

August 15, 2020

Nathan Grubaugh, Ph.D.
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Department of Epidemiology of Microbial Diseases
60 College Street
New Haven, CT 06510

Device: SalivaDirect

Company: Yale School of Public Health, Department of Epidemiology of Microbial Diseases

Indication: Qualitative detection of nucleic acid from SARS-CoV-2 in saliva collected without preservatives in a sterile container from individuals suspected of COVID-19 by their healthcare provider.
Emergency use of this test is limited to authorized laboratories.

Authorized Laboratories: Laboratories designated by the Yale School of Public Health, Department of Epidemiology of Microbial Diseases, that includes the Clinical Molecular Diagnostics Laboratory, Department of Pathology, Yale School of Medicine, located at 310 Cedar St., New Haven, CT 06510, that are also certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a and meet the requirements to perform high complexity tests.

Dear Dr. Grubaugh:

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

¹ For ease of reference, this letter will use the term “you” and related terms to refer to Yale School of Public Health, Department of Epidemiology of Microbial Diseases.

² For ease of reference, this letter will use the term “your product” to refer to the SalivaDirect used for the indication identified above.

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 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, 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 saliva collected without preservatives in a sterile container from individuals suspected of COVID-19 by their healthcare provider. The SARS-CoV-2 nucleic acid is generally detectable in saliva 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. Negative results for SARS-CoV-2 RNA from saliva should be confirmed by testing of an alternative specimen type if clinically indicated.

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.

Testing is limited to laboratories designated by the Yale School of Public Health, Department of Epidemiology of Microbial Diseases, that includes the Clinical Molecular Diagnostics Laboratory, Department of Pathology, Yale School of Medicine, located at 310 Cedar St., New Haven, CT 06510, that are also certified under CLIA, 42 U.S.C. §263a and meet the requirements to perform high complexity tests.

To use your product, authorized laboratories are required to acquire and use, according to the authorized instructions for use, commercially sourced materials or other authorized materials and authorized ancillary reagents commonly used in clinical laboratories as described in the authorized labeling (described below). Saliva is first treated with proteinase K followed by a heat inactivation step, and is then directly used as input where the SARS-CoV-2 nucleic acid is reverse transcribed into cDNA followed by PCR amplification and detection using an authorized real-time (RT) PCR instrument.

Your product requires the following control materials, or other authorized control materials (as specified under Condition O 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 authorized labeling:

- Internal Control - RNase P (RP) control in clinical samples: The RP primer and probe set is included in each run to test for human RP, which controls for specimen quality and demonstrates that nucleic acid was generated by the extraction process.
- Negative Extraction Control (NEC)- Nuclease-free, molecular-grade water processed in the same manner as the clinical specimens and monitors for contamination during saliva processing.
- Negative Template Control (NTC)– Nuclease-free, molecular-grade water added to every PCR plate with specimens and monitors for contamination of the PCR reagents.
- Positive - external control that contains synthetic SARS-CoV-2 RNA and monitors functioning of RT- qPCR reagents.

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 used pursuant to the “SalivaDirect Instructions for Use” (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 accompanied by the following product-specific information pertaining to the emergency use, which you and authorized laboratories are required to make available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Yale School of Public Health, Department of Epidemiology of Microbial Diseases - SalivaDirect
- Fact Sheet for Patients: Yale School of Public Health, Department of Epidemiology of Microbial Diseases - SalivaDirect

The above described product, when used pursuant to the “SalivaDirect Instructions for Use,” and

the EUA Summary (identified above) and accompanied by 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 authorized 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.

IV. Conditions of Authorization

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

Yale School of Public Health, Department of Epidemiology of Microbial Diseases (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 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).
- 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 your product and authorized labeling.
- 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 laboratories you designate as authorized laboratories and you will also maintain records of test usage by all such authorized laboratories.
- H. You 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.
- 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 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 in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- L. You may request the addition of other specimen processing 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). After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of and concurrence with the data, 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.
- R. Upon request, you will conduct post-authorization studies and/or data analysis concerning the performance of saliva specimens with your authorized test. Such studies and/or data analysis will be agreed upon between you and FDA. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of the data, FDA will consider whether additional action is appropriate, such as revision or revocation of the EUA.
- S. You will track adverse events, including any occurrence of false results and report to FDA pursuant to 21 CFR Part 803.

Authorized Laboratories

- T. 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.
- U. 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

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

types, authorized control materials, authorized ancillary reagents and authorized materials required to use your product are not permitted.

- V. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- W. 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.
- X. 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 (salivadirect@gmail.com) 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.
- Y. 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.

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- Z. 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

- AA. All descriptive printed matter, including advertising and promotional materials, relating to the use of your product 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.
- BB. 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.
- CC. 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 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