June 10, 2021

Niall J. Lennon, Ph.D.
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320 Charles Street
Cambridge, MA 02141

Device:	CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay
Laboratory:	Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard
Indication:	Qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal, oropharyngeal, anterior nasal (nasal), and mid-turbinate swabs, nasopharyngeal wash/aspirate and nasal aspirate specimens, and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their healthcare provider (Version 1). Emergency use of this test is limited to the authorized laboratory.
Authorized Laboratory:	Testing is limited to the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard located at 320 Charles Street, Cambridge, MA 02141 which is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

Dear Dr. Lennon:

On July 8, 2020, based on your[1] request the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay for the qualitative detection of nucleic acid from SARS-CoV-2 in upper respiratory specimens (such as nasopharyngeal, oropharyngeal, nasal, and mid-turbinate swabs, nasopharyngeal wash/aspirate or nasal aspirate specimens) and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their healthcare provider, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). Testing was limited to the CRSP, LLC at the Broad Institute of MIT and Harvard located at 320 Charles Street, Cambridge, MA 02141 which is certified under CLIA, 42 U.S.C. §263a, and meets requirements to perform high complexity tests. Based on your

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard.

requests, FDA granted updates to the authorized labeling on August 31, 2020,[2] as well as reissued the letter on October 23, 2020 and December 18, 2020.[3, 4]

On June 3, 2021, you requested to further revise your Emergency Use Authorization (EUA). Based on these requests, and having concluded that revising the December 18, 2021, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the December 18, 2020, letter in its entirety with the revisions incorporated.[5] Pursuant to section 564 of the Act and the Scope of Authorization (Section II) and Conditions of Authorization (Section IV) of this reissued letter, your product[6] is now authorized for use consistent with the indication described above.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.[7]

[2] On August 31, 2020, your request was granted to update the authorized labeling of your product to add use of spun polyester swabs placed into empty, sterile tubes (termed dry swabs) for collection of anterior nares specimens tested using Version 2 of the assay. FDA also updated the Healthcare Provider and Patient Fact Sheets to reflect more recent authorizations.

[3] On October 23, 2020, the revisions to the July 8, 2020, letter and authorized labeling included: (1) revisions to the intended use and authorized labeling documents to clarify which Version of your product can be use for specific indications, (2) revisions to the intended use and authorized labeling documents to include testing of dry nasal swab specimens self-collected unsupervised using the CRSP Self Swab kit using Version 2, (3) revisions to the intended use and authorized labeling documents to include testing of self-collected nasal swab specimens unsupervised at home or in a healthcare setting using the Color COVID-19 Self-Swab Collection Kit using Version 2, and (3) revisions to the intended use, Healthcare Provider and Patient Fact Sheets to reflect language more consistent with recent authorizations.

[4] On December 18, 2020, the revisions to the October 23, 2020, letter and authorized labeling included revisions to the intended use and authorized labeling documents to include testing of self-collected nasal swab specimens at home (which includes a community based setting) using the binx health At-home Nasal Swab COVID-19 Sample Collection Kit using Version 2.

[5] The revisions to the December 18, 2020, letter and authorized labeling include: (1) revisions to the intended use and authorized labeling documents to remove all testing assocatied with Version 2 of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay, which is no longer used for testing clinical specimens having been superseded by Version 3 – authorized under EUA210089, (2) updates to the EUA Summary, Fact Sheet for Healthcare Providers and Fact Sheet to Patients to reflect the updated intended use and reflect language used in more recent authorizations, (3) remove the laboratory SOPs related to Version 2 "CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Testing and Calling Processes Assay Version 2 (V2)" and "CRSP SARS-CoV2 Diagnostic Testing Sample Drop off and Inspection SOP", and (4) updating the Conditions of Authorization as a result of the change to the intended use and to reflect language used in more recent authorizations.

[6] For ease of reference, this letter will use the term "your product" to refer to the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay used for the indication identified above. As described in Section II of this letter and the corresponding EUA Summary this test has Version 1.

[7] 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*

FDA considered the totality of scientific information available in authorizing the emergency use of your product for the indication above. A summary of the performance information FDA relied upon is contained in the EUA Summary (identified below).

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of your product, described in the Scope of Authorization of this letter (Section II), subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

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

1. The SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your product may be effective in diagnosing COVID-19, and that the known and potential benefits of your product when used for diagnosing COVID-19, outweigh the known and potential risks of your product; and

3. There is no adequate, approved, and available alternative to the emergency use of your product for diagnosing COVID-19.[8]

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to the indication above.

Authorized Product Details

Your product (Version 1) is a qualitative test for the detection of nucleic acid from SARS-CoV-2 in nasopharyngeal, oropharyngeal, anterior nasal (nasal), and mid-turbinate swabs, nasopharyngeal wash/aspirate and nasal aspirate specimens, and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their health care provider.

Testing is limited to the CRSP, LLC at the Broad Institute of MIT and Harvard, located at 320 Charles Street, Cambridge, MA 02141 which is certified under CLIA, 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

The SARS-CoV-2 nucleic acid is generally detectable in respiratory specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 nucleic acid; clinical correlation with patient history and other diagnostic information is necessary to

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Cosmetic Act, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 7, 2020).

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

determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

To use your product, SARS-CoV-2 nucleic acid is first extracted and purified from the specimens. The purified nucleic acid is then reverse transcribed into cDNA followed by PCR amplification and detection using an authorized real-time (RT) PCR instrument described in the authorized labeling (described below).

The product uses all commercially sourced materials or other authorized materials and authorized ancillary reagents commonly used in clinical laboratories as described in the authorized labeling.

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

- No template (negative) control (NTC) - used for every run and needed to confirm that there is no contamination for the assay.
- Positive template control - targeting the SARS-CoV-2 N-gene (N1 and N2) is used for every run and needed to confirm that the assay is completed by the intended design.
- Internal control primer/probe set, targeting the human RNase P gene - used for every patient sample to confirm appropriate specimen collection and to monitor the integrity of nucleic acid extraction and RT-PCR reactions.
- Human specimen (HSC) extraction control - included in each run to test for failure in lysis and extraction and potential contamination during extraction.

The above described product is authorized to be accompanied with laboratory procedures (described below), and the EUA Summary (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), and the following information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard - CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay
- Fact Sheet for Patients: Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard - CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay

The above described product, when accompanied by the "CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Testing and Calling Processes Assay Version

1 (V1)", "CRSP SARS-CoV2 Diagnostic Testing Receipt and Accessioning SOP", the EUA Summary (identified above) and the two Fact Sheets (collectively referenced as "authorized labeling" is authorized to be used by the authorized laboratory under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your product, when used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your product.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that your product may be effective in diagnosing COVID-19, when used consistent with the Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that your product (as described in the Scope of Authorization of this letter (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) of the Act described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1) of the Act, your product is authorized for the indication above.

III. Waiver of Certain Requirements

I am waiving the following requirements for your product during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, distribution, and storage of your product.

IV. Conditions of Authorization

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

Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard (You)

A. Your product must comply with the following labeling requirements under FDA regulations: the intended use statement (21 CFR 809.10(a)(2), (b)(2)); adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)); appropriate limitations on

the use of the device including information required under 21 CFR 809.10(a)(4); and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

B. You must make available on your website(s), if applicable, the Fact Sheet for Healthcare Providers, the Fact Sheet for Patients.

C. You must inform relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

D. You must collect information on the performance of your product. You will report to Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) (via email: CDRH-EUA-Reporting@fda.hhs.gov) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the product of which you become aware.

E. You must ensure that any records associated with this EUA, including test usage, are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

F. You are authorized to make available additional information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.

G. You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling. Any request for changes to this EUA should be submitted to the DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.

H. You must have a process in place to track adverse events, including any occurrence of false results with your product, and report any such events to FDA in accordance with 21 CFR Part 803. Serious adverse events, especially unexpected biosafety concerns, should immediately be reported to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov).

I. You must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

J. 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.

K. You must use your product as outlined in the authorized labeling. Deviations from the

authorized laboratory procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and/or authorized materials required to use your product are not permitted.

L. You must evaluate the analytical limit of detection and assess traceability of your product with any FDA-recommended reference material(s), if requested by FDA[9]. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review and concurrence with the data the EUA summary will be updated to reflect the additional testing. Such updates must be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

M. All laboratory personnel using your product must be appropriately trained in molecular techniques and use appropriate laboratory and personal protective equipment when handling this product, and use your product in accordance with the authorized laboratory procedure.

Conditions Related to Printed Materials, Advertising and Promotion

N. All descriptive printed matter, advertising, and promotional materials relating to the use of your product shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and meet the requirements set forth in section 502(a), (q)(1), and (r) of the Act and FDA implementing regulations.

O. No descriptive printed matter, advertising, or promotional materials relating to the use of your product may represent or suggest that this test is safe or effective for the detection of SARS-CoV-2.

P. All descriptive printed matter, advertising, and promotional materials relating to the use of your product shall clearly and conspicuously state that:

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by 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.

[9] Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material. FDA may request, for example, that you perform this study in the event that we receive reports of adverse events concerning your product.

The emergency use of your product as described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure