U.S. FOOD & DRUG ADMINISTRATION

September 2, 2021

Sally Howard
VP Regulatory and Quality
Adaptive Biotechnologies Corporation
1551 Eastlake Avenue E, Ste. 200
Seattle, WA 98102

Device:	T-Detect COVID Test
EUA Number:	EUA203162
Company:	Adaptive Biotechnologies Corporation
Indication:	A multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) based assay to detect and identify rearranged T-cell receptor beta (TCR β) gene sequences from human genomic DNA (gDNA) isolated from venous whole blood using di-potassium ethylenediaminetetraacetic acid (K2 EDTA) as an anticoagulant. The T-Detect COVID Test is intended for use as an aid in identifying individuals with an adaptive T-cell immune response to SARS-CoV-2, indicating recent or prior infection with SARS-CoV-2. Specimens should only be tested from individuals that are 15 days or more post-symptom onset. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Laboratories designated by Adaptive Biotechnologies Corporation that includes the Adaptive Biotechnologies Lab located at 1551 Eastlake Ave E Ste. 200, Seattle, Washington, which is also certified under the Clinical Laboratory Improvements Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high-complexity tests.

Dear Sally Howard:

On March 5, 2021, based on your[1] request the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the T-Detect COVID Test pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) for the detection and identification of rearranged T-cell receptor beta (TCR β) gene sequences from human genomic DNA (gDNA) isolated from venous whole blood using di-potassium ethylenediaminetetraacetic acid (K2 EDTA) as an anticoagulant. The T-Detect COVID Test is

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Adaptive Biotechnologies Corporation.

intended for use as an aid in identifying individuals with an adaptive T-cell immune response to SARS-CoV-2, indicating recent or prior infection with SARS-CoV-2. Testing was limited to laboratories designated by Adaptive Biotechnologies Corporation that includes the Adaptive Biotechnologies Lab located at 1551 Eastlake Ave E Ste. 200, Seattle, Washington, which is also certified under the Clinical Laboratory Improvements Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high-complexity tests.

On July 15, 2021, you requested to revise your Emergency Use Authorization (EUA). Based on this request, and having concluded that revising the March 5, 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 March 5, 2021, letter in its entirety with the revisions incorporated.[2] 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[3] is now authorized for use consistent with the indication described above.

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]

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:

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2 The revisions to the March 5, 2021, letter and authorized labeling include: 1) revisions to the letter and Conditions of Authorization (Section IV) to remove Condition J (of the March 5, 2021, letter) related to the required testing (fulfilled) and the addition of new Conditions related to circulating variants (new Conditions M and N below), and (2) update the Healthcare Provider Fact Sheet and the Recipient Fact sheet to reflect language used in more recent authorizations.

3 For ease of reference, this letter will use the term "your product" to refer to the T-Detect COVID Test 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).

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 recent or prior infection with SARS-CoV-2 by identifying individuals with a T-cell immune response to the virus that causes COVID-19, and that the known and potential benefits of your product when used for such use, 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 multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) based assay to identify rearranged T-cell receptor beta (TCR β) gene sequences from human genomic DNA (gDNA) isolated from venous whole blood using K2 EDTA as an anticoagulant. The T-Detect COVID Test is intended for use as an aid in identifying individuals with an adaptive T-cell immune response to SARS-CoV-2, indicating recent or prior infection with SARS-CoV-2.

At this time, it is unknown how long the T-cell immune response persists following infection and what level of protection may be conferred by the presence of a T-cell immune response. Your product should not be used to diagnose or exclude acute SARS-CoV-2 infection. Testing is limited to laboratories designated by Adaptive Biotechnologies Corporation that includes the Adaptive Biotechnologies Lab located at 1551 Eastlake Ave E Ste. 200, Seattle, Washington, which is also certified under the Clinical Laboratory Improvements Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high-complexity tests.

Results are for identification of specific T-cell receptor beta (TCR β) gene sequences specific for SARS-CoV-2 from human gDNA. It may take several days after initial infection to prime and expand adaptive T cell immune responses, although the duration of time the adaptive T cell immune responses are present is not well characterized for SARS-CoV-2. The sensitivity of your product early after infection is unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing using a FDA approved, cleared, or authorized molecular or antigen test for SARS-CoV-2 is necessary. The results from the assay should always be used in combination with the clinical examination, patient medical history, and other findings. Incorrect results for T-Detect COVID Test may occur due to biologic variation of the T-cell receptor (TCR) repertoire or other possible causes. Specimens should only be tested from individuals that are 15 days or more post-symptom onset.

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

To use your product, human genomic DNA is extracted from the patient's venous whole blood specimen. Following extraction, a multiplex PCR strategy is used to amplify rearranged TCR β sequences from gDNA, reference loci, synthetic TCR β molecules, and synthetic reference molecules. The resulting amplicon libraries are then sequenced and the rearranged TCR β sequences in the specimen are quantified. A machine learning algorithm developed specifically for use as part of your product is employed to identify patients with an immune response to SARS-CoV-2 based on the observed rearranged TCR β sequences identified by your product.

Your product requires the following control materials, or other authorized control materials (as may be requested under Condition H. below), that are processed along with the patient samples and are required to be included with each specimen 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 EUA Summary:

- **DNA Extraction controls** - Each batch extraction (up to 22 samples) is performed with one positive control (Whole Human Blood Frozen with 10% DMSO) and one negative extraction control (Molecular Grade Water). The extraction negative control is used to confirm lack of contamination during the extraction process and is processed through amplification and sequencing in the same fashion as samples.
- **TCR β synthetic templates** - Each PCR reaction includes a spike-in of synthetic molecules that mimic biological TCR β sequence amplicons. The synthetic TCR β molecules allow for measurement and correction of residual amplification bias.
- **Non-TCR β control loci** – Each PCR reaction includes primer sets to amplify control loci. These control loci are used to estimate the absolute number of nucleated human cells in a biological sample and provide information on the quality of the reaction by estimating the number of molecules of template present in the PCR.
- **PCR Amplification Controls** - A positive and negative amplification control are PCR-amplified along with each set of test samples. The amplification controls are subsequently prepared for sequencing and sequenced in the same manner as the test samples.
- **Sequencing Process Controls** - The Illumina PhiX sequencing control is added to every flow cell along with test samples to estimate sequencing error rate for every sequencing run.
- **Other Controls -** A previously characterized COVID-positive sample is included periodically (greater than once per week).

Your product also requires the use of additional authorized materials and authorized ancillary reagents as described in the EUA Summary.

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), the following laboratory SOPs; "Acceptance and DNA Quantification", "Analytical Method for the Characterization of Human T Cell Beta Receptors – 1 Reaction Assay", "Analytical Method for gDNA Extraction from Peripheral Blood Using the KingFisher", "T-Detect Clinical QC Data Review", "T-Detect Reporting", "TCRB_1rxn assay- QC flag specification", and the following fact sheets pertaining to the emergency use, are required to be made available as set forth in the

Conditions of Authorization (Section IV), and are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: Adaptive Biotechnologies Corporation - T-Detect COVID Test
- Fact Sheet for Patients: Adaptive Biotechnologies Corporation - T-Detect COVID Test

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 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 recent or prior infection with SARS-CoV-2 by identifying individuals with an T-cell immune response to the virus that causes 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:

Adaptive Biotechnologies Corporation (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 authorized Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.

D. 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.

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 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 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) (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 product of which you become aware.

H. 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. Any request for changes to this EUA should be submitted to the DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.

I. 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 and concurrence with the data by FDA, you must update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require

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

concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

J. You must further evaluate the clinical cross reactivity performance of your product in an FDA agreed upon post authorization study within 12 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you must update authorized 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 further implement updates to the T-Detect algorithm software used as part of your product to ensure its performance is not degrading in the context of new variant strains, in an FDA agreed upon post authorization software update within 6 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the information and data by FDA, you must update authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH, prior to implementation.

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

M. 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.

N. 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

O. 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.

P. 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.

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

R. 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.

S. 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 (clinicalservices@adaptivebiotech.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.

T. All laboratory personnel using your product must be appropriately trained in molecular techniques and next generation sequencing and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

Adaptive Biotechnologies Corporation (You) and Authorized Laboratories

U. 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

V. 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 and FDA implementing regulations.

W. 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.

X. 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 been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for detecting and identifying the presence of an adaptive T-cell immune response to 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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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure