U.S. FOOD & DRUG ADMINISTRATION

October 8, 2021

Michael J. Wagner, Esq.
Senior Corporate Counsel
Quest Diagnostics Infectious Disease, Inc.
33608 Ortega Highway Bldg B-West Wing
San Juan Capistrano, CA 92675

Device:	SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR
EUA Number:	EUA200015
Company:	Quest Diagnostics Infectious Disease, Inc. ("Quest Diagnostics")
Indication:	This test is authorized for the following indications for use in individuals suspected of COVID-19 by their healthcare provider: Qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens (such as nasopharyngeal or oropharyngeal swabs, sputum, tracheal aspirates, and bronchoalveolar lavage). Qualitative detection of nucleic acid from SARS-CoV-2 in anterior nasal swab specimens that are collected using the Quest Diagnostics Collection Kit for COVID-19 when used consistent with its authorization. Qualitative detection of nucleic acid from SARS-CoV-2 in pooled samples containing up to four of the individual upper respiratory swab specimens (nasopharyngeal, mid-turbinate nasal, anterior nasal or oropharyngeal swabs) that were collected in individual vials containing transport media. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Testing is limited to laboratories designated by Quest Diagnostics that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests.

Dear Mr. Wagner:

On March 17, 2020, based on your[1] request, the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR (also known as the Quest SARS-CoV-2 rRT-PCR).[2]

Subsequently, FDA granted your requests to update the authorized labeling on March 26, 2020, July 28, 2020, and November 13, 2020.[3,4,5] Based on your requests, FDA also reissued the letter in its entirety with revisions incorporated on May 27, 2020, July 18, 2020, and August 7, 2020.[6,7,8] In addition, FDA established additional Conditions of Authorization in response to the continued emergence of new variants of SARS-CoV-2 on September 23, 2021.[9]

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[1] For ease of reference, this letter will use the term "you" and related terms to refer to Quest Diagnostics Infectious Disease, Inc. ("Quest Diagnostics").

[2] The SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR was authorized for the qualitative detection of nucleic acid from SARS-CoV-2 in upper and lower respiratory specimens (such as nasopharyngeal or oropharyngeal swabs, sputum, lower respiratory tract aspirates, bronchoalveolar lavage, and nasopharyngeal wash/aspirate or nasal aspirate) 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 was limited to Quest Diagnostic Laboratories or other laboratories designated by Quest Diagnostics that were also certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high complexity tests.

[3] On March 26, 2020, your request was granted to update the Instructions for Use (IFU) of your product to: (1) change the SARS-CoV-2 primer-probes target combination from N1+N2 (separate wells) to N1+N3 (same well) in order to double testing capacity, and (2) temporarily allow use of a DNA-based internal process control in situations where supply chain issues limited the availability of the RNA-based internal process control.

[4] On July 28, 2020, your request was granted to update the IFU of your product to add use of the Mag-Bind Viral RNA Xpress Kit (Omega Bio-Tek, Cat. M6219-2304) with the Hamilton MagEx STAR ("Omega Method") as an additional extraction method, and the associated updated instructions and performance data.

[5] On November 13, 2020, your request was granted to update the IFU of your product to: (1) change the language in the pooling disclosure to patients, (2) update the pooling monitoring plan to be consistent with more recent authorizations, and (3) modify the limitation statement regarding the lack of RNaseP specimen adequacy control. FDA updated the Fact Sheet for Healthcare Providers accordingly and made updates to the Intended Use statement and IFU to reflect recent policy.

[6] On May 27, 2020, the revisions to the March 17, 2020, letter and authorized labeling included: (1) revised intended use to include nasal swab specimens self-collected at home or in a healthcare setting by individuals using an authorized home-collection kit, specified in this EUA's authorized labeling, when determined appropriate by a healthcare provider, (2) added the Quest Diagnostics Self-collection Kit for COVID-19 as an authorized home-collection kit, (3) added labeling documents and conditions of authorization specific to home specimen collection; and, (4) updated healthcare provider and patient fact sheets to reflect language used in more recent authorizations.

[7] On July 18, 2020, the revisions to the May 27, 2020, letter and authorized labeling included: (1) revised intended use to include use with pooled samples containing up to four individual upper respiratory swab specimens (nasopharyngeal, mid-turbinate, anterior nares or oropharyngeal swabs) collected under observation, in individual vials containing transport media, from individuals suspected of COVID-19 by their healthcare provider, (2) updated labeling documents to include the "Protocol for Monitoring of Specimen Pooling Testing Strategies," (3) added conditions of authorization specific to sample pooling; and, (4) updated healthcare provider and patient fact sheets to reflect more recent authorizations.

[8] On August 7, 2020, the revisions to the July 18, 2020, letter and authorized labeling included: (1) removal of the RNaseP internal control requirement for unobserved self-collected samples, (2) updated labeling documents to remove the requirement to run the RNaseP internal control (3) added conditions of authorization specific to removal of the RNaseP internal control, (4) updated healthcare provider and patient fact sheets to include some additional warnings/precautions around the absence of an RNaseP internal control when unobserved self-collected specimens are tested, and (5) minor updates to the intended use to remove "individual" from the nasal swab specimens that are self-collected at home or in a healthcare setting to allow them to be considered for pooling and other minor clarifications in the pooling section to reflect language used in more recent authorizations.

[9] The Viral Mutation Revision Letter – September 23, 2021, can be accessed at: https://www.fda.gov/media/152406/download.

On July 21, 2021, you requested to amend your Emergency Use Authorization (EUA) again. Based on that request, and having concluded that revising the August 7, 2020, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the August 7, 2020, letter in its entirety with the revisions incorporated.[10] Pursuant to section 564 of the Act and the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter, your product[11] is now intended for the indication described above.

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.[12]

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 included in the Package Insert (identified below, also referred to as the Instructions for Use).

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 as 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:

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[10] The revisions to the August 7, 2020, letter and authorized labeling include: (1) updating the intended use and authorized labeling with respect to anterior nasal swab specimens collected using the Quest Diagnostics Collection Kit for COVID-19 when used consistent with its authorization, (2) clarifying anterior nares as anterior nasal and mid-turbinate as mid-turbinate nasal swabs in the intended use and authorized labeling, (3) updating authorized labeling to fulfill Condition of Authorization (1) in the Viral Mutation Revision Letter – September 23, 2021, (4) updating the performance section of the IFU to remove data from the Quest Diagnostics Collection Kit for COVID-19 which has a standalone EUA, (5) updating the Fact Sheets for Healthcare Providers and Patients to reflect language used in more recent authorizations, (6) updating to add Conditions of Authorization (2) and (3) from the Viral Mutation Revision Letter – September 23, 2021 to the letter (I and J below), and (7) updating the Conditions of Authorization, including to revise S below, consolidating several conditions in G below, updating based on the revised intended use, and to reflect language used in more recent letters of authorization.

[11] For ease of reference, this letter will use the term "your product" to refer to the SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR (or Quest SARS-CoV-2 rRT-PCR test) used for the indication identified above.

[12] 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).

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 such product; and

3. There is no adequate, approved, and available alternative to the emergency use of your product for diagnosing COVID-19.[13]

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.

The Authorized Product

Your product is a qualitative test for the detection of nucleic acid from the SARS-CoV-2 in upper and lower respiratory specimens (such as nasopharyngeal or oropharyngeal swabs, sputum, tracheal aspirates, and bronchoalveolar lavage) collected from individuals suspected of COVID-19 by their healthcare provider.

Your test is also authorized for use with anterior nasal swab specimens that are collected using the Quest Diagnostics Collection Kit for COVID-19 when used consistent with its authorization.

Finally, your product is also authorized for use to detect nucleic acid from the SARS-CoV-2 in pooled samples containing up to four of the individual upper respiratory swab specimens (nasopharyngeal, mid-turbinate nasal, anterior nasal or oropharyngeal swabs) that were collected in individual vials containing transport media from individuals suspected of COVID-19 by their healthcare provider. Negative results from pooled testing should not be treated as definitive. If a patient's clinical signs and symptoms are inconsistent with a negative result or results are necessary for patient management, then the patient should be considered for individual testing. Specimens included in pools with a positive, inconclusive, or invalid result must be tested individually prior to reporting a result. Specimens with low viral loads may not be detected in sample pools due to the decreased sensitivity of pooled testing.

Testing is limited to laboratories designated by Quest Diagnostics that are certified under CLIA and meet the requirements to perform high complexity tests.

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. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

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

Specimens that are collected will not be tested with an internal control to confirm that the specimen was properly collected. As such, collected specimens from SARS-CoV-2 positive individuals may return negative results if the specimen was not collected properly.

To perform the SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR test, SARS-CoV-2 nucleic acid is first extracted, isolated and purified from upper and lower respiratory specimens (such as nasopharyngeal or oropharyngeal swabs, sputum, tracheal aspirates, and bronchoalveolar lavage). The purified nucleic acid is then reverse transcribed into cDNA followed by PCR amplification and detection with the SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR test on with the Applied Biosystems 7500 Real Time PCR System (or ABI 7500 fast system run as a standard ABI 7500), or other authorized instruments and/or other authorized software. Your product includes the following materials or other authorized materials: buffers, extraction reagents, 1-Step RT-qPCR Master Mix, Primer/Probe Master Mixes, exogenous RNA internal control reagents, Positive Control, and Negative Control.

Your product requires the following control materials, or other authorized control materials (as may be requested under Condition G. below), that are processed in the same way as the patient specimens and are required to be included with each batch of specimens tested. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Package Insert (identified below):

- Internal Process Control – Exogenous RNA control material which is required as an extraction, reverse transcription and PCR amplification positive control. This control should be added to each sample aliquot prior to extraction.

- Positive Control - contains the SARS-CoV-2 synthetic RNA. The positive control is used to monitor for failures of rRT-PCR reagents and reaction conditions.

- Negative Control - used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents.

Your product also requires the use of additional authorized materials and authorized ancillary reagents that are not included with the test and are described in the authorized labeling.

Your product described above is authorized to be accompanied with the labeling entitled "SARS-CoV-2 RNA, Qualitative Real-Time RT-PCR (Test Code 39433) Package Insert" (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), and the following product-specific information pertaining to the emergency use, is required to be made available to healthcare providers and patients (collectively referenced as "authorized labeling"):

- Fact Sheet for Healthcare Providers: Quest Diagnostics - Quest SARS-CoV-2 rRT-PCR
- Fact Sheet for Patients: Quest Diagnostics - Quest SARS-CoV-2 rRT-PCR

The above described product, when accompanied by the authorized labeling is authorized to be distributed to and used by authorized laboratories, 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 such a 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 for 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.

IV. Conditions of Authorization

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

Quest Diagnostics (You)

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)); 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 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.

C. You must make your product available with the authorized labeling to authorized laboratories.

D. You must make available on your website(s) the authorized labeling.

E. You must ensure that the authorized laboratories using your product have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

F. You must maintain records of the laboratories you designate as authorized laboratories and you must also maintain records of test usage by all such authorized laboratories.

G. You 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.

H. 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. Any request for changes to this EUA should be submitted to the 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) and require appropriate authorization from FDA prior to implementation.

I. You must evaluate the analytical limit of detection and assess traceability[14] of your product with any FDA-recommended reference material(s). After submission to and concurrence of the data by FDA, you will update its 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.

J. You must evaluate the impact of SARS-CoV-2 viral mutations 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 (via email: CDRH-EUA-Reporting@fda.hhs.gov).

K. If requested by FDA, you must update your labeling within 7 calendar days to include

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

any additional labeling risk mitigations identified by FDA regarding the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

L. You must have a process in place to track adverse events, including with the Quest Diagnostics collection Kit for COVID-19, including any occurrence of false results with your product and report any such events to FDA pursuant to 21 CFR Part 803. Serious adverse events, especially unexpected biosafety concerns, should immediately be reported to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov).

Authorized Laboratories

M. 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.

N. 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 perform the test are not permitted.

O. Authorized laboratories testing authorized specimens collected using the Quest Diagnostics Collection Kit for COVID-19 with your product must follow the Quest Diagnostics' "Unobserved Collected Sample Processing for COVID-19 Molecular Testing" Non-Technical Standard Operating Procedure (SOP) when accepting specimens for testing.

P. Authorized laboratories testing authorized specimens collected using the Quest Diagnostics Collection Kit for COVID-19 must include in the test report for specific patients whose specimen(s) were collected without observation the following limitation: "*Specimens that are collected using the Quest Diagnostics Collection Kit for COVID-19 were not tested with an internal control to confirm that the specimen was properly collected. As such, unobserved collected specimens using the Quest Diagnostics Collection Kit for COVID-19 from SARS-CoV-2 positive individuals may yield negative results if the specimen was not collected properly.*"

Q. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run the test prior to initiating testing.

R. 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.

S. 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 (michael.j.wagner@questdiagnostics.com) 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.

T. Authorized laboratories using specimen pooling strategies when testing patient specimens with your product must include with negative test result reports for specific patients whose specimen(s) were the subject of pooling, a notice that pooling was used during testing and that "*In very rare cases, estimated at about 1 in 1,000 (0.1%) or less patient specimens with low viral loads may not be detected in sample pools due to the decreased sensitivity of pooled testing.*"

U. Authorized laboratories implementing pooling strategies for testing patient specimens must use the "Protocol for Monitoring of Specimen Pooling Testing Strategies" recommendations available in the authorized labeling to evaluate the appropriateness of continuing to use such strategies based on the recommendations in the protocol.

V. Authorized laboratories must keep records of specimen pooling strategies implemented including type of strategy, date implemented, and quantities tested, and test result data generated as part of the "Protocol for Monitoring of Specimen Pooling Testing Strategies." For the first 12 months from the date of their creation, such records will be made available to FDA within 48 business hours for inspection upon request, and will be made available within a reasonable time after 12 months from the date of their creation.

W. 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.

Quest Diagnostics (You) and Authorized Laboratories

X. You 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

Y. All descriptive printed matter, 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.

Z. 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.

AA. 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 by FDA under an EUA for use by authorized laboratories;

- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, 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 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,

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Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosure