March 23, 2021

Shakil Ahmed
Sr. Director, Quality Assurance
Twist Bioscience Corporation
681 Gateway Boulevard
South San Francisco, CA 94080

Device:	SARS-CoV-2 NGS Assay
Company:	Twist Bioscience Corporation
Indication:	Qualitative detection of the SARS-CoV-2 RNA from nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal wash/aspirate specimens and bronchoalveolar lavage (BAL) specimens that are collected from individuals suspected of COVID-19 by their healthcare provider. 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 Shakil Ahmed:

This letter is in response to your[1] 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 Twist Bioscience Corporation.
[2] For ease of reference, this letter will use the term "your product" to refer to the SARS-CoV-2 NGS Assay 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]

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 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.[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 a next-generation sequencing (NGS) in vitro diagnostic test on the Illumina NextSeq 500, NextSeq 550, and NextSeq 550Dx Sequencing System intended for the qualitative detection of the SARS-CoV-2 RNA from nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal wash/aspirate specimens and bronchoalveolar lavage (BAL) specimens that are collected from individuals suspected of COVID-19 by their healthcare provider. The SARS-CoV-2 nucleic acid is generally detectable in respiratory 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.

[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.

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.

To use your product, SARS-CoV-2 nucleic acid from the patient specimen is first isolated and purified by extraction. The extracted and purified patient RNA is then converted to cDNA through random priming before being converted to Illumina TruSeq-compatible libraries. Each library is then quantified to determine size and concentration and then pooled using 8 uniquely barcoded libraries per pool, to create 12 distinct 8-plex reactions. Target enrichment is then done using a hybrid capture onto beads that are washed several times to reduce the number of human libraries in the sequencing pool. The enriched library pools are then sequenced with 150 bp single-end reads on the Illumina NextSeq 500, NextSeq 550, or NextSeq 550Dx Sequencing System and the resulting sequencing data analyzed using a cloud-based Biotia COVID-DX (v1.0) software, that is optimized for the SARS-CoV-2 NGS Assay, and generates a clinical report including presence/absence of the SARS-CoV-2 RNA.

The SARS-CoV-2 NGS Assay includes the following materials or other authorized materials (as may be requested under Condition J below): Twist Synthetic SARS-CoV-2 RNA Control 2, Twist Library Preparation Kit 2, Twist Library Preparation EF Kit 1, Twist Universal Adapter System - Plate A, Twist SARS-CoV-2 Research Panel, Twist Universal Blockers, Twist Binding and Purification Beads, Twist Fast Hybridization Reagents, Twist Fast Wash Buffers, and Biotia COVID-DX (v1.0) software.

Your product requires the following control materials, or other authorized control materials (as may be requested under Condition J below), that are required to be included with each batch of specimens tested with your product. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- Negative/ no template control (NTC) – Viral transport media (VTM) which does not contain human DNA or human cellular material. NTC monitors for sample contamination on the assay run and is used with each extraction batch through sequencing.
- Negative extraction control (NEC) – VERO E6 cells spiked into VTM is used to monitor for any cross-contamination that occurs during the extraction process, as well as validate extraction reagents and successful RNA extraction.
- Positive control (PC) – Positive Twist RNA template control - Synthetic SARS-CoV-2 RNA Control 2 in Agilent Gene Expression Universal Reference RNA (Human). PC is needed to verify that the assay run is performing as intended.
- Internal control (IC) - Agilent Gene Expression Universal Reference RNA (Human). IC is used to validate the SARS-CoV-2 reagents and successful library generation, hybridization, and post- hybridization PCR.

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 labeling entitled “SARS-CoV-2 NGS Assay” Instructions for Use, (available at

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas), Twist SARS-CoV-2 NGS Assay Product Information Cards (box 1,2,3), and the following product-specific information pertaining to the emergency use, is 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: Twist Bioscience Corporation - SARS-CoV-2 NGS Assay
- Fact Sheet for Patients: Twist Bioscience Corporation - SARS-CoV-2 NGS 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 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, 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:

Twist Bioscience Corporation (You) and Authorized Distributor(s)[5]

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) must include a physical copy of the authorized Twist SARS-CoV-2 NGS Assay Product Information Cards with each shipped product to authorized laboratories, and will make the authorized "SARS-CoV-2 NGS Assay" Instructions for Use 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 of your products they distribute.

G. You and authorized distributor(s) must collect information on the performance of your product. You must 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 information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.

[5] "Authorized Distributor(s)" are identified by you, Twist Bioscience Corporation, in your EUA submission as an entity allowed to distribute your product.

Twist Bioscience Corporation (You)

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

J. 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).

K. 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.

L. 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).

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

N. 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.

O. 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 will update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

P. You must further develop a laboratory procedure whereby authorized laboratories can verify that the RUO instruments authorized with your product is capable of performing the SARS-CoV-2 NGS Assay with sufficient accuracy, as stated in the authorized labeling. You should submit the procedure to FDA within 21 calendar days of

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

authorization. After DMD/OHT7-OIR/OPEQ/CDRH's review and concurrence, you will update the authorized labeling to reflect the laboratory procedure within 45 calendar days of authorization.

Q. You must further evaluate the clinical performance of your product in an FDA agreed upon post authorization clinical evaluation study within 4 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.

R. You must further evaluate the *in silico* inclusivity analysis, to include all US SARS-CoV-2 sequences in the GISAID database, of your product in an FDA agreed upon post authorization analytical study within 1 month 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 will update your 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 further evaluate the cybersecurity of your product as agreed on with FDA and implement and test the agreed upon cybersecurity controls within 2 months from the date of this letter. You must report to FDA any suspected occurrence of cybersecurity related incidents to FDA within 7 days of their occurrence. After submission to and concurrence with the information and data by FDA, you must update you product accordingly. Any product updates related to cybersecurity will be made in consultation with, and require concurrence of, DMD/OHT7- OIR/OPEQ/CDRH.

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

Authorized Laboratories

U. 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.

V. 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.

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

X. 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.

Y. 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 (via email: customersupport@twistbioscience.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.

Z. All laboratory personnel using your product must be appropriately trained in NGS, PCR techniques, in vitro diagnostic procedures and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

Twist Bioscience Corporation (You), Authorized Distributor(s) and Authorized Laboratories

AA. You, authorized distributor(s), 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

BB. 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.

CC. No descriptive printed matter, advertising, and 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.

DD. 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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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure