U.S. FOOD & DRUG ADMINISTRATION

September 14, 2020

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Director, Regulatory Affairs
Roche Molecular Systems, Inc.
4300 Hacienda Drive
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Device:	cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System
Company:	Roche Molecular Systems, Inc.
Indication:	An automated multiplexed real-time RT-PCR assay for the simultaneous rapid *in vitro* qualitative detection and differentiation of SARS-CoV-2, influenza A and/or influenza B virus RNA in healthcare provider-collected nasopharyngeal and nasal swabs and self-collected nasal swabs (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. 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, to perform moderate or high complexity tests. The cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System is also authorized for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

Dear Ms. Nakajima:

This letter is in response to your[1] request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of your product,[2] 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

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Roche Molecular Systems, Inc.

[2] For ease of reference, this letter will use the term "your product" to refer to the cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System used for the indication identified above.

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.[3]

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. 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 contained in the Instructions for Use (identified below).

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.[4]

II. Scope of Authorization

[3] 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).

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

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

Your product is an automated multiplexed nucleic acid test for use on the cobas Liat System intended for the simultaneous rapid *in vitro* qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and or influenza B virus RNA in healthcare provider-collected nasopharyngeal and nasal swabs and self-collected nasal swabs (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. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar.

Your product is intended for use with the cobas Liat System in the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A and/or influenza B virus nucleic acids in clinical specimens and is not intended to detect influenza C virus. SARS-CoV-2, influenza A and influenza B viral RNA is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of active infection but do not rule out bacterial infection or co-infection with other pathogens not detected by the test. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definite cause of disease. 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 patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

To use your product, SARS-CoV-2, influenza A, and/or influenza B nucleic acid are first extracted, isolated and purified from nasopharyngeal or nasal 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 Nucleic Acid Test for use on the cobas Liat System 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 control, SARS-CoV-2 sequences and influenza A and influenza B sequences.

Your product also requires the use of positive and negative controls which are not included with the kit but are available from you and are run as outlined in the authorized labeling.

The following control materials, or other authorized control materials (as may be requested under Condition N below), that are processed in the same way as the patient 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:

- Negative Control – universal transport media; needed to ensure that each lot of reagents and the cobas Liat analyzer have not become contaminated with template nucleic acid.
- Positive Control – lyophilized inactivated influenza A and B viruses and a DNA plasmid encoding the SARS-CoV-2 RdRp sequence; needed to ensure that all

components and processes of each lot of reagents are functioning properly, including sample preparation, reverse transcription and nucleic acid amplification.

- Internal Process Control (IC) – inactivated MS2 bacteriophage containing an RNA template. The IC is mixed with sample during the first step of the automated process and is subsequently lysed, reverse transcribed, amplified and detected along with SARS CoV-2, influenza A and influenza B targets when present.

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 labeling entitled "cobas SARS-CoV-2 & Influenza A/B Nucleic acid test for use on the cobas Liat System" Instructions for Use, (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas), the "cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System Quick Reference Instructions" the Product Information Card (PIC card), and the following fact sheets pertaining to the emergency use, which are required to be made available as set forth in the Conditions of Authorization (Section IV), are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: Roche Molecular Systems, Inc. – cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the cobas Liat System
- Fact Sheet for Patients: Roche Molecular Systems, Inc. – cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test for use on the Cobas Liat System

The above described product, with the authorized labeling provided as set forth in the Conditions (Section IV), 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, 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)[5]

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 and authorized distributor(s) will include a physical copy of the authorized PIC card with each shipped kit, and at least 1 physical copy of the Quick Reference Instructions with each order of your product to authorized laboratories, and will make the authorized Instructions for Use electronically available with the opportunity to request a copy in paper form, and after such request, promptly provide the requested information without additional cost. You may request changes to the authorized labeling. Such requests will be made in consultation with, and require concurrence of, 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).

C. You and authorized distributor(s) will make available on your website(s) the authorized labeling.

D. You and authorized distributor(s) will inform authorized laboratories and relevant

[5] "Authorized Distributor(s)" are identified by you, Roche Molecular Systems, Inc., in your EUA submission as an entity allowed to distribute your device.

public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product, 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 (You)

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 DMD/OHT7-OIR/OPEQ/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 L (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/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.

O. You will evaluate the analytical limit of detection and assess traceability[6] of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA, you will update your 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 DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you will update your 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. You will complete the agreed upon real-time stability study for your product. After submission to and concurrence with the data by FDA, you will update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

R. You will have process in place for collecting and reporting, and will report to FDA pursuant to 21 CFR Part 803, adverse events (including any occurrence of false results) of which you become aware.

Authorized Laboratories

S. Authorized laboratories using your product will 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.

T. 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.

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

V. 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.

W. Authorized laboratories will collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-

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

Reporting@fda.hhs.gov) and you (https://www.roche.com/about/business/roche_worldwide.htm) 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.

X. 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

Y. 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

Z. 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.

AA. 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.

BB. 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 acid 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 Federal Food, Drug, and Cosmetic 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,

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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure