July 8, 2022

Richard A. Montagna, Ph.D., FACB
Senior Vice President, Scientific & Clinical Affairs
Rheonix, Inc.
2680 Grand Island Boulevard, Suite 1
Grand Island, NY 14072

Device:	Rheonix COVID-19 MDx Assay
EUA Number:	EUA200240
Company:	Rheonix, Inc.
Indication:	This test is authorized for the following indications for use: Qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal swabs, oropharyngeal (throat) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal washes, nasal aspirates and bronchoalveolar lavage (BAL) fluid from individuals who are suspected of COVID-19 by their healthcare provider. This test is also authorized for the qualitative detection of nucleic acid from SARS-CoV-2 in saliva specimens collected without preservatives in a sterile tube in a healthcare setting from individuals who are 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 moderate or high complexity tests.

Dear Dr. Montagna:

On April 29, 2020, based on your[1] request, the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the Rheonix COVID-19 MDx Assay for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal swabs, oropharyngeal (throat) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal washes, nasal aspirates and bronchoalveolar lavage (BAL) fluid from individuals who are suspected of COVID-19 by their

[1] For ease of reference, this letter will use the term "you" and related terms to refer to Rheonix, Inc.

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 laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests. Based on your request, FDA granted updates to the authorized labeling on September 15, 2020[2] and July 1, 2021[3], as well as revised and reissued the letter on December 3, 2020[4]. In addition, FDA established additional Conditions of Authorization in response to the continued emergence of new variants of SARS-CoV-2 on September 23, 2021.[5]

On September 30, 2021, and November 16, 2022, you requested to revise your Emergency Use Authorization (EUA). Based on that request, and having concluded that revising the December 3, 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 December 3, 2020, letter in its entirety with the revisions incorporated.[6] 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[7] is now intended for the indications 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

[2] On September 15, 2020, your request was granted to update the Instructions for Use (IFU) of your product to add the results of the FDA reference panel testing for upper respiratory specimens.
[3] On July 1, 2021, your request was granted to update the IFU of your product to add the results of the FDA reference panel testing for saliva specimens.
[4] On December 3, 2020, the revisions to the April 29, 2020, letter and authorized labeling included: (1) the addition of qualitative detection of nucleic acids from SARS-CoV-2 in saliva specimens collected without preservatives in a sterile tube in a healthcare setting from individuals suspected of COVID-19 by their healthcare provider, (2) modification of existing packaging and labeling to gain efficiencies in manufacturing and packaging operations, (3) modification of the IFU to reflect addition of saliva as a specimen type, (4) modification of the IFU to update the in silico analysis of assay inclusivity, and (4) updates to the healthcare provider and patient fact sheets to include some additional warnings/precautions around the use of saliva specimens and to reflect language used in more recent authorizations.
[5] The Viral Mutation Revision Letter – September 23, 2021, can be accessed at: https://www.fda.gov/media/152406/download.
[6] The revisions to the December 3, 2020, letter and authorized labeling include: (1) an update to the intended use to extend testing to laboratories that meet the requirement to perform moderate complexity tests, (2) an update to the assay protocol to replace the manual external control validation step with an automated software guided external control validation, (3) addition of a limitation statement regarding emerging variants in accordance with the September 23, 2021, Viral Mutation Revision Letter, (4) addition of a limitation statement related to the use of saliva specimens, to be consistent with more recent authorizations that include saliva specimen claims, (5) modification of warnings to reflect language used in more recent authorizations, (6) addition of two conditions of authorization related to conducting an appropriate product stability study to support the indicated storage temperatures (U. and V. below), and (7) updates to the healthcare provider and patient fact sheets to reflect language used in more recent authorizations.
[7] For ease of reference, this letter will use the term "your product" to refer to the Rheonix COVID-19 MDx Assay used for the indication identified above.

vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.[8]

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 included in the Instructions for Use (identified below).

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

I. Criteria for Issuance of Authorization

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

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

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

3. There is no adequate, approved, and available alternative to the emergency use of your product.[9]

II. Scope of Authorization

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

Authorized Product Details

Your product is a qualitative test for the detection of nucleic acid from SARS-CoV-2 in nasopharyngeal swabs, oropharyngeal (throat) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal washes, nasal aspirates and bronchoalveolar lavage (BAL) fluid from individuals who are suspected of COVID-19 by their healthcare provider.

Your product is also for use with saliva specimens collected without preservatives in a sterile tube in a healthcare setting (supervised) from individuals who are suspected of COVID-19 by their healthcare provider. As specified in the Instructions for Use, the sterile tube is a 15 ml conical tube (Laboratory Product Sales, Rochester, NY, Catalog L262960, or equivalent).

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[8] 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).

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

Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests.

The SARS-CoV-2 nucleic acid is generally detectable in respiratory and saliva 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 infections 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 for SARS-CoV-2 nucleic acid from saliva should be confirmed by testing of an alternative specimen type, if clinically indicated.

Your product, when used with the Rheonix Encompass MDx Workstation (includes Encompass MDx Workstation Operator Manual), or other authorized system (as may be requested under Condition K. below), automates all aspects of nucleic acid testing including external control validation, specimen preparation, nucleic acid extraction and amplification, and detection of the SARS-CoV-2 targeted sequences using reverse transcriptase PCR assays in a single use cartridge detected using microarray technology. The Rheonix COVID-19 MDx Assay includes the materials (or other authorized materials as may be requested under Condition K. below) described in the Instructions for Use.

Your product also includes the control material (or other authorized control materials as may be requested under Condition K. below) that are described in the Instructions for Use.

You also recommend use of external positive and negative controls which are not included with the kit but are available commercially and are run as outlined in the Instructions for Use, described below. 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 "Rheonix COVID-19-MDx Assay 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) and the following fact sheets pertaining to the emergency use, are 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: Rheonix COVID-19 MDx Assay
- Fact Sheet for Patients: Rheonix COVID-19 MDx Assay

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

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that

the known and potential benefits of your product, when used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your product.

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

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

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

III. Waiver of Certain Requirements

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

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

IV. Conditions of Authorization

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

Rheonix, Inc. (You) and Authorized Distributor(s)[10]

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.

[10] "Authorized Distributor(s)" are identified by you, Rheonix, Inc., in your EUA submission as an entity allowed to distribute your product.

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

D. You and authorized distributor(s) must include a physical copy of the "Rheonix COVID-19-MDx Assay Instructions for Use" with each shipped product to authorized laboratories.

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/or 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 your product they distribute.

G. You and authorized distributor(s) must collect information on the performance of your product. You must report to FDA any suspected occurrence of false positive and false negative results and significant deviations from the established performance characteristics of your 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.

Rheonix, Inc. (You)

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

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

K. You may request changes to this EUA, 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 he authorized labeling, and not exceed the terms of authorization of this letter. Any request for changes to this EUA should be submitted to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) and require appropriate authorization from FDA prior to implementation.

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

M. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must ensure that the tests released for distribution have 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[11] of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA, you must update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

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

Q. You must submit to FDA a summary report within 30 calendar days of authorization summarizing the results of any testing performed using saliva specimens collected during that timeframe, including the positivity rate for saliva specimens.

R. Upon request, you must conduct post-authorization studies and/or data analysis concerning the performance of saliva specimens with your authorized test. Such studies and/or data analysis must be agreed upon between you and FDA. After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of the data, FDA will consider whether additional action is appropriate, such as revision or revocation of the EUA.

S. 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 (via email: CDRH-EUA-Reporting@fda.hhs.gov).

T. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA regarding the impact of viral mutations on test performance. Such updates will be made in consultation with, and

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

require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

U. You must further evaluate the stability of the Rheonix COVID-19 MDx Assay Kit, including the COVID-19 Reagent Pack (Pack A), COVID-19 PCR Mix (Pack B) and Sample Buffer in an agreed upon Real-time Reagent Stability Study that encompasses the full range of claimed reagent storage conditions. Within 1 month of the date of this letter you will submit a plan for your Real-time Reagent Stability Study and will commence the study after receiving concurrence from DMD/OHT7-OIR/OPEQ/CDRH regarding its design. If requested by FDA, you must submit the results of your Real-time Reagent Stability Study within 48 hours of the request. During your on-going Real-time Reagent Stability Study, if the results fail to support the claimed duration and temperature of reagent storage, you must notify FDA immediately (via email: CDRH-EUA-Reporting@fda.hhs.gov).

V. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA relating to reagent stability. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

Authorized Laboratories

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

X. Authorized laboratories using your product must use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.

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

Z. 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.

AA. 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 (1-844-RHEONIX (1-844-743-6649)) 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.

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

Rheonix, Inc. (You), Authorized Distributor(s) and Authorized Laboratories

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

Conditions Related to Printed Materials, Advertising and Promotion

DD. 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.

EE. 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.

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

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and,
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

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

V. Duration of Authorization

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

Sincerely,

Jacqueline A. O'shaughnessy -S

Digitally signed by Jacqueline A. O'shaughnessy -S
Date: 2022.07.08 12:00:37 -04'00'

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

Enclosure