March 12, 2020

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

Dear Mrs. Hoady:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the Roche Molecular Systems, Inc.(RMS) cobas SARS-CoV-2 test for use on the cobas 6800/8800 Systems for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal and oropharyngeal swab samples from patients who meet COVID-19 clinical and/or epidemiological criteria, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). The cobas SARS-CoV-2 test is for use only under EUA in United States (U.S.) in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate complexity tests and in U.S. laboratories certified under CLIA to perform high complexity tests, by clinical laboratory personnel who have received specific training on the use of the cobas 6800/8800 Systems.[1]

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. [2] 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]

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the

[1] For ease of reference, this letter will refer to, "United States (U.S.) laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate complexity tests and in U.S. laboratories certified under CLIA to perform high complexity tests" as "authorized laboratories."
[2] On February 11, 2020, the virus tentatively named 2019-nCoV was formally designated as Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Also on February 11, 2020, the disease caused by SARS-CoV-2 was formally designated as Coronavirus Disease 2019 (COVID-19). This document uses the updated names.
[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*. February 4, 2020.

Act are met, I am authorizing the emergency use of the cobas SARS-CoV-2 test (as described in the scope Section of this letter (Section II)) in individuals who meet COVID-19 clinical and/or epidemiological criteria for the detection of SARS-CoV-2 by authorized laboratories, subject to the terms of this authorization.

## I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the cobas SARS-CoV-2 test in individuals who meet COVID-19 clinical and/or epidemiological criteria for testing 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 the cobas SARS-CoV-2 test may be effective in diagnosing COVID-19, and that the known and potential benefits of the cobas SARS-CoV-2 test, 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 the cobas SARS-CoV-2 test for diagnosing COVID-19.[4]

## 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 cobas SARS-CoV-2 test by authorized laboratories for the detection of SARS-CoV-2 in individuals who meet COVID-19 clinical and/or epidemiological criteria for testing.

## The Authorized cobas SARS-CoV-2

The cobas SARS-CoV-2 test is a qualitative test, for use on the cobas 6800 System and cobas 8800 System for the detection of nucleic acid from SARS-CoV-2 in nasopharyngeal and oropharyngeal swab samples collected in Copan Universal Transport Medium System (UTM-RT) or BD Universal Viral Transport System (UVT), or other authorized swab transport systems from patients who meet COVID-19 clinical and/or epidemiological criteria for testing. Results are for the detection of nucleic acid from SARS-CoV-2 that are detectable in nasopharyngeal and oropharyngeal swab samples during 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 cobas SARS-CoV-2 test is based on fully automated sample preparation (nucleic acid extraction and purification) followed by reverse transcription, PCR amplification and detection on the cobas 6800/8800 system, or other authorized instruments. Automated data management is performed by the cobas 6800/8800 software, or otherwise authorized software, which assigns test results for all tests. Results can be reviewed directly on the system screen, and printed as a report.

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

The cobas SARS-CoV-2 test requires an RNA Internal Control, or other authorized internal control material, consisting of non-Sarbecovirus related armored RNA construct, that is added to each specimen and used as an extraction control that is extracted and tested concurrently with each specimen. The internal control is detected by an internal control specific primer and probe set and is used to monitor the entire sample preparation and PCR amplification process.

Nucleic acid from patient samples and added internal control RNA (RNA IC) molecules are simultaneously extracted and purified. Selective amplification of SARS-CoV-2 target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for two SARS-CoV-2 targets, one from the SARS-CoV-2 specific ORF1 region and one from a conserved region of the envelope E-gene common to all SARS-like Coronaviruses (called Sarbecoviruses). The two targets are detected by sequence specific probes labeled with different fluorophores. The pan-Sarbecovirus detection sets will also detect the SARS-CoV-2 virus.

The cobas SARS-CoV-2 test includes the following materials or other authorized materials:

- cobas SARS-CoV-2 test cassettes containing all necessary reagents for the SARS-CoV-2 specific RT-PCR reaction including the RNA Internal Control RNA and the primers and probes for amplification and detection of the internal control and the SARS-CoV-2 sequences
- cobas SARS-CoV-2 Control Kit containing the SARS-CoV-2 Positive Control

In addition, the cobas SARS-CoV-2 test requires the following external control materials, or other authorized control materials, that are processed in the same way as the patient samples and are required to be included with each batch of specimens tested with the cobas SARS-CoV-2 test. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the cobas SARS-CoV-2 test Instructions for Use:

- SARS-CoV-2 Positive Control: non-infectious plasmid DNA that include the following sequences: SARS-COV-2 sequence, pan-Sarbecovirus 1 sequence, and pan-Sarbecovirus sequence. The positive control is used to monitor for failures of rRT-PCR reagents and reaction conditions.
- cobas Buffer Negative Control: Tris buffer used to monitor for reagent and system contamination that is run with each batch of specimens.

The cobas SARS-CoV-2 test 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 cobas SARS-CoV-2 test Instructions for Use, including but not limited to the following:

- cobas Buffer Negative Control Kit
- cobas omni reagents and materials

The above described cobas SARS-CoV-2 test, when labeled consistently with the labeling authorized by FDA, entitled “cobas SARS-CoV-2 Instructions for Use” (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-

authorizations), which may be revised by RMS 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 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.

The above-described cobas SARS-CoV-2 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: cobas SARS-CoV-2
- Fact Sheet for Patients: cobas SARS-CoV-2

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 cobas SARS-CoV-2 test, when used for the detection of SARS-CoV-2 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 FDA, that it is reasonable to believe that the authorized cobas SARS-CoV-2 test may be effective in the detection of SARS-CoV-2, when used consistently 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 the cobas SARS-CoV-2 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 cobas SARS-CoV-2 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), cobas SARS-CoV-2 test described above is authorized to detect SARS-CoV-2 in individuals who meet COVID-19 clinical and/or epidemiological criteria for 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 cobas SARS-CoV-2 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, storage, and distribution of the cobas SARS-CoV-2 test

## 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, (RMS) and Its Authorized Distributor(s)**

A. This device 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)); 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).

B. RMS and its authorized distributor(s) will make available the authorized cobas SARS-CoV-2 test with the authorized labeling to authorized laboratories. RMS may request changes to the authorized labeling. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

C. RMS and its authorized distributor(s) will provide to authorized laboratories the authorized cobas SARS-CoV-2 test Fact Sheet for Healthcare Providers and the authorized cobas SARS-CoV-2 test Fact Sheet for Patients.

D. RMS and its authorized distributor(s) will make available on their website(s) the authorized cobas SARS-CoV-2 test Fact Sheet for Healthcare Providers and the authorized cobas SARS-CoV-2 test Fact Sheet for Patients.

E. RMS and its 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 the cobas SARS-CoV-2 test, authorized labeling and authorized Fact Sheets.

F. Through a process of inventory control, RMS and its authorized distributor(s) will maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.

G. RMS and its authorized distributor(s) will collect information on the performance of the test. RMS 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 RMS becomes aware.

H. RMS and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized cobas SARS-CoV-2 test that is consistent with, and does not exceed, the terms of this letter of authorization.

I. RMS and its authorized distributor(s) will send out a Customer Letter to authorized laboratories to inform them of acceptable material(s), other than clinical specimens, that will aid the authorized laboratories in verification of the authorized cobas SARS-CoV-2 test. RMS will notify DMD/OHT7-OIR/OPEQ/CDRH when this condition has been completed.

**Roche Molecular Systems, Inc, (RMS)**

J. RMS will notify FDA of any authorized distributor(s) of the cobas SARS-CoV-2 test, including the name, address, and phone number of any authorized distributor(s).

K. RMS will provide its authorized distributor(s) with a copy of this EUA and communicate to its authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).

L. RMS may request changes to the authorized cobas SARS-CoV-2 test Fact Sheet for Healthcare Providers and the authorized cobas SARS-CoV-2 test Fact Sheet for Patients. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

M. RMS may request changes to the Scope of Authorization (Section II in this letter) of the authorized cobas SARS-CoV-2 test. Such requests will be made by RMS in consultation with DMD/OHT7-OIR/OPEQ/CDRH, 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.

N. RMS may request the addition of other instruments and associated software for use with the authorized cobas SARS-CoV-2 test. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

O. RMS may request the addition of other swab transport systems for use with the authorized cobas SARS-CoV-2 test. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

P. RMS may request the addition of other specimen types for use with the authorized cobas SARS-CoV-2 test. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

Q. RMS may request the addition and/or substitution of primers or probes for use with the authorized cobas SARS-CoV-2 test. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

R. RMS may request the addition and/or substitution of other ancillary reagents and materials for use with the authorized cobas SARS-CoV-2 test. Such requests will be made by RMS in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

S. RMS will evaluate the analytical limit of detection and assess traceability[5] of the cobas SARS-CoV-2 test with any FDA-recommended reference material(s). After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, RMS 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.

T. RMS will track adverse events, including any occurrence of false results and report to FDA under 21 CFR Part 803.

**Authorized Laboratories**

U. Authorized laboratories using the cobas SARS-CoV-2 test will include with result reports of the cobas SARS-CoV-2 test, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

V. Authorized laboratories using the cobas SARS-CoV-2 test will perform the cobas SARS-CoV-2 test as outlined in the cobas SARS-CoV-2 Instructions for Use. 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 cobas SARS-CoV-2 test are not permitted.

W. Authorized laboratories that receive the cobas SARS-CoV-2 test must notify the relevant public health authorities of their intent to run the test prior to initiating testing.

X. Authorized laboratories using the cobas SARS-CoV-2 test will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

Y. Authorized laboratories 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 Roche Diagnostics US Customer Technical Support 1-800-526-1247 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.

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

Z. 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.

**RMS, Its Authorized Distributor(s), and Authorized Laboratories**

AA. RMS, its authorized distributor(s) and authorized laboratories using the cobas SARS-CoV-2 test 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 Advertising and Promotion**

BB. All advertising and promotional descriptive printed matter relating to the use of the authorized cobas SARS-CoV-2 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.

CC. All advertising and promotional descriptive printed matter relating to the use of the authorized cobas SARS-CoV-2 test 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 detection of nucleic acid from SARS-CoV-2, 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 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.

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

The emergency use of the authorized cobas SARS-CoV-2 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 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

Enclosures