS-CoV-2 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

Enclosures