U.S. FOOD & DRUG ADMINISTRATION

October 29, 2021

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| Device: | SalivaDirect for use with DTC Kits |
| EUA Number: | EUA210506 |
| Laboratory: | Yale School of Public Health, Department of Epidemiology of Microbial Diseases |
| Indication: | A direct to consumer product for testing saliva specimens self-collected at home (which includes in a community-based setting) using the SalivaDirect DTC Saliva Collection Kit when used consistent with its authorization by any individual including individuals without symptoms or other reasons to suspect COVID-19.<br><br>This test is also for the qualitative detection of nucleic acid from the SARS-CoV-2 in pooled samples containing up to five individual saliva specimens self-collected at home (which includes in a community-based setting) using the SalivaDirect DTC Saliva Collection Kit and tested using specified workflows.<br><br>Emergency use of the SalivaDirect for use with DTC Kits 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. Wylie:

On August 27, 2021, based on your[1] request, the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of SalivaDirect for use with DTC Kits, a direct to consumer product for testing saliva specimens self-collected at home (which includes in a community-based setting) using the SalivaDirect DTC Saliva Collection Kit when used consistent with its authorization by any individual including individuals without symptoms or other reasons to suspect COVID-19, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). Testing was 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 the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a and meet the requirements to perform high complexity tests.

On October 21, 2021, you requested to amend the Emergency Use Authorization (EUA). Based on that request, and having concluded that revising the August 27, 2021, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the August 27, 2021, letter in its entirety with the revisions incorporated.[2] Accordingly, your product[3] is hereby authorized pursuant to section 564 of the Act when used pursuant to the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter.

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.[4]

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[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] The revisions to the August 27, 2021, letter and authorized labeling include: (1) modification of the intended use to include pooling of up to five individual saliva specimens self-collected at home (which includes in a community based setting) using the SalivaDirect DTC Saliva Collect Kit and tested using specified workflows and addition of the Protocol for Monitoring of Specimen Pooling Strategies to the Instructions for Use (IFU), (2) addition of the following thermocyclers: Roche LightCycler 480, ABI StepOne Plus, CHAI Open qPCR, and the following automated liquid handler platforms: Tecan Fluent 780 and Tecan Fluent 480 (96 and 384 well), (3) addition of a new RT-PCR reagent and an additional N1 external positive control, (4) updates to the Conditions of Authorization to add new Conditions of Authorization related to pooling (new Conditions BB, CC, and DD below), and update an email address in Condition V, and (5) updates to the assay IFU and Fact Sheets for Healthcare Providers and Patients to include language related to pooling.

[3] For ease of reference, this letter will use the term "your product" to refer to the SalivaDirect for use with DTC Kits used for the indication identified above.

[4] 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 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.[5]

**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 direct to consumer product for testing saliva specimens self-collected at home (which includes in a community-based setting) using the SalivaDirect DTC Saliva Collection Kit when used consistent with its authorization by any individual including individuals without symptoms or other reasons to suspect COVID-19.

This test is also for the qualitative detection of nucleic acid from the SARS-CoV-2 in pooled samples containing up to five individual saliva specimens that are self-collected at home (which includes in a community-based setting) using the SalivaDirect DTC Saliva Collection Kit and tested using specified workflows. Negative results from pooled testing should not be treated as definitive. If a patient's clinical signs and symptoms are inconsistent with a negative result or results are necessary for patient management, then the patient should be considered for individual testing. Specimens included in pools with a positive or invalid result must be tested

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

individually prior to reporting a result. Specimens with low viral loads may not be detected in sample pools due to the decreased sensitivity of pooled testing.

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.

Results are for the detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in saliva specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA. 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. The agent detected may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2 infection.

Negative test results are provided to the user via text, email and/or online portal. Individuals with positive, or invalid test results will be contacted by a healthcare provider. The direct to consumer home collection system is intended to enable users to access information about their COVID-19 infection status that could aid with determining if self-isolation or quarantine is appropriate and to assist with healthcare decisions after discussion with a healthcare provider.

Use of your product is not a substitute for visits to a healthcare provider. The information provided by this product should not be used to start, stop, or change any course of treatment unless advised by a healthcare provider.

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 I 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 and run as outlined in the authorized labeling. 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 test is authorized to be used pursuant to the "SalivaDirect for use with DTC Kits 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/in-vitro-diagnostics-euas), and accompanied by the following fact sheets 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 for use with DTC Kits
- Fact Sheet for Individuals: Yale School of Public Health, Department of Epidemiology of Microbial Diseases – SalivaDirect for use with DTC Kits

The above described test, when used pursuant to the "SalivaDirect for use with DTC Kits Instructions for Use", and the EUA Summary and accompanied by the two Fact Sheets (collectively referred to 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) 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.

## 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 pursuant to 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 must make your product available with the authorized labeling to authorized laboratories.

C. You must make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.

D. You must 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. You must also ensure that authorized laboratories using your product have a process in place for providing test results via the agreed upon process as authorized by the SalivaDirect for use with DTC Kits EUA.

E. You must maintain records of the laboratories you designate as authorized laboratories, and you must also maintain records of test usage by all such authorized laboratories.

F. You must 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.

G. You must collect information on the performance of your product. You will report to 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) 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.

H. 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.

I. 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.

J. You must evaluate the analytical limit of detection and assess traceability[6] 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 must 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.

K. You must have lot release procedures for lots of reagents needed to run the SalivaDirect DTC for use with DTC Kits, and the lot release procedures, including the study design, acceptance criteria and statistical power, must be sufficient to ensure that your product can achieve the clinical and analytical performance claimed in the authorized labeling. You must make lot numbers of qualified lots available to designated laboratories to use with your product.

L. Upon request, you must 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.

M. You must submit to DMD/OHT7-OIR/OPEQ/CDRH on a monthly basis (unless otherwise notified by DMD/OHT7-OIR/OPEQ/CDRH) a current list of the authorized laboratories designated by you to use the SalivaDirect DTC for use with DTC Kits.

N. You must submit to FDA a summary report within 30 calendar days of authorization summarizing the results of any testing performed using specimens collected with the SalivaDirect DTC Saliva Collection Kit for use with your product during that timeframe, including how many specimens were received, how many specimens had

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

to be rejected during accession and the main reasons for rejection, and the positivity rate for specimens collected with the authorized self-collection kit.

O. You must have a process in place to track adverse events, including any occurrence of false results with your product, including with the SalivaDirect DTC Saliva Collection Kit, from testing at your institution and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) pursuant to 21 CFR Part 803 and via Medwatch by submitting the online FDA Form 3500 (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home) or by calling 1-800-FDA-1088.

P. You must evaluate the impact of SARS-CoV-2 viral mutations on your product's performance. Such evaluations must occur on an ongoing basis and must include any additional data analysis that is requested by FDA in response to any performance concerns you or FDA identify during routine evaluation. Additionally, if requested by FDA, you must submit records of these evaluations for FDA review within 48 hours of the request. If your evaluation identifies viral mutations that affect the stated expected performance of your device, you must notify FDA immediately.

Q. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA, such as those related to the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

**Authorized Laboratories**

R. Authorized laboratories using your product must 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.

S. Authorized laboratories using your product must 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.

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

U. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

V. Authorized laboratories must collect information on the performance of your product and report any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your

product, including with the SalivaDirect DTC Saliva Collection Kit, of which they become aware to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov), you (info@salivadirect.org) and Medwatch by submitting the online FDA Form 3500 (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home) or by calling 1-800-FDA-1088

W. 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.

X. Authorized laboratories must make available all instructions related to the self-collection of saliva specimens using the SalivaDirect DTC Saliva Collection Kit, both in the shipped kit and on their website.

Y. Through a process of inventory control, authorized laboratories must maintain records of the numbers of SalivaDirect DTC Saliva Collection Kit they distribute.

Z. Authorized laboratories must maintain customer complaint files on record and must report to FDA (See Condition V) any significant complaints about usability or deviations from the established performance characteristics of the SalivaDirect DTC Saliva Collection Kit.

AA. When testing authorized specimens self-collected using the SalivaDirect DTC Saliva Collection Kit, authorized laboratories must follow any specimen accessioning protocols provided with the self-collection kit when accepting specimens for testing. Authorized laboratories testing specimen self-collected using the SalivaDirect DTC Saliva Collection Kit must have in place a suitable specimen receipt and accessioning SOP or follow the "Self-Collection Specimen Receipt and Accessioning SOP" standard operating procedure when accepting specimens for testing.

BB. Authorized laboratories using specimen pooling strategies when testing patient specimens with your product must include with negative test results for specific patients whose specimen(s) were the subject of pooling, a notice that pooling was used during testing and that "Patient specimens with low viral loads may not be detected in sample pools due to the decreased sensitivity of pooled testing."

CC. Authorized laboratories implementing pooling strategies for testing patient specimens must use the "Protocol for Monitoring of Specimen Pooling Testing Strategies" available in the authorized labeling to evaluate the appropriateness of continuing to use such strategies based on the recommendations in the protocol.

DD. Authorized laboratories must keep records of specimen pooling strategies implemented including type of strategy, date implemented, and quantities tested, and

test result data generated as part of the Protocol for Monitoring of Specimen Pooling Testing Strategies. For the first 12 months from the date of their creation, such records must be made available to FDA within 48 business hours for inspection upon request and must be made available within a reasonable time after 12 months from the date of their creation.

**Yale School of Public Health, Department of Epidemiology of Microbial Diseases (You) and Authorized Laboratories**

EE. You and authorized laboratories using your product must 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**

FF. 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 meet the requirements set forth in section 502(a), (q)(1), and (r) of the Act, as applicable, and FDA implementing regulations.

GG. No descriptive printed matter, 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.

HH. All descriptive printed matter, advertising and promotional materials relating to the use of your product shall clearly and conspicuously state that:

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and
- The emergency use of this product 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 declaration is terminated or authorization is 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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Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosure