



November 15, 2021

To: Laboratories That Have Developed Certain Molecular-Based Tests for SARS-CoV-2

Authorized Tests: Certain RT-PCR Molecular-Based Tests for Detection of Nucleic Acid from SARS-CoV-2 from Anterior Nasal Respiratory Specimens for Use as part of a Serial Testing Program

Authorized Laboratories: Testing is limited to the single laboratory that developed the authorized test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3(b)(1)(C)), 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.¹

On November 15, 2021, pursuant to Section 564 of the Act, in response to public health needs to maintain the nation's testing capacity and adapt to current testing uses,² FDA is issuing this letter to authorize certain tests that are within the Scope of this Authorization (Section II). Under this Emergency Use Authorization (EUA), authorized tests are authorized for use only in the single laboratory that developed the authorized test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, and meets requirements to perform high complexity tests.

¹ 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)

² Many laboratories have been providing SARS-CoV-2 testing with tests that are not FDA authorized for emergency use, including as discussed in FDA policies in place earlier in the public health emergency. This authorization is intended to provide an efficient mechanism by which some of these tests can become authorized.

As set forth throughout, this EUA authorizes certain tests that are within the Scope of this Authorization (Section II) for certain specified indications for use.³ This letter authorizes tests (also referred to as products) for multiple indications for use as set forth in the appendices. These indications all contain these essential elements: use with individual or pooled anterior nasal specimens to test individuals, including individuals without symptoms or other epidemiological reasons to suspect COVID-19, when tested at least once per week. This means that tests authorized by this letter may be used with individual or pooled anterior nasal respiratory specimens from individuals with or without known or suspected exposure to COVID-19 when such individuals are tested at least once per week, such as testing at regular intervals as part of a testing program implemented by schools, workplaces, or community groups. The indications in each appendix (A-K) differ in the number of specimens that can be tested or pooled (i.e., 1, up to 3, up to 5, or up to 10), the type of pooling that can be done (i.e., media or swab pooling), and whether the test is authorized for use with home collected specimens. A test is authorized by this EUA if it has been validated in accordance with Appendix A. Appendix A includes the base validation requirements and indication but does not authorize testing of pooled specimens or testing with home collected specimens. Appendices B- K set forth the validation requirements for the pooling and home collection indications. FDA will add tests to Exhibit 1 once it confirms it has received a complete notification as set forth in Section II of this letter. Exhibit 1 will be annotated with the authorized indication(s) for each test and will be maintained on FDA’s webpage.⁴

FDA’s determination that the tests authorized by this EUA meet the criteria for issuance under Section 564(c) of the Act is based on the available scientific evidence, including recent studies involving antigen tests used in a serial manner, knowledge of recently authorized antigen and molecular tests, our experience with SARS-CoV-2 tests since the start of the emergency, as well as the inclusion of additional risk mitigations, such as limiting the use to serial testing.

Having concluded, based on the available scientific evidence, that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of the authorized tests identified in the Scope of this Authorization (Section II) and subject to the Conditions of Authorization (Section IV), for use in the single laboratory that developed the authorized test and that is certified under the CLIA, 42 U.S.C. § 263a and meets the requirements to perform high complexity tests, to detect SARS-CoV-2 in anterior nasal respiratory specimens from individuals.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the authorized tests meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

³ For ease of reference, this letter uses the phrase “authorized tests” to refer to molecular-based tests that are developed and used by the single laboratory, that is certified under CLIA and meets requirements to perform high complexity tests, that developed the test and that are within the Scope of Authorization (Section II).

⁴ CDRH IVD EUA webpage <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>.

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 the authorized tests may be effective in diagnosing infection with SARS-CoV-2 by detecting the presence of SARS-CoV-2 viral material for the indications set forth in the appendices, and that the known and potential benefits of the authorized tests when used for such use, outweigh the known and potential risks of the authorized tests; and
3. There are no adequate, approved, and available alternatives to the emergency use of the authorized tests.⁵

II. Scope of this Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to the tests described below for the indication in Appendix A and any additional indication(s) for use⁶ given in the applicable appendix(es) for which the test is validated consistent with, for use in the single laboratory that developed the authorized test and that is certified under CLIA, 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

Authorized Tests

Tests that meet all of the following eligibility criteria are authorized consistent with this letter:

1. The test is an RT-PCR test that is **not** already authorized for emergency use as of today's date for the qualitative detection of SARS-CoV-2 in respiratory specimens collected by anterior nasal swabs;
2. The test is validated in accordance with Appendix A (base validation);
3. The test is validated in accordance with the applicable Appendix B -K if indicated for more than the base indication set forth in Appendix A;
4. The test detects two or more viral targets on the SARS-CoV-2 genome;
5. The test includes a chemical lysis step followed by a nucleic acid isolation step (e.g., silica bead extraction);
6. The test detects only SARS-CoV-2;
7. The test is designed, manufactured, and used within a single CLIA certified laboratory that meets requirements to perform high complexity tests;
8. The test is for prescription (Rx) use only; and
9. The test uses a combination of control materials that control for specimen quality and test

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

⁶ The indications for use for tests authorized by this EUA are limited to anterior nasal swab specimens in dry tubes or tubes containing viral transport media (VTM), saline, or phosphate-buffered saline (PBS) and do not include any indications for other specimen types, such as saliva. The indications for use for tests authorized by this EUA also do not include specimens in tubes containing inactivating transport media (ITM), such as those containing guanidine thiocyanate or similar chemicals.

system performance.⁷

Authorized tests are qualitative tests for the detection of nucleic acid from SARS-CoV-2 in anterior nasal respiratory specimens from individuals, including those without symptoms or other reasons to suspect COVID-19, when tested at least once per week, as set forth in Appendix A and any additional appendix(es) that the test is validated consistent with.

The SARS-CoV-2 nucleic acid is generally detectable in anterior nasal swab 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 from pooled testing should not be treated as definitive. If a patient's clinical signs and symptoms are inconsistent with a negative result or results are necessary for patient management, then the patient should be considered for individual testing. Specimens included in pools with a positive or invalid result must be reported as presumptive positive or tested individually prior to reporting a result. Individuals included in a pool that returns a positive or invalid result should be treated as a presumptive positive unless or until they receive a negative result when re-tested individually. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, they should isolate until receiving a negative result when re-tested individually and should not be cohorted with other individuals who have received a positive or presumptive positive result. Specimens with low viral loads may not be detected with pooled testing due to decreased sensitivity or increased interference from pooled testing.

For serial testing programs, additional confirmatory testing for negative results may be necessary, if there is a high likelihood of COVID-19, such as an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Additional confirmatory testing for positive results may also be necessary if there is a low likelihood of COVID-19, such as in individuals without known exposure to COVID-19 or residing in communities with low prevalence of infection.

Authorized tests must be accompanied by labeling that is consistent with this letter. For this EUA, such labeling must include the test procedures, a Fact Sheet for Healthcare Providers, a Fact Sheet for Patients, and a Test Summary. Developers must include, at a minimum, the relevant information in the applicable appendix (see Appendices L-N) and the following statement: This test is authorized under the Umbrella EUA for SARS-CoV-2 Molecular

⁷ Examples include: (1) Process Controls such as endogenous or exogenous RNA controls, included in each clinical sample or on each plate to control for reagent quality; (2) Extraction Controls such as a previously characterized negative patient sample to confirm the performance of extraction reagents and successful RNA extraction; (3) External Positive Controls or Positive Template Controls such as in vitro transcript SARS-CoV-2 RNA or a previously characterized positive patient sample, to monitor for failures of analyte specific rRT-PCR reagents and reaction conditions; and (4) No Template (Negative) Controls such as nuclease-free, molecular-grade water or buffer, to monitor for non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents.

Diagnostic Tests for Serial Testing [include link to this letter] for use in [the single laboratory (CLIA certified and meets the requirements to perform high complexity tests) in which it was developed] for [insert indication(s) from applicable appendix(es)] using the test procedures validated in accordance with the requirements of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing.

In addition, the Fact Sheets are required to be made available to healthcare providers and patients receiving test results.

Authorized tests, when labeled consistent with this letter and subject to the Conditions of Authorization (Section IV) of this letter, are authorized to be used in accordance with the Scope of this Authorization (Section II) and the Conditions of Authorization (Section IV) by the laboratory that developed the authorized test, despite the fact that they do not meet certain requirements otherwise required by applicable federal law.

Addition to Exhibit 1

A test will be added to Exhibit 1 after FDA confirms that the required documentation set forth below has been submitted via email to FDA. At that time, FDA will notify the developer of the inclusion of its test(s) in Exhibit 1 by replying to the email. Please note that being added to Exhibit 1 does not necessarily mean that FDA has reviewed the underlying validation data submitted or has confirmed that the test is appropriately validated. Instead, being added to Exhibit 1 only means that the developer has submitted complete documentation. However, if FDA determines that a test listed on Exhibit 1 does not meet one or more of the nine eligibility criteria listed above, it will remove the test from Exhibit 1. Tests removed from Exhibit 1 will be included in a list maintained on FDA’s EUA webpage.

To be added to Exhibit 1, developers must notify FDA by sending an email to FDA with the subject line “Addition to Exhibit 1 of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing” to CDRH-EUA-Templates@fda.hhs.gov with the information below:

- Developer (laboratory) name
- Contact individual’s name, address, phone number, email address
- Test name
- The specific indication(s), referenced by noting the applicable appendix
- The required information, including validation data, as set forth in the applicable appendices
- Authorized labeling (i.e., Test Summary, test procedure(s), Fact Sheet for Healthcare Providers, and Fact Sheet for Patients) as set forth above and required by Condition of Authorization A
- The following information on testing capacity:
 - i. The number of individual tests that can be run with normal operation in a 24-hour period; and
 - ii. The number of individual samples that can be tested in a 24-hour period if all samples are pooled at the maximum ratio authorized pursuant to

the applicable appendix of this letter.

- Statement certifying that the nine eligibility criteria listed above are met and that all information submitted is truthful and accurate, for example:
 - I certify that, in my capacity as [the position held in laboratory] of [laboratory name], I believe to the best of my knowledge that all nine eligibility criteria described in FDA's November 15, 2021, letter have been met and that all data and information I am submitting are truthful and accurate and no material fact has been omitted.

Your Fact Sheets and Test Summary will be added to FDA's webpage when your test is added to Exhibit 1.

Conclusions

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 the authorized tests, when used consistent with the Scope of this Authorization (Section II), outweigh the known and potential risks of such authorized tests.

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 the authorized tests may be effective in diagnosing infection with SARS-CoV-2 by detecting the presence of SARS-CoV-2 viral material as set forth in Section I of this letter, when used consistent with the Scope of this Authorization (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 the authorized tests (as described in the Scope of this Authorization of this letter (Section II)) meet the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized tests under this EUA must be consistent with, and may not exceed the terms of this letter, including the Scope of this 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, the authorized tests are authorized for the indication(s) set forth in Appendix A and any additional appendix for which the test is validated consistent with.

III. Waiver of Certain Requirements

I am waiving the following requirements for the authorized tests 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:

Authorized Laboratories (You)

- A. Your product's labeling must be consistent with the information set forth in this letter and must consist of, at a minimum, a Fact Sheet for Healthcare Providers, a Fact Sheet for Patients, a Test Summary, and test procedure(s). Your Fact Sheet for Healthcare Providers and Fact Sheet for Patients must include the relevant information set forth in Appendices L and M, respectively. Your Test Summary must include the relevant information set forth in Appendix N. Additionally, all of your authorized labeling must include the following statement: This test is authorized under the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing [include link to this letter] for use in [the single laboratory (certified under the CLIA and meets requirements to perform high complexity tests) in which it was developed] for [insert indication(s) from applicable appendix(es)] using the test procedures validated in accordance with the requirements of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing. Your product's labeling must not include any information that is inconsistent with this authorization.
- B. 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 product, you must notify FDA immediately (via email: CDRH-EUA-Reporting@fda.hhs.gov).
- C. If requested by FDA, you must update your labeling within 7 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.
- D. Your authorized 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 product, including requirements under 21 CFR 809.10(b)(12).

- E. You must make available on your website(s), if applicable, the Fact Sheet for Healthcare Providers and Fact Sheet for Patients.
- F. You are authorized to make available additional information relating to the emergency use of your authorized product that is consistent with, and does not exceed, the terms of this letter of authorization.
- G. You may make modifications to your authorized product and implement such changes if the test continues to be within the Scope of this Authorization (Section II), and the modifications do not change the indication for use set forth in the applicable appendix(es) (e.g., including new/different extraction kits or instruments) and do not change the analyte specific reagents (e.g., PCR primers and/or probes).⁸ Prior to implementing modifications under this Condition of Authorization, you must first validate your modified test in accordance with the requirements in the applicable appendix(es) and notify FDA by submitting any information set forth in Section II that has changed from your prior notification, including updated labeling to reflect the modification(s), to FDA at CDRH-EUA-Templates@fda.hhs.gov using the subject line “Modification to Test on Exhibit 1 of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing”. You must also resubmit the certifying statement required for inclusion in Exhibit 1 as set forth in Section II of this letter. Provided that the modification(s) do not affect whether your product is within the scope of this authorization, the updated labeling will be added to FDA’s website after FDA confirms that the required documentation set forth in Section II has been submitted to FDA. At that time, FDA will notify the developer of the inclusion of its updated labeling on FDA’s website by replying to the email. Please note that adding the updated labeling does not necessarily mean that FDA has reviewed the underlying validation data submitted or has confirmed that the modification(s) is appropriately validated. Instead, being added to FDA’s website only means that the developer has submitted complete documentation as set forth in Section II and consistent with this paragraph.
- H. You must inform relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your authorized product and authorized labeling.
- I. You must notify the relevant public health authorities of your intent to run your product.
- J. You must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- K. You 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.

⁸ Other modifications, including new claimed specimen types or test settings (e.g., point-of-care, home testing), or any other modifications that change the indication for use, are not authorized under this EUA and must be authorized under an individual EUA prior to use.

- L. You must use your product as outlined in the authorized labeling. Your test procedures must include the use of control materials that control for specimen quality and test system performance, as set forth in Section II of this letter. The test procedures must indicate the expected results for each control that are necessary for a test to be considered valid. Deviations from your authorized test procedures, including the instruments extraction methods, clinical specimen types, control materials, other ancillary reagents and materials required to use your product are not permitted. Any modifications to your authorized product, including the authorized labeling, must be made in accordance with Condition of Authorization G of this letter.
- M. All laboratory personnel using your product must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this product and use your product in accordance with the authorized labeling.
- N. Upon request from FDA, 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. After concurrence, the updated labeling will be added to FDA's website.
- O. You must collect information on the performance of your product. You must report to DMD/OHT7-OIR/OPEQ/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 your product of which you become aware.
- P. You must have a process in place to track adverse events of your product in accordance with 21 CFR Part 803. Serious adverse events must be immediately reported to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov).
- Q. You 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.
- R. If your product is used with specimens collected using an authorized home specimen collection kit per Appendix J or K, you must follow any specimen accessioning protocols and other authorized labeling provided with the authorized home specimen collection kit.
- S. If your product is used with specimens collected using an authorized home specimen collection kit per Appendix J or K of this letter, you must have a process in place for

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

informing the manufacturer(s) of any authorized home collection kit used with your authorized product of any adverse events that you become aware of related to such kit(s).

- T. If testing pooled specimens with your product, you must have and follow a pooling protocol that includes instructions for follow-up for positive and invalid pools, including follow-up instructions to be provided to the organizer of the testing program. For media pooling, the instructions for follow up for positive and invalid pools must include deconvoluting to retest individual samples. For swab pooling, the instructions for follow up for positive and invalid pools must include reporting as “presumed positive” unless or until the individual is re-tested individually and must include instructions to collect a new specimen to be tested individually. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, the instructions must indicate that such individuals should isolate until receiving a negative result when re-tested individually and should not be cohorted with other individuals who have received a positive or presumptive positive result.
- U. You must include with test result reports for specific individuals whose specimen(s) were the subject of pooling, a notice that pooling was used during testing and that “Individual specimens with low viral loads may not be detected due to the decreased sensitivity or increased interference when tested with pooled testing.”
- V. If testing pooled specimens with your product, you must include with test result reports for specific individuals whose specimen(s) were the subject of pooling, a notice that their test result is “presumed positive” unless or until they are re-tested individually if the pool in which they were included returns a positive or invalid result. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, the report must include instructions to collect a new specimen to be tested individually and must indicate that such individuals should isolate until receiving a negative result when re-tested individually and should not be cohorted with other individuals who have received a positive or presumptive positive result.
- W. If testing specimens using pooled testing with your product, you must monitor the positivity rate of the specimens tested using pooled testing by calculating the percent positive results using a moving average (such as a rolling average updated daily using data from the previous 7-10 days).
- X. You must keep records of specimen pooling test result data, daily testing totals including number of pooled test results, number of individuals tested and daily running average of percent positive results. For the first 12 months from the date of their creation, such records must be made available to FDA upon request within 48 business hours. After 12 months from the date of their creation, upon FDA request, such records must be made available for inspection within a reasonable time.
- Y. You must evaluate the clinical performance of your product by completing the clinical evaluation study for asymptomatic individuals set forth in Appendix A. If this clinical

evaluation is not included in the original notification submitted to FDA, then these results must be submitted to FDA at CDRH-EUA-Templates@fda.hhs.gov using the subject line “Post-Authorization Screening Data for Test on Exhibit 1 of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing” within 6 months of submitting the notification required by Section II of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). If FDA concurs with the data, you must update your authorized labeling to reflect the additional testing. Such labeling updates must be made only after concurrence by DMD/OHT7-OIR/OPEQ/CDRH. If FDA does not concur that the data submitted meets the validation requirements set forth in Appendix A, FDA may determine that your product is not authorized. As described in Section II, FDA will remove any product from Exhibit 1 that it determines is not authorized, e.g., if such product does not meet the validation requirements set forth in Appendix A.

Conditions Related to Printed Materials, Advertising and Promotion

- Z. 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.
- AA. No descriptive printed matter, advertising, or promotional materials relating to the use of your product may represent or suggest that this product is safe or effective for the detection of SARS-CoV-2.
- BB. All descriptive printed matter, advertising, and promotional materials relating to the use of your test 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 the authorized laboratory;
 - 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,

Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Enclosure

Appendix A

Base Validation for Testing Individual Specimens

As explained in Section II of this letter, all tests must be validated in accordance with this appendix in order to be authorized. After the test is validated, the developer must notify FDA by submitting the information set forth in Section II to FDA at CDRH-EUA-Templates@fda.hhs.gov using the subject line “Addition to Exhibit 1 of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing”. Developers who wish to be authorized for additional indications (e.g., pooling) must also validate their test in accordance with the applicable Appendices B-K.

As noted in Appendices B-K, all tests must validate consistent with this appendix (including all protocols outlined below) in order to be authorized. If no other indication(s) is requested in the notification described in Section II, then the indication noted in this appendix will be the only indication for which the test is authorized under this EUA.

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in this appendix:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swab samples collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

Tests will be added to Exhibit 1 for this indication after FDA determines it has received a complete notification.

Validation specific to this indication, and needed prior to performing validation for any indications set forth in other appendices in this letter, includes the four validation protocols outlined below: (1) Limit of Detection (LoD); (2) Validation for Inclusivity (Analytical Reactivity); (3) Validation for Cross-Reactivity (Analytical Specificity); and (4) Clinical Evaluation.

As part of the notification to FDA, methodology and summary data must be submitted for each validation protocol. This includes line data with the Ct score for each sample tested in the clinical evaluation. If you are leveraging data from another developer’s EUA-authorized test, such as *in silico* or cross-reactivity data, you must submit a right of reference from that developer

as part of your notification or indicate that you intend to leverage the CDC's general right of reference.¹⁰

1. Limit of Detection (LoD)

You must determine the LoD of the test utilizing all components of the test system from sample preparation and extraction to detection. Testing quantified live or inactivated virus (i.e., heat treated, chemically modified, or irradiated virus) spiked into real clinical matrix (anterior nasal swab or nasopharyngeal swab samples) for LoD determination is acceptable since this most closely represents a clinical sample. Quantified known positive clinical specimen, as determined by an EUA authorized test, can be used to create dilutions in clinical matrix for LoD determination. Synthetic RNA is not an acceptable test material for the LoD studies. Anterior nasal swab or nasopharyngeal swab samples collected from SARS-CoV-2 negative individuals can be used as clinical matrix. You must determine a preliminary LoD by testing a 2-3 fold dilution series of three replicates per concentration. The lowest concentration that gives positive results 100% of the time is defined as the preliminary LoD. During the preliminary LoD determination at least one concentration that does not yield 100% positive results must be tested. The final LoD concentration must be confirmed by testing 20 individual extraction replicates at the preliminary LoD. For this letter, the LoD is the lowest concentration at which $\geq 19/20$ replicates are positive.

You must determine the LoD of your test for each type of media you intend to use with your test (e.g., saline, PBS, VTM, dry swab reconstituted with PBS).

As part of the notification to FDA, you must provide documentation of the methodology and results of your LoD determination.

2. Validation for Inclusivity (Analytical Reactivity)

Genetic variants of SARS-CoV-2 are emerging which may have the potential to impact test performance. This is discussed in the FDA guidance [Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests](#), which includes recommendations for evaluating the potential impact of emerging and future viral mutations of SARS-CoV-2 on COVID-19 tests.¹¹

¹⁰ The Centers for Disease Control and Prevention (CDC) has granted a right of reference to the performance data contained in the CDC's EUA request for the [CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel \(CDC\)](#) (FDA submission number EUA200001) to any entity seeking authorization for a COVID-19 diagnostic device. The CDC has also granted a right of reference to the performance data contained in the CDC's EUA request for their [Influenza SARS-CoV-2 \(Flu SC2\) Multiplex Assay](#) (FDA submission number EUA201781) to any entity seeking authorization for a multi-analyte respiratory panel that includes SARS-CoV-2. CDC has published the primer and probe sequences for the Influenza SARS-CoV-2 Multiplex Assay on [the CDC website](#).

¹¹ Available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests>.

You must perform an *in silico* inclusivity analysis by conducting sequence alignment of the primer/probe sequences of your test with publicly available SARS-CoV-2 genomes, such as those in the GISAID database.

As part of the notification to FDA, you must provide documentation of the specific primer and probe sequences for your test and the methodology and results of your *in silico* inclusivity analysis. Include a discussion of your *in silico* analysis results for the particular SARS-CoV-2 variants that are circulating with high prevalence (i.e., B.1.617.2 and sub-lineages at the time of issuance of this letter).¹²

Repeat the *in silico* inclusivity analysis on a regular basis (at least monthly) prior to and after authorization.

Your *in silico* inclusivity analysis (initial and recurring) must demonstrate, for at least one of the viral targets in your test, 100% homology to at least 95% of sequences (when analyzing at least 2000 sequences within the last 30 days prior to your submission) representing circulating SARS-CoV-2 variants.

3. Validation for Cross-reactivity (Analytical Specificity)

You must assess the potential cross-reactivity of your test with the organisms listed in the table below to demonstrate that the test does not react with related pathogens, high prevalence disease agents and normal or pathogenic flora that are reasonably likely to be encountered in a clinical specimen. Specifically, conduct sequence alignment of the primer/probe sequences of your test with publicly available genome sequences for the organisms listed in the table below to determine the extent to which cross-reactivity may impact test performance.

Your validation must demonstrate <80% homology between potential cross-reacting microorganism(s) and your test primers/ probe(s).

As part of the notification to FDA, you must provide documentation of the methodology and results of your cross-reactivity validation.

High priority pathogens from the same genetic family	High priority organisms likely present in respiratory specimens
Human coronavirus 229E	Adenovirus (e.g., C1 Ad. 71)
Human coronavirus OC43	Human Metapneumovirus (hMPV)
Human coronavirus HKU1	Parainfluenza virus 1-4
Human coronavirus NL63	Influenza A & B
SARS-CoV-1	Enterovirus (e.g., EV68)

¹² For additional information on the estimated proportions of SARS-CoV-2 lineages, see:
<https://covid.cdc.gov/covid-data-tracker/#variant-proportions>

High priority pathogens from the same genetic family	High priority organisms likely present in respiratory specimens
MERS-coronavirus	Respiratory syncytial virus
	Rhinovirus
	<i>Chlamydia pneumoniae</i>
	<i>Haemophilus influenzae</i>
	<i>Legionella pneumophila</i>
	<i>Streptococcus pneumoniae</i>
	<i>Streptococcus pyogenes</i>
	<i>Bordetella pertussis</i>
	<i>Mycoplasma pneumoniae</i>
	<i>Candida albicans</i>
	<i>Pseudomonas aeruginosa</i>
	<i>Staphylococcus epidermidis</i>
	<i>Streptococcus salivarius</i>

4. Clinical Evaluation

You must perform a clinical evaluation to determine the clinical sensitivity and specificity of your test using natural clinical specimens. Test a minimum of 30 positive and 30 negative specimens collected from a total of 60 patients suspected of SARS-CoV-2 infection by a healthcare provider in COVID-19 disease endemic region(s).

You must also test an additional 20 positive and 100 negative specimens collected from individuals without symptoms or other reasons to suspect COVID-19 in COVID-19 disease endemic region(s). As explained in Condition of Authorization Y of this letter, this information must be submitted to FDA as part of your initial notification or within 6 months of your notification date.

Acceptable Specimens:¹³

Positive specimens must be individual natural (prospective or retrospective or leftover samples) positive clinical specimens collected in COVID-19 disease endemic region(s).

20-25% of the positive specimens must be “low positive” by the comparator method, meaning the specimen is no more than 3 Ct below the mean Ct of the target with the highest Ct (if there are multiple targets) at the LoD of the comparator test. If collecting specimens prospectively and fewer than 20% of comparator positive specimens

¹³ Prospective collection of clinical specimens should be done in accordance with regulations for human subject protection, including IRB approval and informed consent. Use of leftover de-identified samples may follow the policy outlined in the FDA Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable, available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-informed-consent-vitro-diagnostic-device-studies-using-leftover-human-specimens-are-not>.

representing low positives as per the comparator assay are obtained, supplement the prospective specimens with additional low positive specimens such as archived samples or samples collected from convalescent patients.

The use of frozen samples is acceptable if an analytical study is performed and demonstrates that preservation of samples (e.g., by freezing at $\leq 70^{\circ}\text{C}$) does not change the sensitivity of your test by more than 3 Ct at LoD when compared to freshly prepared samples.

Samples previously tested positive by another highly sensitive EUA RT-PCR assay (defined below) may be used without additional comparator testing.

Negative specimens must be individual negative samples acquired from the following acceptable sources: (1) prospective samples from individuals suspected of COVID-19 by their healthcare provider, (2) archived/retrospective respiratory samples collected from patients with signs and symptoms of respiratory infection, and (3) other subjects that are expected to be negative for SARS-CoV-2, such as specimens collected prior to COVID-19 pandemic in the U.S.

Comparator Method:

As your comparator method, you must use a highly sensitive EUA (or cleared) RT-PCR assay that uses a chemical lysis step followed by a nucleic acid isolation step (e.g., silica bead extraction), and generates Ct values. An EUA RT-PCR assay is considered highly sensitive when the test's authorized labeling, posted on FDA's website,¹⁴ indicates a PPA $\geq 95\%$ based on validation with positive patient specimens. The EUA authorized comparator assay must be used according to authorized labeling (e.g., using only claimed matrices, etc.).

The comparator assay may have the same, or different, targets as your assay.

Validation:

Test clinical specimens in accordance with your proposed diagnostic algorithm (i.e., tested using your proposed test procedure), including retesting when appropriate. The limited volume of natural specimens may preclude retesting. In instances where retesting is indicated per your proposed test procedure but not performed, calculate your test's performance using the initial results, where equivocal/indeterminate/inconclusive results will count against your final performance.

Test specimens in a blinded fashion (e.g., present positive and negative samples to the end user in a blinded fashion), including blinding the end user to the results of any

¹⁴ Currently authorized molecular diagnostic tests for SARS-CoV-2 can be found at: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2#individual-molecular>

comparator method testing.

Investigate potential false results using an additional highly sensitive EUA RT-PCR assay and/or Sanger sequencing. The results of the discordant analysis can be footnoted in your final performance table but cannot be used to change the final performance calculations.

Test Performance:

Calculate positive percent agreement (PPA) by comparing the results for each specimen tested with your test compared to the comparator assay.

Calculate negative percent agreement (NPA) by comparing the results for each specimen tested with your test compared to the comparator assay (for prospectively collected samples) or as agreement with expected results if samples were collected from individuals known to be negative for SARS-CoV2 (e.g., collected before December 2019).

Calculate positive and negative percent agreement separately for the two datasets (i.e., specimens collected from patients suspected of SARS-CoV-2 infection by a healthcare provider and specimens collected from individuals without symptoms or other reasons to suspect COVID-19), as well as combined.

Your validation must demonstrate a minimum of 95% positive and negative percent agreement.

Documentation:

Provide documentation of the methodology and results, including line data and Ct scores, of your clinical evaluation. Results from specimens collected from patients suspected of SARS-CoV-2 infection by a healthcare provider must be provided as part of your notification to FDA required by Section II of this letter. Results from specimens collected from individuals without symptoms or other reasons to suspect COVID-19 may be provided either in your notification to FDA or post-authorization as set forth in Condition of Authorization Y of this letter.

Appendix B
Swab pooling up to n=3

Subject to the terms of this EUA, a test that is within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing up to 3 individual human anterior nasal swabs placed in a single vial after being collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Appendix C **Swab pooling up to n=5**

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing up to 5 individual human anterior nasal swabs placed in a single vial after being collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Validation specific to this indication must include both validation protocols outlined below, “*Validation of Expected Limit of Detection (LoD)*” and “*Validation of High Viral Concentrations*”. As part of the notification to FDA, summary data must be submitted, including the percent of positive pools detected, the Ct score difference, and the line data including the Ct score for each pool and individual sample tested.

1. Validation of Expected Limit of Detection (LoD)

Use either diluted positive clinical samples quantified in copies/mL using a standard curve, or inactivated virus of a known quantity represented as copies/mL. Prepare samples using negative anterior nasal clinical matrix (collection from healthy individuals is acceptable) using sample volumes you intend to include in your procedure for testing 5-swab pools.

To generate a 5-swab pool positive for SARS-CoV-2, prepare a single positive swab by spiking a known amount of inactivated virus or quantified positive patient sample onto the swab prior to immersion in the volume of media you intend to include in your procedure for 5-swab pooling. Add an additional four swabs containing only negative patient clinical matrix. The final viral analyte concentration in the media must be approximately 3x the LoD determined when performing the validation as set forth in Appendix A for testing an individual specimen. To ensure this concentration is achieved, factor in how much volume the swab absorbs, and the SARS-CoV-2 concentration needed on the single positive swab to achieve a final concentration of approximately 3x the LoD in the media. This is the concentration you should use to prepare the positive swabs for your validation study.

Test at least 20 independent extraction replicates of individual swabs in the same volume of buffer used in the LoD study as set forth in Appendix A for validation of individual specimen testing, using the testing protocol in your test's procedure for testing an individual specimen, validated as set forth in Appendix A. Test 20 paired 5-swab pools in parallel, each containing a single positive swab and 4 individual negative swabs in the volume of media you intend to include in your procedure for testing 5-swab pools, using the testing protocol you intend to include in your procedure for testing 5-swab pools.

Your validation must demonstrate that:

- $\geq 95\%$ of pooled replicates are detected as positive using the swab pooling protocol;
- The Ct score difference between the pooled and single swab protocols does not exceed 1.7 Ct; and
- The invalid rate in the swab pooling protocol does not exceed 5%.

2. *Validation of High Viral Concentrations*

Prepare three swabs simulating high viral concentrations by spiking 10^6 copies/mL of inactivated virus or quantified positive patient sample. Test 10 replicates of media containing the three spiked positive swabs and 2 individual negative swabs in the volume of media you intend to include in your procedure for testing 5-swab pools, using the testing protocol you intend to include in your procedure for testing 5-swab pools.

Your validation must demonstrate that:

- All 10 replicates are detected as positive; and
- The invalid rate in the swab pooling protocol does not exceed 5%.

Appendix D **Swab pooling up to n=10**

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing up to 10 individual human anterior nasal swabs placed in a single vial after being collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Validation specific to this indication must include both validation protocols outlined below, “*Validation of Expected Limit of Detection (LoD)*” and “*Validation of High Viral Concentrations*”. As part of the notification to FDA, summary data must be submitted, including the percent of positive pools detected, the Ct score difference, and the line data including the Ct score for each pool and individual sample tested.

1. Validation of Expected Limit of Detection (LoD)

Use either diluted positive clinical samples quantified in copies/mL using a standard curve, or inactivated virus of a known quantity represented as copies/mL. Prepare samples using negative anterior nasal clinical matrix (collection from healthy individuals is acceptable) using sample volumes you intend to include in your procedure for testing 10-swab pools.

To generate a 10-swab pool positive for SARS-CoV-2, prepare a single positive swab by spiking a known amount of inactivated virus or quantified positive patient sample onto the swab prior to immersion in the volume of media you intend to include in your procedure for 10-swab pooling. Add an additional nine swabs containing only negative patient clinical matrix. The final viral analyte concentration in the media must be approximately 3x the LoD determined when performing the validation as set forth in Appendix A for testing an individual specimen. To ensure this concentration is achieved, factor in how much volume the swab absorbs, and the SARS-CoV-2 concentration needed on the single positive swab to achieve a final concentration of approximately 3x the LoD in the media. This is the concentration you should use to prepare the positive swabs for your validation study.

Test at least 20 independent extraction replicates of individual swabs in the same volume of buffer used in the LoD study as set forth in Appendix A for validation of individual specimen testing, using the testing protocol in your test's procedure for testing an individual specimen, validated as set forth in Appendix A. Test 20 paired 10-swab pools in parallel, each containing a single positive swab and 9 individual negative swabs in the volume of media you intend to include in your procedure for testing 10-swab pools, using the testing protocol you intend to include in your procedure for testing 10-swab pools.

Your validation must demonstrate that:

- $\geq 95\%$ of pooled replicates are detected as positive using the swab pooling protocol;
- The Ct score difference between the pooled and single swab protocols does not exceed 1.7 Ct; and
- The invalid rate in the swab pooling protocol does not exceed 5%.

2. *Validation of High Viral Concentrations*

Prepare three swabs simulating high viral concentrations by spiking 10^6 copies/mL of inactivated virus or quantified positive patient sample. Test 10 replicates of media containing the three spiked positive swabs and 7 individual negative swabs in the volume of media you intend to include in your procedure for testing 10-swab pools, using the testing protocol you intend to include in your procedure for testing 10-swab pools.

Your validation must demonstrate that:

- All 10 replicates are detected as positive; and
- The invalid rate in the swab pooling protocol does not exceed 5%.

Appendix E
Media pooling up to n=3

Subject to the terms of this EUA, a test that is within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing aliquots of media from up to 3 individual human anterior nasal swab specimens that were collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19 and placed in individual vials when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Appendix F

Media pooling up to n=5 – validation option 1

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing aliquots of media from up to 5 individual human anterior nasal swab specimens that were collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19 and placed in individual vials, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Validation specific to this indication must include the validation protocol outlined below, “*Validation of Expected Limit of Detection (LoD)*”. As part of the notification to FDA, summary data must be submitted, including the percent of positive pools detected, the Ct score difference, and the line data including the Ct score for each pool and individual sample tested.

1. Validation of Expected Limit of Detection (LoD)

Use either diluted positive clinical samples quantified in copies/mL using a standard curve, or inactivated virus of a known quantity represented as copies/mL. Prepare samples using negative anterior nasal clinical matrix (collection from healthy individuals is acceptable) using sample volumes you intend to include in your procedure for testing 5-sample pools.

Prepare positive samples for your validation study at 5x the LoD determined when performing the validation as set forth in Appendix A for testing an individual specimen.

Test at least 20 independent extraction replicates of individual samples using the testing protocol in your test’s procedure for testing an individual specimen, validated as set forth in Appendix A. Test 20 paired 5-sample pools in parallel, each containing aliquots from a single positive sample and 4 individual negative samples, using the volumes and testing protocol you intend to include in your procedure for testing 5-sample pools.

Your validation must demonstrate that:

- ≥95% of pooled replicates are detected as positive using the sample pooling protocol;

- The Ct score difference between the pooled and single swab protocols does not exceed 1.7 Ct; and
- The invalid rate in the swab pooling protocol does not exceed 5%.

Appendix G

Media pooling up to n=10 – validation option 1

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing aliquots of media from up to 10 individual human anterior nasal swab specimens that were collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19 and placed in individual vials, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Validation specific to this indication must include the validation protocol outlined below, “*Validation of Expected Limit of Detection (LoD)*”. As part of the notification to FDA, summary data must be submitted, including the percent of positive pools detected, the Ct score difference, and the line data including the Ct score for each pool and individual sample tested.

1. Validation of Expected Limit of Detection (LoD)

Use either diluted positive clinical samples quantified in copies/mL using a standard curve, or inactivated virus of a known quantity represented as copies/mL. Prepare samples using negative anterior nasal clinical matrix (collection from healthy individuals is acceptable) using sample volumes you intend to include in your procedure for testing 10-sample pools.

Prepare positive samples for your validation study at 10x the LoD determined when performing the validation as set forth in Appendix A for testing an individual specimen.

Test at least 20 independent extraction replicates of individual samples using the testing protocol in your test’s procedure for testing an individual specimen, validated as set forth in Appendix A. Test 20 paired 10-sample pools in parallel, each containing aliquots from a single positive sample and 9 individual negative samples, using the volumes and testing protocol you intend to include in your procedure for testing 10-sample pools.

Your validation must demonstrate that:

- ≥95% of pooled replicates are detected as positive using the sample pooling protocol;

- The Ct score difference between the pooled and single swab protocols does not exceed 1.7 Ct; and
- The invalid rate in the swab pooling protocol does not exceed 5%.

Appendix H

Media pooling up to n=5 – validation option 2

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following additional indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing aliquots of media from up to 5 individual human anterior nasal swab specimens that were collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19 and placed in individual vials, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Validation specific to this indication must include the validation protocol outlined below, “*Validation of the Effect on the Percent Agreement*”. As part of the notification to FDA, summary data must be submitted, including the percent of positive pools detected, the Ct score difference, and the line data including the Ct score for each pool and individual sample tested.

1. Validation of the Effect on the Percent Agreement

Test at least 20 individual positive clinical specimens using the testing protocol in your test’s procedure for testing an individual specimen, validated as set forth in Appendix A. Test 20 paired 5-sample pools in parallel, each containing aliquots from a single positive specimen and 4 randomly selected individual negative clinical specimens (collection of negative anterior nasal specimens from healthy individuals is acceptable), using the testing protocol you intend to include in your procedure for testing 5-sample pools.

20 unique positive specimens and 80 unique negative specimens are needed to comprise twenty 5-sample pools. At least 20% of positive clinical specimens used for this validation study must be low positives, where, for 5-sample pooling, a low positive is within 2.32 Ct of the mean Ct at the LoD determined when performing the validation as set forth in Appendix A for testing an individual specimen.

Archived individual clinical anterior nasal specimens are acceptable for this validation study, if available, given they contain enough volume for both individual and 5-sample pool testing. If archived specimens are used, the original diagnostic results are acceptable in lieu of repeating the individual specimen testing, if the original diagnostic results were acquired according to your test’s procedure for testing an individual specimen, validated as set forth in Appendix A.

If you cannot acquire at least 20% low positive samples as natural clinical specimens, you may dilute positive clinical specimens into pooled negative anterior nasal clinical matrix prepared as described here. Use either diluted positive clinical samples quantified in copies/mL using a standard curve, or inactivated virus of a known quantity represented as copies/mL. Prepare samples using negative anterior nasal clinical matrix (collection from healthy individuals is acceptable) using sample volumes you intend to include in your procedure for testing 5-sample pools.

Your validation must demonstrate that:

- $\geq 85\%$ agreement between pooled testing and individual testing; and
- The invalid rate in the pooling protocol does not exceed 5%.

Appendix I

Media pooling up to n=10 – validation option 2

Subject to the terms of this EUA, a test that is otherwise within the Scope of this Authorization (Section II) is authorized for the following additional indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swabs or pooled samples containing aliquots of media from up to 10 individual human anterior nasal swab specimens that were collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP from individuals, including individuals without symptoms or other reasons to suspect COVID-19 and placed in individual vials, when tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Validation specific to this indication must include the validation protocol outlined below, “*Validation of the Effect on the Percent Agreement*”. As part of the notification to FDA, summary data must be submitted, including the percent of positive pools detected, the Ct score difference, and the line data including the Ct score for each pool and individual sample tested.

1. Validation of the Effect on the Percent Agreement

Test at least 20 individual positive clinical specimens using the testing protocol in your test’s procedure for testing an individual specimen, validated as set forth in Appendix A. Test 20 paired 10-sample pools in parallel, each containing aliquots from a single positive specimen and 9 randomly selected individual negative clinical specimens (collection of negative anterior nasal specimens from healthy individuals is acceptable), using the testing protocol you intend to include in your procedure for testing 10-sample pools.

20 unique positive specimens and 180 unique negative specimens are needed to comprise twenty 10-sample pools. At least 20% of positive clinical specimens used for this validation study must be low positives, where, for 10-sample pooling, a low positive is within 3.32 Ct of the mean Ct at the LoD determined when performing the validation as set forth in Appendix A for testing an individual specimen.

Archived individual clinical anterior nasal specimens are acceptable for this validation study, if available, given they contain enough volume for both individual and 10-sample pool testing. If archived specimens are used, the original diagnostic results are acceptable in lieu of repeating the individual specimen testing, if the original diagnostic results were acquired according to your test’s procedure for testing an individual specimen, validated as set forth in Appendix A.

If you cannot acquire at least 20% low positive samples as natural clinical specimens, you may dilute positive clinical specimens into pooled negative anterior nasal clinical matrix prepared as described here. Use either diluted positive clinical samples quantified in copies/mL using a standard curve, or inactivated virus of a known quantity represented as copies/mL. Prepare samples using negative anterior nasal clinical matrix (collection from healthy individuals is acceptable) using sample volumes you intend to include in your procedure for testing 10-sample pools.

Your validation must demonstrate that:

- $\geq 85\%$ agreement between pooled testing and individual testing; and
- The invalid rate in the pooling protocol does not exceed 5%.

Appendix J

Individual Home Specimen Collection

Subject to the terms of this EUA, a test that is within the Scope of this Authorization (Section II) is authorized for the following indication and may be used for this indication after validation is completed as set forth in this appendix and Appendix A:

Qualitative detection of RNA from SARS-CoV-2 in individual human anterior nasal swab samples collected by a healthcare provider (HCP), self-collected under the supervision of an HCP, or self-collected at home using the following authorized home collection kit(s): [insert authorized home collection kit with which your test was validated], when used consistent with the home collection kit's authorization for individuals tested at least once per week.

This test is authorized for use in the single laboratory that developed the test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

A list of authorized home collection kits can be found on FDA's website, available here: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2#individual-molecular>.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Developers who seek this indication must confirm that the transport media used in the authorized home collection kit is the same transport media used for the validation set forth in Appendix A, or, for specimens collected in dry tubes, that the media used for reconstitution of specimens collected with the authorized home collection kit is the same media used for reconstitution of specimens for the validation set forth in Appendix A. If the validation set forth in Appendix A was completed using a different media than used with the authorized home collection kit, an additional LoD determination, as set forth in Appendix A, must be completed for specimens collected with the authorized home collection kit, with results demonstrated that the LoD is within 3x of the LoD determined with the original validation.

Moreover, developers must clearly include in their test's authorized labeling that the authorized home collection kit must be used consistent with the home collection kit's authorization.

Appendix K

Pooled Home Specimen Collection

Subject to the terms of this EUA, a test that is within the Scope of this Authorization (Section II) and validated for at least one of the indications set forth in Appendices B-I, is also authorized for use with anterior nasal swab specimens collected using an authorized home collection kit after validation is completed as set forth in this appendix and Appendix A.

The indication of such a test, as set forth in the applicable Appendix B-I, shall include the following clause after “self-collected under the supervision of an HCP”, replacing “from individuals, including individuals without symptoms or other reasons to suspect COVID-19 and placed in individual vials, when tested at least once per week.”:

“or self-collected at home using the following authorized home collection kit(s): [insert authorized home collection kit with which your test was validated] when used consistent with the home collection kit’s authorization for individuals tested at least once per week.”

Such that the portion of the indication discussing specimen collection shall read:

“... human anterior nasal swab specimens that were collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP or self-collected at home using the following authorized home collection kit(s): [insert authorized home collection kit with which your test was validated] when used consistent with the home collection kit’s authorization for individuals tested at least once per week.”

A list of authorized home collection kits can be found on FDA’s website, available here:
<https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2#individual-molecular>.

This indication will be added to Exhibit 1 for the relevant test after FDA determines it has received a complete notification.

Developers who seek this indication must confirm that the transport media used in the authorized home collection kit is the same transport media used for the validation set forth in Appendix A, or, for specimens collected in dry tubes, that the media used for reconstitution of specimens collected with the authorized home collection kit is the same media used for reconstitution of specimens for the validation set forth in Appendix A. If the validation set forth in Appendix A was completed using a different media than used with the authorized home collection kit, an additional LoD determination, as set forth in Appendix A, must be completed for specimens collected with the authorized home collection kit, with results demonstrated that the LoD is within 3x of the LoD determined with the original validation.

Moreover, developers must clearly include in their test’s authorized labeling that the authorized home collection kit must be used consistent with the home collection kit’s authorization.

Appendix L

Fact Sheet for Healthcare Providers

As set forth in Section II of this letter and required by Condition of Authorization A of this letter, your test's labeling must include a Fact Sheet for Healthcare Providers that includes the relevant information in this appendix. FDA has provided a template for a Fact Sheet for Healthcare Providers on the FDA website with this letter to facilitate the creation of your test specific fact sheet.

You must include the following in your Fact Sheet for Healthcare Providers:

Fact Sheet for Healthcare Providers
[DATE]
[LABORATORY NAME]
[DEVICE/TEST NAME]

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the [DEVICE/TEST NAME].

The [DEVICE/TEST NAME] is authorized for use with anterior nasal respiratory specimens from individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.

All patients whose specimens are tested with this assay will receive the Fact Sheet for Patients: [LABORATORY NAME] - [DEVICE/TEST NAME].

What are the symptoms of COVID-19?

Many patients with COVID-19 have developed fever and/or symptoms of acute respiratory illness (e.g., cough, dyspnea), although some individuals experience only mild symptoms or no symptoms at all. The current information available to characterize the spectrum of clinical illness associated with COVID-19 suggests that, when present, symptoms include cough, shortness of breath or dyspnea, fever, chills, myalgias, headache, sore throat, new loss of taste or smell, nausea or vomiting or diarrhea. Signs and symptoms may appear any time from 2 to 14 days after exposure to the virus, and the median time to symptom onset is approximately 5 days. For further information on the symptoms of COVID-19 please see the link provided in “*Where can I go for updates and more information?*” section.

Public health officials have identified cases of COVID-19 throughout the world, including the United States. Please check the CDC COVID-19 webpage (see link provided in “*Where can I go for updates and more information?*” section at the end of this document) or your local jurisdictions website for the most up to date information.

What do I need to know about COVID-19 testing?

Current information on COVID-19 for healthcare providers is available at CDC's webpage, *Information for Healthcare Professionals* (see links provided in “Where can I go for updates and more information?” section).

This test is to be performed only using anterior nasal respiratory specimens from individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.

- The [DEVICE/TEST NAME] can be used to test anterior nasal respiratory specimens.
- The [DEVICE/TEST NAME] should be ordered for the detection of SARS-CoV-2 in individuals, including individuals without symptoms or other reasons to suspect COVID-19, when tested at least once per week.
- [INCLUDE THE FOLLOWING BULLET IF YOUR TEST INCLUDES USE OF AN AUTHORIZED HOME COLLECTION KIT – MODIFY TO INCLUDE HOME COLLECTION INDICATION BASED ON THE APPENDIX YOU ARE CLAIMING]: The [DEVICE/TEST NAME] can also be used to test anterior nasal respiratory specimens collected by a healthcare provider (HCP) or self-collected under the supervision of an HCP or self-collected at home using the following authorized home collection kit(s) [INCLUDE NAME OF AUTHORIZED KIT]].
- [INCLUDE THE FOLLOWING BULLET IF YOUR TEST ALLOWS SPECIMEN POOLING – BASED ON THE APPENDIX YOU ARE CLAIMING]: The [DEVICE/TEST NAME] can also be used to test up to [INCLUDE POOLING INDICATION BASED ON THE APPENDIX YOU ARE CLAIMING].
- The [DEVICE/TEST NAME] is only authorized for use at the [NAME OF LABORATORY] that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

Specimens should be collected with appropriate infection control precautions. Current guidance is available at the CDC's website (see links provided in “Where can I go for updates and more information?” section).

When collecting and handling specimens from individuals suspected of being infected with the virus that causes COVID-19, appropriate personal protective equipment should be used as outlined in the CDC *Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)*. For additional information, refer to CDC *Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19)* (see links provided in “Where can I go for updates and more information?” section).

What does it mean if the specimen tests positive for the virus that causes COVID-19?

A positive test result for COVID-19 indicates that RNA from SARS-CoV-2 was detected, and therefore the patient is infected with the virus and presumed to be contagious. Laboratory test results should always be considered in the context of clinical observations and epidemiological data (such as local prevalence rates and current outbreak/epicenter locations) in making a final diagnosis and patient management decisions. Patient management should be made by a healthcare provider and follow current CDC guidelines.

The [DEVICE/TEST NAME] has been designed to minimize the likelihood of false positive test results. However, it is still possible that this test can give a false positive result, even when used in locations where the prevalence is below 5%. In the event of a false positive result, risks to patients could include the following: a recommendation for isolation of the patient, monitoring of household or other close contacts for symptoms, patient isolation that might limit contact with family or friends and may increase contact with other potentially COVID-19 patients, limits in the ability to work, delayed diagnosis and treatment for the true infection causing the symptoms, unnecessary prescription of a treatment or therapy, or other unintended adverse effects.

[INCLUDE THIS TEXT IF YOUR INDICATION INCLUDES POOLING: Individuals included in a pool that returns a positive or invalid result should be treated as a presumptive positive unless or until they receive a negative result when re-tested individually. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, they should isolate until receiving a negative result when re-tested individually and should **not** be cohorted with other individuals who have received a positive or presumptive positive result.]

All laboratories using this test must follow the standard testing and reporting guidelines according to their appropriate public health authorities.

What does it mean if the specimen tests negative for the virus that causes COVID-19?

A negative test result for this test means that SARS-CoV-2 RNA was not present in the specimen above the limit of detection. However, a negative result does not rule out COVID-19 and should not be used as the sole basis for treatment or patient management decisions. It is possible to test a person too early or too late during SARS-CoV-2 infection to make an accurate diagnosis via [DEVICE/TEST NAME].

In addition, asymptomatic people infected with the virus that causes COVID-19 may not shed enough virus to reach the limit of detection of the test, giving a false negative result. In the absence of symptoms, it is difficult to determine if asymptomatic people have been tested too late or too early. Therefore, negative results in asymptomatic individuals may include individuals who were tested too early and may become positive later, individuals who were tested too late and may have serological evidence of infection, or individuals who were never infected.

[INCLUDE THIS TEXT IF YOUR INDICATION INCLUDES POOLING: Specimens with low viral loads may not be detected in sample pools due to the decreased sensitivity or increased interference of pooled testing. Your interpretation of negative results should take into account clinical and epidemiological risk factors.]

When diagnostic testing is negative, the possibility of a false negative result should be considered in the context of a patient's recent exposures and the presence of clinical signs and symptoms consistent with COVID-19. The possibility of a false negative result should especially be considered if the patient's recent exposures or clinical presentation indicate that COVID-19 is likely, and diagnostic tests for other causes of illness (e.g., other respiratory illness) are negative.

If COVID-19 is suspected based on exposure history together with other clinical findings, re-testing using a new sample with a sensitive method [INCLUDE THIS TEXT IF YOUR INDICATION INCLUDES POOLING: or without pooling] should be considered by healthcare providers in consultation with public health authorities. Additional testing may be helpful to ensure testing was not conducted too early.

Risks to a patient of a false negative test result include: delayed or lack of supportive treatment, lack of monitoring of infected individuals and their household or other close contacts for symptoms resulting in increased risk of spread of COVID-19 within the community, or other unintended adverse events.

The performance of this test was established based on the evaluation of a limited number of clinical specimens. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation.

Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

What is an EUA?

The United States FDA has made this test available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by the Secretary of Health and Human Service's (HHS's) declaration that circumstances exist to justify the emergency use of in vitro diagnostics (IVDs) for the detection and/or diagnosis of the virus that causes COVID-19. An IVD made available under an EUA has not undergone the same type of review as an FDA-approved or cleared IVD. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives, and based on the totality of scientific evidence available, it is reasonable to believe that this IVD may be effective in diagnosing COVID-19.

This test is authorized under the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing [include link to this letter] for use in [the specific laboratory, that is certified under CLIA and meets requirements to perform high complexity tests, in which it was developed] for [insert indication(s) from applicable appendix(es)] using the test procedures validated in accordance with the requirements of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing.

The EUA for this test is in effect for the duration of the COVID-19 declaration justifying emergency use of IVDs, unless terminated or revoked (after which the test may no longer be used).

What are the approved available alternatives?

Any tests that have received full marketing status (e.g., cleared, approved), as opposed to an EUA, by FDA can be found by searching the medical device databases here: <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases>. A cleared or approved test should be used instead of a test made available under an EUA, when appropriate and available. FDA has issued EUAs for other tests that can be found at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>.

Where can I go for updates and more information?

CDC webpages:

General: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>

Symptoms:

<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

Healthcare Professionals:

<https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>

Information for Laboratories:

<https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html>

Laboratory Biosafety: <https://www.cdc.gov/coronavirus/2019-nCoV/lab-biosafety-guidelines.html>

Isolation Precautions in Healthcare Settings:

<https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html>

Specimen Collection: <https://www.cdc.gov/coronavirus/2019-nCoV/guidelines-clinical-specimens.html>

Infection Control: <https://www.cdc.gov/coronavirus/2019-ncov/php/infection-control.html>

FDA webpages:

General: www.fda.gov/novelcoronavirus

EUAs: (includes links to fact sheet for individuals and manufacturer's instructions) <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>

LABORATORY NAME:

ADDRESS LINE 1

ADDRESS LINE 2

Customer Support:

+1 800 XXX-XXXX

customersupportemail@company.com

Technical Support:

+1 800 XXX-XXXX

techsupportemail@company.com

Report Adverse events, including problems with test performance or results, to MedWatch by submitting the online FDA Form 3500

(<https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home>) or by calling **1-800-FDA-1088**

Appendix M

Fact Sheet for Patients

As set forth in Section II of this letter and required by Condition of Authorization A of this letter, your test's labeling must include a Fact Sheet for Patients that includes the relevant information in this appendix. FDA has provided a template for a Fact Sheet for Patients on the FDA website with this letter to facilitate the creation of your test specific fact sheet.

You must include the following in your Fact Sheet for Patients:

Fact Sheet for Patients

[DATE]

[LABORATORY NAME]

[DEVICE/TEST NAME]

You are being given this Fact Sheet because your sample(s) was tested for the Coronavirus Disease 2019 (COVID-19) using the [DEVICE/TEST NAME].

This Fact Sheet contains information to help you understand the risks and benefits of using this test for the diagnosis of COVID-19. After reading this Fact Sheet, if you have questions or would like to discuss the information provided, please talk to your healthcare provider.

For the most up to date information on COVID-19 please visit the CDC Coronavirus Disease 2019 (COVID-19) webpage:

<https://www.cdc.gov/COVID19>

What is COVID-19?

COVID-19 is caused by the SARS-CoV-2 virus which is a new virus in humans causing a contagious respiratory illness. COVID-19 can present with a mild to severe illness, although some people infected with COVID-19 may have no symptoms at all. Older adults and people of any age who have underlying medical conditions have a higher risk of severe illness from COVID-19. Serious outcomes of COVID-19 include hospitalization and death. The SARS-CoV-2 virus can be spread to others not just while one is sick, but even before a person shows signs or symptoms of being sick (e.g., fever, coughing, difficulty breathing, etc.). A full list of symptoms of COVID-19 can be found at the following link:

<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>.

What is the [DEVICE/TEST NAME]?

The test is designed to detect the virus that causes COVID-19 in anterior nasal swabs .

Why was my sample tested?

You were tested because your healthcare provider believes you may have been exposed to the virus that causes COVID-19 based on your signs and symptoms (e.g., fever, cough, difficulty breathing), and/or because:

- You are being tested at regular intervals (serial testing) even though you do not have symptoms or risk factors for COVID-19; or

- You live in or have recently traveled to a place where transmission of COVID-19 is known to occur; or
- You have been in close contact with an individual suspected of or confirmed to have COVID-19; or
- You and your healthcare provider believe there is another reason to investigate your COVID-19 status.

Testing of the samples will help find out if you may have COVID-19.

[INCLUDE THIS TEXT IF YOUR INDICATION INCLUDES POOLING: Laboratories may use pooling when testing your specimen, which means they combine your sample with other individuals samples prior to testing and test them as a “pool”. The laboratory may return a result for the entire pool together or may return individual results.]

What are the known and potential risks and benefits of the test?

Potential risks include:

- Possible discomfort or other complications that can happen during sample collection.
- Possible incorrect test result (see below for more information).

Potential benefits include:

- The results, along with other information, can help your healthcare provider make informed recommendations about your care.
- The results of this test may help limit the spread of COVID-19 to your family and those you come in contact with.

What does it mean if I have a positive test result?

If you have a positive test result, it is very likely that you have COVID-19. Therefore, it is also likely that you may be placed in isolation to avoid spreading the virus to others. You should follow CDC guidance to reduce the potential transmission of disease.

[INCLUDE THIS TEXT IF YOUR INDICATION INCLUDES POOLING: If you were tested as part of a pool that returned a positive or invalid test result, you may have COVID-19 and should consider yourself to have a positive test result unless or until you receive a negative test result when re-tested individually. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, you should isolate until receiving a negative result when re-tested individually and should not be grouped with other individuals who have received a positive or presumptive positive result.]

There is a smaller possibility that this test can give a positive result that is wrong (a false positive result) particularly when used in a population without many cases of COVID-19 infection. Your healthcare provider will work with you to determine how best to care for you based on the test results along with medical history, and your symptoms

What does it mean if I have a negative test result?

A negative test result means that the virus that causes COVID-19 was not found in your sample.

However, it is possible for this test to give a negative result that is incorrect (false negative) in some people with COVID-19. You might test negative if the sample was collected early during your infection. You could also be exposed to COVID-19 after your sample was collected and then have become infected.

In particular, people infected with COVID-19 but who have no symptoms may not shed enough virus to trigger a positive test. This means that you could possibly still have COVID-19 even though the test result is negative. If your test is negative, your healthcare provider will consider the test result together with all other aspects of your medical history (such as symptoms, possible exposures, and geographical location of places you have recently traveled) in deciding how to care for you.

[INCLUDE THIS TEXT IF YOUR INDICATION INCLUDES POOLING: If your test result indicates your specimen was pooled and you have a negative test result there is a small chance that your result is incorrect. You should talk with your healthcare provider if you are concerned.]

If you have no symptoms but have been tested because your healthcare provider thought you may have been exposed to COVID-19, you should continue to monitor your health and let your healthcare provider know if you develop any symptoms of COVID-19. If you develop symptoms you may need another test to determine if you have contracted the virus causing COVID-19.

If you develop symptoms or your symptoms get worse you should seek medical care. If you have the following symptoms you should seek immediate medical care at the closest emergency room:

- Trouble breathing
 - Persistent pain or pressure in the chest
 - New confusion
 - Inability to wake up or stay awake
 - Bluish lips or face
-

It is important that you work with your healthcare provider to help you understand the next steps you should take.

Is this test FDA-approved or cleared?

No. This test is not yet approved or cleared by the United States FDA. FDA may issue an Emergency Use Authorization (EUA) when certain criteria are met, which includes that there are no adequate, approved, available alternatives. The EUA for this test is supported by the Secretary of Health and Human Service's (HHS's) declaration that circumstances exist to justify the emergency use of in vitro diagnostics for the detection and/or diagnosis of the virus that causes COVID-19. This EUA will remain in effect (meaning this test can be used) for the duration of the COVID-19 declaration justifying the emergency use of in vitro diagnostics, unless it is terminated or revoked by FDA (after which the test may no longer be used).

This test is authorized under the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing [include link to this letter] for use in [the specific laboratory, that is certified under CLIA and meets requirements to perform high complexity tests, in which it was developed] for [insert indication(s) from applicable appendix(es)] using the test procedures validated in accordance with the requirements of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing.

What are the approved alternatives?

Any tests that have received full marketing status (e.g., cleared, approved), as opposed to an EUA, by FDA can be found by searching the medical device databases here: <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases>. A cleared or approved test should be used instead of a test made available under an EUA, when appropriate and available. FDA has issued EUAs for other tests that can be found at:

<https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>

Where can I go for updates and more information? The most up-to-date information on COVID-19 is available at the CDC General webpage: <https://www.cdc.gov/COVID19>. In addition, please also contact your healthcare provider with any questions/concerns.

Appendix N

Authorized Test Summary

As set forth in Section II of this letter and required by Condition of Authorization A, your test's labeling must include a Test Summary that includes the relevant information in this appendix. FDA has provided a template for a Test Summary on the FDA website with this letter to facilitate the creation of your test specific summary.

You must include the following information in your Test Summary, replacing text highlighted in yellow **[Text]** with information applicable to your specific test:

TEST SUMMARY

For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only

The **[test name]** will be performed at the **[laboratory name]** located at **[laboratory address]**, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high complexity tests.

INTENDED USE

The **[test name]** is intended for the *in vitro* **[insert indication(s) from applicable appendix(es)]**. Testing is limited to **[laboratory name]** laboratory located at **[laboratory address]**, which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high-complexity testing.

The **[test name]** is intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and *in vitro* diagnostic procedures. The **[test name]** is only for use under the Food and Drug Administration's Emergency Use Authorization.

Results are for the detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 nucleic acid is generally detectable in anterior nasal swab specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease.

Negative results do not preclude SARS-CoV-2 infection 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.

Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

[INCLUDE THIS PARAGRAPH IF YOUR INDICATION INCLUDES POOLING:] Negative results from pooled testing should not be treated as definitive. If a patient's clinical signs and symptoms are inconsistent with a negative result or results are necessary for patient management, then the patient should be considered for individual testing. Specimens included in pools with a positive or invalid result must be reported as presumptive positive or tested individually prior to reporting a result. Individuals included in a pool that returns a positive or invalid result should be treated as a presumptive positive unless or until they receive a negative result when re-tested individually. However, as most individuals in a positive pool will likely receive a negative result when re-tested individually, they should isolate until receiving a negative result when re-tested individually and should not be cohorted with other individuals who have received a positive or presumptive positive result. Specimens with low viral loads may not be detected with pooled testing due to decreased sensitivity or increased interference from pooled testing.

For serial testing programs, additional confirmatory testing for negative results may be necessary, if there is a high likelihood of COVID-19, such as an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Additional confirmatory testing for positive results may also be necessary, if there is a low likelihood of COVID-19, such as in individuals without known exposure to COVID-19 or residing in communities with low prevalence of infection.

1) Special Conditions for Use Statements:

For use under Emergency Use Authorization (EUA) only
For prescription use only
For *in vitro* diagnostic use only

[INCLUDE THIS PARAGRAPH IF YOUR INDICATION INCLUDES HOME COLLECTION:] Testing of specimens self-collected at home is limited to specimens collected with the **[name of authorized home collection kit with which your test is validated]** by **[the patient population authorized in the home collection kit EUA]**.

This test is authorized under the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing [include link to this letter] for use in [the specific laboratory, that is certified under CLIA and meets requirements to perform high complexity tests, in which it was developed] for [insert indication(s) from applicable appendix(es)] using the test procedures validated in accordance with the requirements of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The [**Test Name**] assay is a reverse transcription polymerase chain reaction (RT -PCR) test. The

SARS-CoV-2 primer and probe set(s) is designed to detect RNA from the SARS-CoV-2 [genes/regions] in anterior nasal swab specimens that were collected from individuals, including individuals without symptoms or other reasons to suspect COVID-19.

[Describe the processes used to perform the test, including, as applicable, 1) nucleic acid extraction, 2) reverse transcription of target RNA to cDNA, 3) PCR amplification of target and internal control, and 4) simultaneous detection of PCR amplicons by fluorescent dye labeled probes. Include key parameters such as input volumes, reverse transcription (RT) time and temperature, PCR cycling parameters including dwell temperature and dwell times.]

INSTRUMENTS USED WITH TEST

Instruments

The [test name], a real-time RT-PCR test, is to be used with the [list extraction kit(s)] and the [list RT-PCR Instrument(s)] and [RT-PCR Instrument Software].

Collection Kits (if applicable)

This assay can be used with the [list EUA authorized Home Collection Kit(s)].

Reagents

The primary reagents used in [test name] assay:

Kits and Reagents	Manufacturer	Catalog #

CONTROL MATERIAL(s) TO BE USED WITH [test name]:

[List all control materials used with the test and describe what they are, how they are expected to work, where in the testing process they are used, and the frequency of use. If a control is commercially available, provide supplier's name and catalog number or other identifier; if your device relies on external controls that are manufactured by a third party please note that these controls must also be validated within your analytical and clinical studies.]

Controls that are used with the test include:

- a) A “no template” (negative) control is needed to **[describe need]** and is used **[describe use – please also specify frequency of use]**
- b) A positive template control is needed to **[describe need]** and is used **[describe use – please specify the concentration of the positive control relative to the LoD of your test (note that ideally the positive control concentration should be such that it is close to the LoD of your test) and also specify frequency of use]**
- c) An extraction control **[describe control]** is needed to **[describe need]** and is used **[describe use – please also specify frequency of use]**. Please note that if the no template control and positive control, are taken through the entire sample processing procedure, including the extraction, then a separate extraction control is not required.
- d) An internal control **[describe control]** is needed to **[describe need]** and is used **[describe use]**.

INTERPRETATION OF RESULTS

All test controls must be examined prior to interpretation of patient results. If the controls are not valid, the patient results cannot be interpreted. Appropriate control interpretation criteria and result interpretation criteria are described here. You must describe if a Ct cutoff is used as part of your testing algorithm and/or if the end user is required to review curves before final result interpretation. Although not typical for molecular-based tests, if the test result involves the use of an algorithm/calculation, for example a ratio value, when determining the final patient test result, include a detailed description and any additional calibration materials that may be required.

1. Examination and Interpretation of Control Results

[Describe in detail the expected results generated, including acceptance criteria, for all the controls used in test. Describe the measured values (if applicable) for valid and invalid controls and outline the actions to take in the event of an invalid control result.]

2. Examination and Interpretation of Patient Specimen Results:

Assessment of clinical specimen test results must be performed after the controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted.

[Describe when clinical specimen test results should be assessed and outline the criteria for test validity. Clearly indicate how to interpret numeric test values (if applicable) as positive or negative for presence of SARS-CoV-2. Indicate if the end user is required to review curves before final result interpretation and, if applicable, how to identify indeterminate/inconclusive-equivocal results. When applicable, we

recommend providing a table clearly describing the possible combinations of test result values for each primer/probe set. Describe how they should be combined into a final interpretation of the result for your test. If the test produces an equivocal or indeterminate result, please indicate what follow-up testing/process should be conducted, if applicable.]

[If your test is indicated for pooling, also include a pooling results interpretation table, indicating how to interpret each possible result, including when samples should be retested individually.]

PERFORMANCE EVALUATION

1) Limit of Detection (LoD) -Analytical Sensitivity:

The LoD for the **[test name]** was evaluated and verified using **[validation material, e.g., SARS-CoV-2 inactivated virus (e.g., heat treated or irradiated)]** per the validation required by Appendix A of the Umbrella EUA for SARS-CoV-2 Molecular Diagnostic Tests for Serial Testing. Nucleic acid was extracted from the swabs using **[specify nucleic acid extraction]** and the reverse transcription RT-PCR was performed using the **[specify RT-PCR Instrument and, if applicable, interpretive software version]**. Preliminary and Confirmation LoD results are included in the tables below.

[insert table such as:] Table Example: Preliminary Determination of LoD

Virus Concentration	Target 1 Ct Value	Target 2 Ct Value	Internal Control Ct Value	# of Replicates

[insert table such as:] Table Example: LoD Confirmation

Targets	Target 1	Target 2
Analyte Concentration		
Positives/Total		
% Detected		
Mean Ct		
Mean SD		
CV		

The data confirmed the assay analytical sensitivity is **[specify LoD represented as genome copies or equivalents/mL]**.

2) Inclusivity (Analytical Reactivity):

An alignment was performed with the oligonucleotide primer and probe sequences of the [test name] with [number of sequences] publicly available SARS-CoV-2 sequences (including mutation variants of high prevalence, i.e., B.1.617.2 and sub-lineages at the time of issuance of this letter) from [specify sequence data base, e.g., GISAID] to demonstrate the predicted inclusivity of the assay.

[Insert summary of results of inclusivity analysis.]

3) Cross-reactivity (Analytical Specificity):

Analytical specificity of the primer/probe combination for [test name] was evaluated by conducting sequence alignment of the primer/probe sequences of the test with publicly available genome sequences for potential cross-reacting microorganisms. The following organisms were tested with [test name] primer probe set.

[insert table such as:] Table Example: Organisms Analyzed for Cross Reactivity

Organism	Strain	Target 1	Target 2

4) Clinical Evaluation:

Clinical evaluation of the [test name] was conducted with 30 individual natural positive and 30 negative anterior nasal swab clinical specimens collected from patients suspected of SARS-CoV-2 infection by a healthcare provider in COVID-19 disease endemic region(s). These specimens were [prospective, retrospective, or leftover samples]. Nucleic acid was extracted from the swabs using [specify nucleic acid extraction] and the reverse transcription RT-PCR was performed using the [specify RT-PCR Instrument and, if applicable, interpretive software version].

Data is summarized in the Table below:

Table: Summary Performance on individual anterior nasal swab specimens in comparison to an FDA-authorized method for specimens collected from individuals suspected of COVID-19 by a healthcare provider

[Test Name]	FDA EUA RT-PCR Assay		Total	% Performance Agreement	95% CI
	Detected	Not Detected			
Detected	A	B	A+B	PPA= 100% x A/(A+C)	
Not Detected	C	D	C+D	NPA= 100% x D/(B+D)	
Total	A+C	B+D			

[IF VALIDATION WAS ALSO COMPLETED WITH SPECIMENS COLLECTED FROM INDIVIDUALS WITHOUT SYMPTOMS OR OTHER REASONS TO SUSPECT COVID-19, ALSO INCLUDE THOSE RESULTS:] Clinical evaluation of the **[test name]** was conducted with 20 positive and 100 negative specimens collected from individuals without symptoms or other reasons to suspect COVID-19 in COVID-19 disease endemic region(s). These specimens were **[prospective, retrospective, or leftover samples]**. Nucleic acid was extracted from the swabs using **[specify nucleic acid extraction]** and the reverse transcription RT-PCR was performed using the **[specify RT-PCR Instrument and, if applicable, interpretive software version]**.

Data is summarized in the Table below:

Table: Summary Performance on individual anterior nasal swab specimens in comparison to an FDA-authorized method for specimens collected from individuals without symptoms or other reasons to suspect COVID-19

[Test Name]	FDA EUA RT-PCR Assay		Total	% Performance Agreement	95% CI
	Detected	Not Detected			
Detected	A	B	A+B	PPA= 100% x A/(A+C)	
Not Detected	C	D	C+D	NPA= 100% x D/(B+D)	
Total	A+C	B+D			

5) Additional Validation for [indication provided by appendix(es) B -K, e.g., Media Pooling up to n=10 with validation option 2]:

[For each additional indication, include a section with the required validation and documentation from the applicable appendix.]

LIMITATIONS

- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between [include collection window dates between MONTH, YEAR AND MONTH, YEAR and the location(s) of clinical evaluation (Country(ies)– identify if it was multiple sites in the country or limited locations – if known)]. The clinical performance of this test has not been established in all circulating variants but is anticipated to be reflective of the variants in circulation at the time and location(s) of the clinical evaluation. As such, performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2, and their prevalence, which change over time.
- [IF EVALUATION OF SPECIMENS COLLECTED FROM INDIVIDUALS WITHOUT SYMPTOMS OR OTHER REASONS TO SUSPECT COVID-19 HAVE NOT YET BEEN EVALUATED, INCLUDE THIS STATEMENT:] Clinical performance has been established in specimens collected from subjects suspected of COVID-19 by a healthcare provider. Performance of specimens collected from individuals without symptoms or other reasons to suspect COVID-19 has not been established. A study to determine the performance in individuals without symptoms or other reasons to suspect COVID-19 will be completed.

WARNINGS:

- This product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization (EUA) for use by the laboratory that developed the test and which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high complexity tests.
- 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.