

July 1, 2020

Ellen Karges, MS
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CENTOGENE US, LLC
99 Erie Street
Cambridge, MA 02139

Device: CentoFast-SARS-CoV-2 RT-PCR Assay
Company: CENTOGENE US, LLC
Indication: Qualitative detection of nucleic acid from SARS-CoV-2 in dry oropharyngeal swab specimens from individuals suspected of COVID-19 by their healthcare provider. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories: Testing is limited to the CENTOGENE US, LLC or other laboratories designated by CENTOGENE US, LLC that are also certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet requirements to perform high complexity tests.

Dear Ms. Karges:

This letter is in response to your¹ 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 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

¹ For ease of reference, this letter will use the term “you” and related terms to refer to CENTOGENE US, LLC.

² For ease of reference, this letter will use the term “your product” to refer to the CentoFast-SARS-CoV-2 RT-PCR Assay used for the indication identified above.

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*

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)), in individuals suspected of COVID-19 by their healthcare provider 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 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, and that the known and potential benefits of your product when used for diagnosing COVID-19, 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 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 indication above.

The Authorized CentoFast-SARS-CoV-2 RT-PCR Assay

Your product is a qualitative test for the detection of nucleic acid from SARS-CoV-2 in dry oropharyngeal swab specimens collected from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to CENTOGENE US, LLC or other laboratories designated by CENTOGENE US, LLC that are also certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet requirements to perform high-complexity tests.

Results are for the detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 nucleic acid is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 nucleic acid; 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 patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

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.

To use your product, SARS-CoV-2 nucleic acid is first extracted, isolated and purified from dry oropharyngeal swab and other authorized specimens. The purified nucleic acid is then reverse transcribed into cDNA followed by PCR amplification and detection using the LightCycler 480 II and other authorized real-time (RT) PCR instrument and software.

Your product uses all commercially sourced materials or other authorized materials and authorized ancillary reagents commonly used in clinical laboratories as described in the authorized labeling.

Your product requires the following 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 your product. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the authorized labeling:

- Empty Swab Control - a negative full process negative control for the entire procedure. It consists of sterile swabs, not used for sampling, and processed through the entire testing procedure.
- Positive Template Control (PC) – a positive full process control for the entire procedure. It consists of artificial SARS-CoV-2 RNA with genomic regions targeted by the kit. The positive control is used to monitor for failures of rRT-PCR reagents and reaction conditions. The Positive Template Control also contains the internal control.
- Negative Template Control (NTC) - Nuclease-free, molecular-grade water used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of RT-PCR reagents. The NTC also contains the internal control.
- Internal Amplification Control – a positive control for the RT-PCR reaction. It consists of artificial RNA sequences of the Equine Arteritis Virus (EAV) and is used to monitor reverse transcription and PCR amplification for each sample. The EAV primer and probe set is included in all clinical samples, the PC and the NTC to control for specimen quality and demonstrates that nucleic acid was reverse transcribed and amplified in the PCR reaction.

The above described product is authorized to be accompanied with laboratory procedures (described below), and the EUA Summary (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: CentoFast-SARS-CoV-2 RT-PCR Assay
- Fact Sheet for Patients: CentoFast-SARS-CoV-2 RT-PCR Assay

The above described product, when accompanied by the “CentoFast-SARS-CoV-2 RT-PCR Assay” laboratory procedures, the EUA Summary (identified 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, 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) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), 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, distribution, and storage of your product.

IV. Conditions of Authorization

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

CENTOGENE US, LLC (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 will make your product available with the authorized labeling to authorized laboratories.
- C. You may request changes to the authorized labeling. Such requests will be made by you in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- D. You will make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.
- E. You will inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to the authorized labeling, including authorized Fact Sheets.
- F. You will 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.
- G. You will maintain records of the authorized laboratories to which you distribute the test and number of tests distributed.
- H. You will collect information on the performance of your product. You will report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the test of which you become aware.
- I. 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.
- J. You may request changes to the Scope of Authorization (Section II in this letter) of your product. Such requests will be made by you 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.
- K. You may request the addition of other instruments and associated software for use with your product. Such requests will be made by you in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- L. You may request the addition of other extraction methods for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- M. You may request the addition of other specimen types for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- N. You may request the addition and/or substitution of primers or probes for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- O. You may request the addition and/or substitution of control materials for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- P. You may request the addition and/or substitution of other ancillary reagents and materials for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- Q. You will evaluate the analytical limit of detection and assess traceability⁵ of your product with any FDA-recommended reference material(s), if requested by FDA. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of and concurrence with the data, FDA will update the EUA summary to reflect the additional testing. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- R. You will track adverse events, including any occurrence of false results with your product and report any such events to FDA under 21 CFR Part 803.

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 using your product must 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

⁵ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material. FDA may request, for example, that you perform this study in the event that we receive reports of adverse events concerning your authorized test.

results to healthcare providers and relevant public health authorities, as appropriate.

- W. 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 CENTOGENE US, LLC (Quality@centogene.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.
- X. 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 test, and use the test in accordance with the authorized labeling.

CENTOGENE US, LLC and Authorized Laboratories

- Y. You 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 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 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