

September 3, 2020

Rita Hoady, MS, RAC, CCRA
Senior Manager, Regulatory Affairs
Roche Molecular Systems, Inc.
4300 Hacienda Drive
Pleasanton, CA 94588

Device: cobas SARS-CoV-2 & Influenza A/B

Company: Roche Molecular Systems, Inc.

Indication: An automated multiplexed real-time RT-PCR assay intended for simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and/or influenza B virus RNA in healthcare provider-collected nasal and nasopharyngeal swab specimens and self-collected nasal swab specimens (collected in a healthcare setting with instruction by a healthcare provider) from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider.¹ Emergency use of this test is limited to authorized laboratories.

Authorized Laboratories: Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests.

Dear Ms. Hoady:

This letter is in response to your² request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of your product,³ 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.

¹ For this EUA, a healthcare provider includes, but is not limited to, physicians, nurses, pharmacists, technologists, laboratory directors, epidemiologists, or any other practitioners or allied health professionals.

² For ease of reference, this letter will use the term “you” and related terms to refer to Roche Molecular Systems, Inc.

³ For ease of reference, this letter will use the term “your product” to refer to the cobas SARS-CoV-2 & Influenza A/B used for the indication identified above.

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.⁴

There are FDA-approved/cleared tests for influenza A virus and influenza B virus, but there are no FDA-approved/cleared multiplexed tests for simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and/or influenza B virus nucleic acids. Respiratory viral infections caused by the influenza A and B viruses 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 and the common influenza viruses that cause seasonal epidemics of flu, influenza A and B (not influenza C) is needed during the flu season that coincides with the COVID-19 pandemic.

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;
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 SARS-CoV-2, influenza A virus, and/or influenza B virus nucleic acids and that the known and potential benefits of your product when used for such a use, 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.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.

Authorized Product Details

⁴ 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).

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

Your product is an automated multiplexed nucleic acid test intended for use on the cobas 6800/8800 Systems for simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and/or influenza B virus RNA in healthcare provider-collected nasal and nasopharyngeal swab specimens and self-collected nasal swab specimens (collected in a healthcare setting with instruction by a healthcare provider) from individuals suspected of respiratory viral infection consistent with COVID-19 by their healthcare provider. Symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar.

Your product is intended for use with the cobas 6800/8800 Systems for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A, and/or influenza B viral Ribonucleic acid (RNA) in patient specimens, and is not intended to detect influenza C. RNA from influenza A, influenza B, and/or SARS-CoV-2 viruses is generally detectable in respiratory specimens during infection. Positive results are indicative of active infection but do not rule out bacterial infection or co-infection with other viruses; 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, influenza A, and/or influenza B infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and/or epidemiological information.

To use your product, SARS-CoV-2, influenza A, and/or influenza B nucleic acids are first extracted, isolated and purified from nasal or nasopharyngeal swab specimens. The purified nucleic acid is then reverse transcribed into cDNA followed by PCR amplification and detection using an authorized real-time (RT) PCR instrument. The cobas SARS-CoV-2 & Influenza A/B assay includes the following materials or other authorized materials: all necessary reagents for the SARS-CoV-2 & Influenza A/B specific PCR reaction including the RNA Internal Control, primers and probes for amplification and detection of the internal controls, the SARS-CoV-2, Influenza A and Influenza B sequences, and the positive and negative control kits.

Your product requires the following control materials, or other authorized control materials (as can be requested under Condition N below), that are processed in the same way as the specimens and are required to be included 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 (described below):

- cobas Buffer Negative Control – tris buffer used to monitor for reagent and system contamination that is run with each batch of specimens
- cobas SARS CoV-2 & Influenza A/B Positive Control – non-infectious plasmid DNA containing SARS-CoV-2, Sarbecovirus, Influenza A and Influenza B sequences; used to monitor for failures of RT-PCR reagents and reaction conditions
- RNA Internal Control- armored RNA of non-related sequence used with each sample to ensure correct processing of each sample and to monitor for potential inhibitors that may be present in the sample.

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 above described product is authorized to be accompanied with the labeling entitled “cobas

SARS-CoV-2 & Influenza A/B” Instructions for Use (available at <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas>) and 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: Roche Molecular Systems, Inc. – cobas SARS-CoV-2 & Influenza A/B
- Fact Sheet for Patients: Roche Molecular Systems, Inc. – cobas SARS-CoV-2 & Influenza A/B

The above described product, when accompanied by the Instructions for Use (described above) and the two Fact Sheets (collectively referenced as “authorized labeling”) 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, through the simultaneous detection and differentiation of SARS-CoV-2, influenza A virus, and/or influenza B virus nucleic acid, 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:

Roche Molecular Systems, Inc. (You) and Authorized Distributor(s)⁶

- 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 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) will make your product available with the authorized labeling to authorized laboratories.
- C. You and authorized distributor(s) will make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.
- D. You and authorized distributor(s) will 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 and authorized Fact Sheets.
- E. Through a process of inventory control, you and authorized distributor(s) will maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.
- F. You and authorized distributor(s) will collect information on the performance of your product. You will report to FDA 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.
- G. 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.

Roche Molecular Systems, Inc. (You)

⁶ “Authorized Distributor(s)” are identified by you, in your EUA submission as an entity allowed to distribute your device.

- H. You will notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).
- I. You will 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).
- J. You may request 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. Such requests will be made in consultation with, and require concurrence of 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).
- K. You will comply with the following requirements under FDA regulations: 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).
- L. 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.
- M. 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.
- N. 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. Such requests should be submitted to the DMD/OHT-7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.
- O. You will evaluate the analytical limit of detection and assess traceability⁷ of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA, you will update 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 will 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 FDA). After submission to and concurrence with the data by FDA, you will update authorized labeling to reflect the additional testing.

⁷ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

Such labeling updates will be made in consultation with, and require concurrence of DMD/OHT7-OIR/OPEQ/CDRH.

- Q. You will track adverse events, including any occurrence of false results and report to FDA pursuant to 21 CFR Part 803.

Authorized Laboratories

- R. Authorized laboratories using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these this labeling may be used, which may include mass media.
- S. Authorized laboratories using your product will 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.
- T. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- U. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- V. Authorized laboratories will 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 at US Customer Technical Support (via telephone number 1-800-526-1247) 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.
- W. All laboratory personnel 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.

Roche Molecular Systems, Inc. (You), Authorized Distributors and Authorized Laboratories

- X. You, authorized distributors, and authorized laboratories using your product 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 Printed Materials, Advertising and Promotion

- Y. 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 the applicable requirements set forth in the Act and FDA regulations.

Z. No descriptive printed matter, including 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, including advertising and promotional materials, relating to the use of your product 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 simultaneous qualitative detection and differentiation of nucleic acids from SARS-CoV-2, influenza A virus, and influenza B virus, and 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 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 authorization is terminated or 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