

April 22, 2021

Karen Gutekunst, Ph.D.
Vice President Regulatory Affairs
Illumina, Inc.
5200 Illumina Way
San Diego, CA 92122

Device: Illumina COVIDSeq Test
EUA Number: EUA201574
Company: Illumina, Inc.
Indication: Qualitative detection of SARS-CoV-2 RNA from nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal aspirates, and bronchoalveolar lavage (BAL) specimens 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, to perform high complexity tests.

Dear Dr. Gutekunst:

On June 9, 2020 based on your¹ request the Food and Drug Administration (FDA) issued 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). Based on your request, FDA has also granted updates to the authorized labeling on August 20, 2020³ and October 28, 2020.⁴

¹ For ease of reference, this letter will use the term “you” and related terms to refer to Illumina, Inc.

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

³ On August 20, 2020, your request was granted to update the Instructions for Use (IFU) of your product to: (1) add the use of the Zymo Quick-DNA/RNA Viral MagBead extraction method, (2) add additional sequencing instruments (NextSeq 500, NextSeq 550, and NextSeq 550Dx) each running software version 4.0, (3) update the Illumina DRAGEN COVIDSeq Test Pipeline to software version 1.2 to accommodate the new sequencing instruments, (4) add the SP flow cell for use on the previously authorized NovaSeq 6000 instrument, (5) replace 6 out of 384 sequencing library indexes for better color balance and read quality, and (6) include cloud-based implementation of DRAGEN COVIDSeq Test Pipeline.

⁴ On October 28, 2020, your request was granted via email to update the EUA Summary to add the results of testing the FDA SARS-CoV-2 Reference Panel Testing.

On October 29, 2020, you requested to amend your Emergency Use Authorization (EUA). Based on this request, and having concluded that revising the June 9, 2020, 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 June 9, 2020, letter in its entirety with the revisions incorporated.⁵ 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 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.⁶

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 Illumina COVIDSeq Test 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

⁵ The revisions to the June 9, 2020, letter and authorized labeling include: (1) revisions to the intended use and authorized labeling documents to include use of the NextSeq 2000 Sequencing System, (2) update to the PCR annealing temperature for the amplification of virus specific sequence, (3) update the Illumina DRAGEN COVIDSeq Test Pipeline to software version 1.3 to accommodate the new sequencing configurations, (4) updates to the NovaSeq 6000 reagent chemistry for certain sequencing configurations, (5) updates to the Fact Sheet for Healthcare Provider and Fact Sheet for Patient to reflect the intended use updates and language consistent with recent authorizations, (6) updates to the letter to use language consistent with recent authorizations and (7) incorporate additional authorized labeling in the letter: “Illumina DRAGEN COVIDSeq Test Pipeline Software Guide”, the “Illumina DRAGEN COVIDSeq Test (EUA) v1.3 App Guide” and the “Illumina COVIDSeq Test” Product Information Card.

⁶ 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).

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.⁷

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 Next-Generation Sequencing (NGS) in vitro diagnostic test on the Illumina NovaSeq 6000 Sequencing System, NextSeq 2000 Sequencing System, NextSeq 500 Sequencing System, NextSeq 550 Sequencing System, or NextSeq 550Dx Instrument intended for the qualitative detection of SARS-CoV-2 RNA from nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal aspirates, and bronchoalveolar lavage (BAL) specimens from individuals suspected of COVID-19 by their healthcare provider. Testing is limited to laboratories certified under CLIA, 42 U.S.C. §263a, that meet requirements to perform high complexity tests. 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. 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 is first extracted, isolated and purified from nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal aspirates, and bronchoalveolar lavage (BAL) specimens. The purified nucleic acid then undergoes reverse transcription, target amplification, library preparation, library pooling, sequencing, and analysis. The Illumina COVIDSeq Test includes the following materials or other authorized materials: Test Box 1- Illumina Tune Beads and Stop Tagment Buffer 2 HT, Test Box 2 - Enrichment BLT HT, Elution Buffer HT, Resuspension Buffer HT, and Tagmentation Wash Buffer HT, Test Box 3 –COVIDSeq Primer Pool 1 HT, COVIDSeq Primer Pool 2 HT, Elution Prime Fragment 3HC Mix HT, Enhanced PCR Mix HT, First Strand Mix HT, Illumina PCR Mix HT, Reverse Transcriptase HT and Tagmentation Buffer 1 HT. In addition your product includes the COVIDSeq Positive Control HT and IDT for Illumina PCR Indexes Sets 1-4. The Illumina COVIDSeq Test is to be used with the Illumina NovaSeq6000 Sequencing System, NextSeq 2000 Sequencing System, NextSeq 500 Sequencing System, NextSeq 550 Sequencing System, or NextSeq 550Dx Instrument.

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

⁷ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

Instructions for Use. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- CCP1 HT (COVIDSeq Primer Pool 1 HT) and CCP2 HT (COVIDSeq Primer Pool 2 HT) – internal control – contains a total of two pools that include SARS-CoV-2 specific primers and a set of primer pairs targeting human transcripts. The targeted human transcripts are commonly prevalent in nasopharyngeal swabs, oropharyngeal swabs, nasal swab, and mid-turbinate specimens. Monitors for successful completion of each step from extraction through Illumina DNA Prep library prep and sequencing to validate negative samples.
- COVIDSeq Positive Control HT - consists of ssRNA fragments that provide coverage of greater than 99.9% of the SARS-CoV-2 viral genome bases, used to monitor detect SARS-CoV-2 and reagent integrity.
- ELB HT (Elution Buffer HT) – used as a no template control (NTC), used to monitor cross-contamination during RNA extraction and downstream library preparation steps and monitor reagent integrity.

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 “Illumina COVIDSeq Test Instructions for Use”, “Illumina DRAGEN COVIDSeq Test Pipeline Software Guide”, the “Illumina DRAGEN COVIDSeq Test (EUA) v1.3 App Guide” and the “Illumina COVIDSeq Test” Product Information Card (available at <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas>), 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 are collectively referred to as “authorized labeling”:

- Fact Sheet for Healthcare Providers: Illumina, Inc. - Illumina COVIDSeq Test
- Fact Sheet for Patients: Illumina, Inc. - Illumina COVIDSeq 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 COVID19, 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:

Illumina, Inc. (You) and Authorized Distributor(s)⁸

- 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 “Illumina COVIDSeq Test” Product Information Card with each shipped product to authorized

⁸ “Authorized Distributor(s)” are identified by you, Illumina, Inc., in your EUA submission as an entity allowed to distribute your product.

laboratories, and must make the authorized “Illumina COVIDSeq Test Instructions for Use”, “Illumina DRAGEN COVIDSeq Test Pipeline Software Guide”, and the “Illumina DRAGEN COVIDSeq Test (EUA) v1.3 App Guide” 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 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) (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 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.

Illumina, Inc. (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 must comply with the following requirements under 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).
- L. 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.

- M. 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.
- 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 DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.
- O. You must evaluate the analytical limit of detection and assess traceability⁹ 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 concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- P. 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

- Q. 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.
- R. Authorized laboratories using your product will use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- S. Authorized laboratories using your product must notify the relevant public health authorities of their intent to run your product.
- T. 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.
- U. 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: techsupport@illumina.com) any suspected occurrence of false positive or false negative results and significant deviations from the

⁹ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

established performance characteristics of your product of which they become aware.

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

Illumina, Inc. (You), Authorized Distributors and Authorized Laboratories

- W. 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

- X. 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.
- Y. 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.
- Z. 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,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure