June 14, 2022

Emi Zychlinsky, Ph.D.
Sr. Vice President, Quality and Regulatory
Standard BioTools Inc.
2 Tower Place, Suite 2000
South San Francisco, CA 94080

Device:	Advanta Dx SARS-CoV-2 RT-PCR Assay
EUA Number:	EUA201725
Company:	Standard BioTools Inc.
Indication:	Qualitative detection of nucleic acid from SARS-CoV-2 in saliva specimens collected without preservatives in a sterile container from individuals suspected of COVID-19 by their healthcare provider. This test is also for use with saliva specimens that are self-collected at home with or without the supervision of a healthcare provider (HCP) with the AZOVA COVID-19 Test Collection Kit from individuals suspected of COVID-19 by their HCP. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity tests.

Dear Dr. Zychlinsky:

On August 25, 2020, based on Fluidigm Corporation's request the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Advanta Dx SARS-CoV-2 RT-PCR Assay, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) for the indication stated in the letter.[1]

[1] The August 25, 2020, letter authorized the Advanta Dx SARS-CoV-2 RT-PCR Assay for the qualitative detection of nucleic acid from SARS-CoV-2 in saliva specimens from individuals suspected of COVID-19 by their healthcare provider. Testing was limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity tests.

Based on Fluidigm Corporation's requests FDA granted updates to the authorized labeling on November 5, 2020,[2] January 8, 2021[3] and February 1, 2022.[4] FDA also reissued the EUA on February 26, 2021, with revisions incorporated. [5] In addition, FDA established additional Conditions of Authorization in response to the continued emergence of new variants of SARS-CoV-2 on September 23, 2021.[6]

On April 15, 2022, you[7] requested to amend the EUA. Based on that request, and having concluded that revising the February 26, 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 February 26, 2021 letter in its entirety with the revisions incorporated.[8] Pursuant to section 564 of the Act and the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter, your product[9] is now intended for the indication described above.

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[2] On November 5, 2020, the request was granted to update the Instructions for Use (IFU) to: (1) update the Biomark Data Collection Software, the Real-Time PCR analysis software and the IFC Controller RX (RX Controller) system software to include the option for a manual Ct threshold adjustment, (2) include a procedure to manually adjust the fluorescence threshold for data analysis, (3) substitute the requirement of using sterile pipette tips with RNase/DNase free pipette tips, and (4) include minor updates to the intended use, IFU and the quick reference guide for the Advanta Dx SARS-CoV-2 RT-PCR Assay Interpretive Software.

[3] On January 8, 2021, the request was granted to update the IFU to: (1) add a new qualified manufacturer for the Advanta Dx SARS-CoV-2 RT-PCR Assay primers and probes, (2) clarify the interpretation of Positive Control, Negative Control and No Template Control results in the IFU and the Software Quick Reference Guide, and (3) minor updates to wording in the IFU and the intended use.

[4] On February 1, 2022, the request was granted to update the authorized labeling to: (1) remove use of CDC's primers and probes manufactured by IDT, (2) update the inclusivity study data, (3) include use of Interpretive Software v1.0.1 with the Real-Time analysis software v4.7.1, Biomark Data Collection Software v4.7.1, and Juno System Software v3.14.1, and (4) include release of software version changes for new customers (Real-Time analysis software v4.8.1, Biomark Data Collection Software v4.8.1, Juno System Software v3.15.1, and Advanta DX SARS-CoV-2 Interpretive Software v2.0.1). FDA also updated the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients to reflect language used in more recent authorizations.

[5] On February 26, 2021 the revisions to the August 25, 2020, letter and authorized labeling included:: (1) revision of the intended use to add the use of the AZOVA COVID-19 Test Collection Kit for self-collection of saliva specimens at home with or without the supervision of a healthcare provider; (2) add an Instrument Qualification Method Protocol (IQM) for validation of RUO instruments; (3) update the healthcare provider fact sheet to include information indicating performance has not been established with all circulating variants and update the patient fact sheets to reflect language use in more recent authorizations, (4) update conditions of authorization consistent with recent authorizations, including additional conditions D., I., J., K., U., V. and CC. (in the February 26, 2021, letter) and consolidation of several conditions in N, and (5) add a limitation regarding performance with circulating variants.

[6] The Viral Mutation Revision Letter – September 23, 2021, can be accessed at: https://www.fda.gov/media/152406/download

[7] For ease of reference, this letter will use the term "you" and related terms to refer to Standard BioTools Inc.

[8] The revisions to the February 26, 2021, letter and authorized labeling include: (1) revision of the Company name from "Fluidigm Corporation" to "Standard BioTools Inc."; (2) add "Instruments and Software Used with the Advanta Dx SARS-CoV-2 RT-PCR Assay" Product Information as authorized labeling, (3) delete Condition of Authorization U. (from the February 26, 2021 letter) as fulfilled through data and information submitted to FDA, (4) add Conditions of Authorization (2) and (3) from the Viral Mutation Revision Letter – September 23, 2021 (U. and V. below), and (5) updates to the Fact Sheet for Healthcare Providers and Fact Sheet for Patients to reflect more recent authorizations.

[9] For ease of reference, this letter will use the term "your product" to refer to the Advanta Dx SARS-CoV-2 RT-PCR Assay.

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.[10]

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 included in the "Advanta Dx SARS-CoV-2 RT-PCR Assay" Instructions for Use (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.[11]

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

[10] 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).

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

Your product is a real-time Reverse Transcription (RT) PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in saliva specimens collected without preservatives in a sterile container from individuals suspected of COVID-19 by their healthcare provider.

The test is also for use with saliva specimens that are self-collected at home with or without the supervision of an HCP with the AZOVA COVID-19 Test Collection Kit from individuals suspected of COVID-19 by their HCP.

Children under the age of 18 may use the self-collection kit, under adult supervision to assist, as needed, with the steps beyond spitting into the collection tube.

Testing is limited to laboratories certified under CLIA that meet requirements to perform high complexity tests.

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.

The AZOVA COVID-19 Test Collection Kit is ordered online. The AZOVA COVID-19 Test Collection Kit provides specimen collection and storage materials as well as materials for user shipment to the testing laboratory, as described in the "AZOVA COVID-19 Test Collection Kit for use with the Advanta Dx SARS-CoV-2 RT-PCR Assay Self-Collection Kit Instructions for Patients".

To use your product, SARS-CoV-2 nucleic acid is released from saliva through a heat-lysis step. The heat-treated saliva is then used directly for testing where the nucleic acid is first reverse transcribed into cDNA followed by a PCR pre-amplification step and then real-time PCR detected using a real-time fluorescence based PCR technology as described in the Instructions for Use. The Advanta Dx SARS-CoV-2 RT-PCR Assay includes the materials (or other authorized materials as may be requested under Condition N. below) described in the authorized labeling.

Your product requires control materials, or other authorized control materials (as may be requested under Condition N. below), that are described in the authorized labeling

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 authorized labeling.

The labeling entitled "Advanta Dx SARS-CoV-2 RT-PCR Assay" Instructions for Use, the "Advanta Dx SARS-CoV-2 RT-PCR Assay Interpretive Software" Quick Reference Guide, the "AZOVA COVID-19 Test Collection Kit for use with the Advanta Dx SARS-CoV-2 RT-PCR Assay Self-Collection Kit Instructions for Patients," the "Instruments and Software Used with

the Advanta Dx SARS-CoV-2 RT-PCR Assay" Product Information and the "Advanta Dx SARS-CoV-2 RT-PCR Assay Instrument Qualification Method (IQM) Protocol" (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas), the Product Information Card (PIC), and the following fact sheets pertaining to the emergency use, is required to be made available as set forth in the Conditions of Authorization (Section IV), and together are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: Standard BioTools Inc. - Advanta Dx SARS-CoV-2 RT-PCR Assay
- Fact Sheet for Patients: Standard BioTools Inc. - Advanta Dx SARS-CoV-2 RT-PCR Assay

The above described product, when accompanied by the authorized labeling provided as set forth in the Conditions of Authorization (Section IV), is authorized to be distributed and used 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, storage, and distribution of your product, but excluding Subpart

H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

IV. Conditions of Authorization

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

Standard BioTools Inc. (You) and Authorized Distributor(s)[12]

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 and authorized distributor(s) must make your product available with the authorized labeling to authorized laboratories.

C. You and authorized distributor(s) must make available on your website(s) the authorized labeling.

D. You and authorized distributor(s) will include a physical copy of the authorized PIC card with each shipped product to authorized laboratories and will make the authorized labeling electronically available with the opportunity to request a copy in paper form, and after such request, you must promptly provide the requested information without additional cost.

E. You and authorized distributor(s) 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.

F. Through a process of inventory control, you and authorized distributor(s) must maintain records of the authorized laboratories to which they distribute your product and number they distribute.

G. You and authorized distributor(s) must 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.

H. You and authorized distributor(s) are authorized to make available additional

[12] "Authorized Distributor(s)" are identified by you, Standard BioTools Inc., in your EUA submission as an entity allowed to distribute your product.

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 and authorized distributors must make available all instructions related to the self-collection of saliva specimens using the AZOVA COVID-19 Test Collection Kit both in the shipped kit and on your website.

J. Through a process of inventory control, you and authorized distributor(s) must maintain records of the numbers and locations to which the AZOVA COVID-19 Test Collection Kit is distributed.

K. You and authorized distributor(s) must maintain customer complaint files concerning the AZOVA COVID-19 Test Collection Kit on record. You will report to FDA any significant complaints about usability or deviations from the established performance characteristics of the product of which you become aware.

Standard BioTools Inc. (You)

L. You must notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).

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

N. 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, including requests to make available additional authorized labeling specific to an authorized distributor. Such additional labeling may use another name for the product but otherwise must be consistent with the authorized labeling, and not exceed the terms of authorization of this letter. Any request for changes to this EUA 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.

O. You must comply with the following requirements pursuant to FDA regulations: 21 CFR 820 Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

P. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must ensure that the tests released for distribution have the clinical and analytical performance claimed in the authorized labeling.

Q. If requested by FDA, you must submit lot release procedures to FDA, including sampling protocols, testing protocols, and acceptance criteria, that you use to release lots of your product for distribution in the U.S. If such lot release procedures are requested by FDA, you must provide it within 48 hours of the request.

R. You must evaluate the analytical limit of detection and assess traceability[13] 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.

S. You must have a process in place to track adverse events, including any occurrence of false results and report to FDA pursuant to 21 CFR Part 803

T. 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.

U. 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 (via email: CDRH-EUAReporting@fda.hhs.gov).

V. 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.

W. You must have a process in place to track adverse events associated with the AZOVA COVID-19 Test Collection Kit, including occurrences of false results and report to FDA pursuant to 21 CFR Part 803. Serious adverse events, especially unexpected biosafety concerns, must be immediately reported to DMD/OHT-7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov).

Authorized Laboratories

X. Authorized laboratories using your product must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for

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

disseminating these Fact Sheets may be used, which may include mass media.

Y. 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.

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

AA. 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.

BB. Authorized laboratories must 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 (techsupport@fluidigm.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.

CC. All laboratory personnel using your product must be appropriately trained in RT-PCR techniques, the specific processes and instruments used in the Advanta Dx SARS-CoV-2 RT-PCR Assay and use appropriate laboratory and personal protective equipment when handling this kit and use your product in accordance with the authorized labeling.

DD. Authorized laboratories testing specimens self-collected using the AZOVA COVID-19 Test Collection Kit must have in place a suitable specimen receipt and accessioning SOP.

Standard BioTools Inc. (You), Authorized Distributors and Authorized Laboratories

EE. You, authorized distributors, 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, 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