July 22, 2021

Mari Meyer
Vice President Regulatory and Clinical Affairs, North America
DiaSorin Molecular LLC
11331 Valley View Street,
Cyress, CA 90630 US

Device:	Simplexa COVID-19 Direct
EUA:	EUA200026
Company:	DiaSorin Molecular LLC
Indication:	Qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in nasopharyngeal swabs (NPS), anterior nasal swabs (NS), nasal washes/aspirates (NW) or bronchoalveolar lavage (BAL) specimens from individuals suspected of COVID-19 by their healthcare provider. Emergency use of this test is limited to authorized laboratories.
Authorized Laboratories:	Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high or moderate complexity tests.

Dear Ms. Meyer:

On March 19, 2020, based on your[1] request the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the Simplexa COVID-19 Direct assay, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3), for the qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in nasopharyngeal swabs (NPS) from individuals suspected of COVID-19 by their healthcare provider. Testing was limited to laboratories certified under CLIA to perform high and moderate complexity tests. Based on your requests, FDA granted updates to the authorized labeling on March 26, 2020,[2] April 13, 2020,[3] June 4, 2020,[4] October 2, 2020[5] and April 1, 2021.[6]

[1] For ease of reference, this letter will use the term "you" and related terms to refer to the DiaSorin Molecular LLC.
[2] On March 26, 2020, your request was granted to update the Instructions for Use (IFU) to add the use of the following transport media; Remel M5, Remel M6, Copan ESwab (Liquid Amies), Puritan UniTranz-RT, and saline (0.9% sodium chloride in water). FDA also concurred with the related updates to the Instructions for Use to reflect the requested update.
[3] On April 13, 2020, your request was granted to update the IFU to add nasal swabs (NS) and bronchoalveolar lavage (BAL) specimen types to the intended use. FDA also concurred with the related updates to the IFU to reflect

On May 26, 2021, you requested to amend your Emergency Use Authorization (EUA). Based on that request and having concluded that revising the March 19, 2020, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), FDA is reissuing the March 19, 2020, letter in its entirety with the revisions incorporated.[7] 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[8] is now intended for 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.[9]

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

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

I. Criteria for Issuance of Authorization

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the requested update and updated the Healthcare Provider Fact Sheet accordingly.

[4] On June 4, 2020, your request was granted to update the IFU to add nasal wash/aspirate (NW) specimen types to the intended use and update the performance section accordingly. FDA also updated the Healthcare Provider and Patient Fact Sheets to reflect the updated intended use.

[5] On October 2, 2020, your supplement was acknowledged via email to update the IFU of you product with results from testing with the FDA SARS-CoV-2 Reference Panel.

[6] On April 1, 2021, your supplement was acknowledged via email to make minor updates to the IFU.

[7] The revisions to the March 19, 2020, letter and authorized labeling include: (1) updates to the indications section of the letter to reflect the current intended use, (2) minor updates to the intended use to reflect language used in more recent authorizations, (3) delete "assay" from the name of the device in the letter (4) updates to the IFU, including the limitations section, to indicate that NPS and NS specimens should be diluted in 3 mL of transport media and also note that use of 1 mL of transport media may result in an increased rate of Internal Control (IC) failures due to elevated inhibitor levels in some patient specimens, (5) update the limitation section to include general variant limitation, (6) updates to the Conditions of Authorization to add new Conditions related to circulating variants (Conditions Q and R), (7) updates to the IFU, Conditions of Authorization (including consolidation of several conditions in new condition K), Healthcare Provider and Patient Fact Sheets to reflect language used in more recent authorizations and (8) revisions to include use of a product information card.

[8] For ease of reference, this letter will use the term "your product" to refer to the Simplexa COVID-19 Direct used for the indication identified above.

[9] 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.

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.[10]

II. Scope of Authorization

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

Authorized Product Details

Your product is for the qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in nasopharyngeal swabs (NPS), anterior nasal swabs (NS), nasal washes/aspirates (NW) or bronchoalveolar lavage (BAL) specimens from individuals suspected of COVID-19 by their healthcare provider. 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. 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.

Testing is limited to laboratories certified under CLIA that meet requirements to perform high or moderate complexity tests.

Your product enables the direct amplification of Coronavirus SARS-CoV-2 RNA from nasopharyngeal swabs (NPS). The product is used with the LIAISON MDX (with LIAISON MDX Studio Software), the Direct Amplification Disc and associated accessories, or other authorized instruments, software or accessories. Fluorescent probes are used together with corresponding forward and reverse primers in your product to amplify and detect the SARS-CoV-2 viral specific RNA and internal control RNA. The Simplexa COVID-19 Direct includes the following materials or other authorized materials: Simplexa COVID-19 Direct Reaction Mix (RM), and Simplexa COVID-19 Direct Barcode Card.

Your product requires the following control material, or other authorized control material (as may be requested under Condition K. below), that are processed in the same way as the patient

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

samples and are required to be included with each batch of specimens tested with your product. The control listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- Internal Control - encapsulated RNA Template control added to the clinical samples positive control, and negative control: controls for viral lysis, reverse transcription and amplification within each reaction.

You also have available additional controls, or other authorized controls that are recommended but not provided with the test kit, and used as outlined in the Instructions for Use:

- Simplexa COVID-19 Positive Control - used to monitor for failures of rRT-PCR reagents and reaction conditions.
- No Template (Negative) Control - used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents.

Your product also requires the use of additional authorized materials and authorized ancillary reagents that are not included with your product and are described in the Instructions for Use.

The labeling entitled "Simplexa COVID-19 Direct" Instructions for Use (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas), the "Product Information Card, Simplexa COVID-19 Direct, catalog number MOL4150, Simplexa COVID-19 Direct Positive Control Pack, catalog number MOL4160," and the following fact sheets pertaining to the emergency use, is required to be made available as set forth in the Conditions of Authorization (Section IV), and are collectively referred to as "authorized labeling":

- Fact Sheet for Healthcare Providers: DiaSorin Molecular LLC - Simplexa COVID-19 Direct
- Fact Sheet for Patients: DiaSorin Molecular LLC - Simplexa COVID-19 Direct

The above described product, when accompanied by the authorized labeling as set forth in the Conditions of Authorization (Section IV) is authorized to be distributed to and used by authorized laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your authorized product, when used for the qualitative detection of SARS-CoV-2 and used consistently with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of such a 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 consistently 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 when used consistent with the Scope of Authorization of this letter (Section II) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

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

III. Waiver of Certain Requirements

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

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of your product, but excluding Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250)

IV. Conditions of Authorization

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

DiaSorin Molecular LLC (You) and Authorized Distributor(s)[11]

A. Your product must comply with the following labeling requirements under FDA regulations: the intended use statement (21 CFR 809.10(a)(2), (b)(2)); adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)); appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4); and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

B. You and authorized distributor(s) must make your product available with the authorized labeling to authorized laboratories.

C. You and authorized distributor(s) must make available on your website(s) the authorized labeling.

[11] "Authorized Distributor(s)" are identified by you, DiaSorin Molecular LLC, in your EUA submission as an entity allowed to distribute your product.

D. You and authorized distributor(s) must include a physical copy of the "Product Information Card, Simplexa COVID-19 Direct, catalog number MOL4150, Simplexa COVID-19 Direct Positive Control Pack, catalog number MOL4160" with each shipped product to authorized laboratories, and will make the authorized "Simplexa COVID-19 Direct" Instructions for Use electronically available with the opportunity to request a copy in paper form, and after such request, you must promptly provide the requested information without additional cost.

E. You and authorized distributor(s) must inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.

F. Through a process of inventory control, you and authorized distributor(s) must maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.

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

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

DiaSorin Molecular LLC (You)

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

J. You must provide authorized distributor(s) with a copy of this EUA and communicate to authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).

K. You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling, including requests to make available additional authorized labeling specific to an authorized distributor. Such additional labeling may use another name for the product but otherwise must be consistent with the authorized labeling, and not exceed the terms of authorization of this letter. Any request for changes to this EUA should be submitted to DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.

L. You must comply with the following requirements pursuant to FDA regulations: 21 CFR 820 Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).

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

N. If requested by FDA, you must submit lot release procedures to FDA, including sampling protocols, testing protocols, and acceptance criteria, that you use to release lots of your product for distribution in the U.S. If such lot release procedures are requested by FDA, you must provide it within 48 hours of the request.

O. You must evaluate the analytical limit of detection and assess traceability[12] of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA you will update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

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

Q. You must evaluate the impact of SARS-CoV-2 viral mutations on your product's performance. Such evaluations must occur on an ongoing basis and must include any additional data analysis that is requested by FDA in response to any performance concerns you or FDA identify during routine evaluation. Additionally, if requested by FDA, you must submit records of these evaluations for FDA review within 48 hours of the request. If your evaluation identifies viral mutations that affect the stated expected performance of your device, you must notify FDA immediately.

R. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA, such as those related to the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

Authorized Laboratories

S. Authorized laboratories using your product must include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

T. Authorized laboratories using your product must use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the

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

authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.

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

V. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

W. Authorized laboratories must collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and You ((800) 838-4548) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.

X. 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 kit, and use your product in accordance with the authorized labeling.

DiaSorin Molecular LLC (You), Authorized Distributors and Authorized Laboratories

Y. You, authorized distributors, and authorized laboratories using your product must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Printed Materials, Advertising and Promotion

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 test is safe or effective for the detection of SARS-CoV-2.

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

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

- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and

- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

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

V. Duration of Authorization

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

Sincerely,

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

Enclosure