



September 29, 2020

Ellen Karges, MS
Senior Vice President Pharma Compliance and Regulatory Affairs
CENTOGENE US, LLC
99 Erie Street
Cambridge, MA 02139

Device: CentoSure 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 without symptoms or other reasons to suspect COVID-19. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories: Testing is limited to the laboratories designated by CENTOGENE US, LLC, which are 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 CentoSure 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 Cosmetic Act*, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 7, 2020).

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 EUA Summary (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 Section 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, 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.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.

Authorized Product Details

Your product is a qualitative test for the detection of nucleic acid from SARS-CoV-2 in dry oropharyngeal swab specimens collected from individuals without symptoms or other reasons to suspect COVID-19. Testing is limited to laboratories designated by CENTOGENE US, LLC which are certified under the CLIA 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 dry oropharyngeal swab 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.

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. 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 (as may be requested under Condition G below), 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 Instructions for Use:

- Internal Control (IC): the endogenous human RNase (RNP) gene monitors improper sampling or sample storage, failures of the extraction process that result in insufficient amounts or quality of the samples RNA, failure of the RT-PCR process and the presence of inhibitory substances present in the extracted RNA sample.
- No template control (NTC): 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.

The above described product is authorized to be accompanied with laboratory procedures entitled “CentoSure SARS-CoV-2 RT-PCR Assay” (SOPeNT-21), 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 product-specific information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: CentoSure SARS-CoV-2 RT-PCR Assay
- Fact Sheet for Patients: CentoSure SARS-CoV-2 RT-PCR Assay

The above described product, when accompanied by the laboratory procedures (identified above), EUA Summary 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 for the qualitative 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 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 for the indication above, 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 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, storage, and distribution 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 available the authorized product with the authorized labeling to authorized laboratories.
- C. You 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.

- D. You will ensure that the authorized laboratories using the authorized product have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- E. You will maintain records of the authorized laboratories to which you distribute the test and the number of tests you distribute.
- F. 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.
- G. 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 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.
- H. You will evaluate the analytical limit of detection and assess traceability of your product with any FDA-recommended reference material(s), if requested by FDA.⁵ After submission to and concurrence by FDA, DMD/OHT7/OIR/OPEQ/CDRH, will update the EUA summary to reflect the additional testing.
- I. You will have a process in place to track adverse events, including any occurrence of false results, with your product and report any such events to FDA pursuant to 21 CFR Part 803.

Authorized Laboratories

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

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.

- M. 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.
- N. 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 (customersupportel@centogene.com; +1(617)580-2102) 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.
- O. 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.

CEN TO GENE US, LLC. and Authorized Laboratories

- P. 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

- Q. 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.
- R. 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.
- S. 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 the authorized laboratory;
 - 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 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,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure

REVOKED