February 9, 2021

Marlene Hanna
Ortho Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, NY 14626

Device:	VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack used in combination with the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator
EUA Number:	EUA202928
Company:	Ortho Clinical Diagnostics, Inc.
Indication:	Qualitative detection of SARS-CoV-2 nucleocapsid protein antigens in nasopharyngeal (NP) swab specimens collected in CDC's formulation of VTM, WHO's formulation of VTM, COPAN Universal Transport Media (UTM), Hardy R99 VTM, FlexTrans Transport Media, saline or phosphate buffered saline (PBS) from individuals who are suspected of COVID-19 by their healthcare provider within seven days of the onset of symptoms using the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems. 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 the requirements to perform moderate or high complexity tests.

Dear Ms. Hanna:

On January 11, 2021, based on your[1] request the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack used in combination with the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator 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 SARS-CoV-2 nucleocapsid protein antigens in nasopharyngeal (NP) swab

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

specimens collected in CDC's formulation of VTM, COPAN Universal Transport Media (UTM), Remel M4RT VTM, or Hardy R99 VTM from individuals who are suspected of COVID-19 by their healthcare provider within seven days of the onset of symptoms using the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems. Testing was limited to laboratories certified under CLIA, 42 U.S.C. §263a, to perform high complexity tests.

On February 7, 2021, you requested to further revise your Emergency Use Authorization (EUA). Based on this request, and having concluded that revising the January 11, 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 January 11, 2021, letter in its entirety with the revisions incorporated.[2] 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[3] 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.[4]

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

[2] The revisions to the January 11, 2021, letter and authorized labeling include: (1) addition of WHO's formulation of VTM, FlexTrans Transport Media, saline or phosphate buffered saline (PBS) to the intended use, (2) removal of Remel M4RT VTM from the intended use and performance characteristics section, (3) addition of the Remel M4RT VTM to the special precautions section and (4) updates to the limitations section and healthcare provider fact sheet to indicate that 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.

[3] For ease of reference, this letter will use the term "your product" to refer to the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack used in combination with the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator used for the indication identified above. CDC refers to the Centers for Disease Control and Prevention. WHO refers to the World Health Organization.

[4] 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.[5]

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 chemiluminescent immunoassay intended for the qualitative detection of SARS-CoV-2 nucleocapsid protein antigens in NP swab specimens collected in CDC's formulation of VTM, WHO's formulation of VTM, COPAN Universal Transport Media (UTM), Hardy R99 VTM, FlexTrans Transport Media, saline or phosphate buffered saline (PBS) from individuals who are suspected of COVID-19 by their healthcare provider within seven days of the onset of symptoms using the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems. Your product does not differentiate between SARS-CoV and SARS-CoV-2. The SARS-CoV-2 nucleocapsid protein antigen is generally detectable in nasopharyngeal swab specimens during the acute phase of infection. Positive results indicate the presence of viral antigens, but clinical correlation with patient history and other diagnostic information is necessary to determine infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. Negative results should be treated as presumptive and confirmation with a molecular assay, if necessary, for patient management, may be performed. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions. Negative results should be considered in the context of a patient's recent exposures, history and presence of clinical signs and symptoms consistent with COVID-19.

Testing of NP swab specimens using your product, as outlined in the "Instructions for Use VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack, VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator," using the VITROS 3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems is limited to

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

laboratories certified under CLIA that meet the requirements to perform moderate or high complexity tests.

To use your product, which is a 2-step chemiluminescent immunometric technique, a NP swab specimen collected from the patient is inserted in either CDC's formulation of VTM, WHO's formulation of VTM, COPAN Universal Transport Media (UTM), Hardy R99 VTM, FlexTrans Transport Media, saline or phosphate buffered saline (PBS). The patient specimen is added to the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Extraction Buffer (not provided with your product) in a sample tube prior to loading onto the instrument. In the first step SARS-CoV-2 nucleocapsid antigen present in the sample binds with monoclonal anti-SARS-CoV-2 coated on the well. Unbound sample is removed by washing. In the second step horseradish peroxidase (HRP)-labeled monoclonal anti-SARS-CoV-2 is added in the conjugate reagent. The conjugate binds specifically to any SARS-CoV-2 nucleocapsid captured on the well during the first step. Unbound conjugate is removed by the subsequent wash step and the remaining bound HRP conjugate is measured by addition of a reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs luminescent reaction emission. Signal to cutoff numerical values will increase as the amount of SARS-CoV-2 antigen present in the specimen increases.

The VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack includes the following materials or other authorized materials: coated wells (rabbit monoclonal anti-SARS-CoV-2 nucleocapsid), assay reagent (buffer with bovine protein stabilizers and antimicrobial agent) and conjugate reagent (HRP-mouse monoclonal anti-SARS-CoV-2 nucleocapsid in buffer with protein stabilizers and antimicrobial agent). The VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator includes the following materials or other authorized materials: VITROS SARS-CoV-2 Antigen Calibrator (recombinant SARS-CoV-2 nucleocapsid antigen in buffer with bovine serum albumin and antimicrobial agent) and 8 calibrator bar code labels.

You also require use of the VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Controls (not provided with your product), or other authorized controls (as may be requested under Condition O. below), that are run as outlined in the Instructions for Use:

- VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Controls – include two VITROS SARS-CoV-2 Antigen Controls (SARS-CoV-2 Ag negative and SARS-CoV-2 Ag positive)

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 "Instructions for Use VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack, VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Calibrator," "VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Controls" and "VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Extraction Buffer" (available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas), and the following fact sheets pertaining

to the emergency use, 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: Ortho Clinical Diagnostics, Inc. - VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack
- Fact Sheet for Patients: Ortho Clinical Diagnostics, Inc. - VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Reagent Pack

The above described product, with 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, 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:

Ortho Clinical Diagnostics, Inc. (You) and Authorized Distributor(s)[6]

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 CFR 809.10(b)(5), (7), and (8)); appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4); and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

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

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

D. You and authorized distributors who make your product available with the Instructions for Use only electronically available will provide with your product the opportunity to request a copy in paper form, and after such request, you must promptly provide the requested information without additional cost. For example, such information may be included on the box label included with your product that complies with Condition A.

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 will report to FDA any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the product of which you become aware.

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

I. You and authorized distributor(s) will make available the VITROS Immunodiagnostic

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

Products SARS-CoV-2 Antigen Extraction Buffer and VITROS Immunodiagnostic Products SARS-CoV-2 Antigen Controls, or other authorized materials or control materials (as may be requested under Condition O. below), at the same time as your product.

Ortho Clinical Diagnostics, Inc. (You)

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

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

L. You must comply with the following requirements pursuant to FDA regulations: 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 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 shall 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.

P. You must evaluate the analytical limit of detection and assess traceability[7] of your product with any FDA-recommended reference material(s). After submission to and review and concurrence with the data by FDA, you must update labeling to reflect the additional testing. Such labeling updates must be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

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

Q. You must complete the agreed upon real-time stability study for your product and notify DMD/OHT7-OIR/OPEQ/CDRH of the testing results as they become available until completion of the study. After submission of the study data, and review and concurrence with the data by FDA, you must update your product labeling to reflect the additional testing. Such labeling updates must be made in consultation with, and require concurrence of, DMD/OHT7- OIR/OPEQ/CDRH.

R. 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.

Authorized Laboratories

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

T. Authorized laboratories using your product must use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including authorized instruments, authorized clinical specimen types, authorized control materials, authorized 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 (at OrthoCareTechnicalSolutions@orthoclinicaldiagnostics.com or via phone by contacting Ortho Customer Support Services at 1-800-421-3311) 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 operators using your product must be appropriately trained in performing and interpreting the results of your product, use appropriate personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

Ortho Clinical Diagnostics, Inc. (You), Authorized Distributor(s) 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 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, advertising, and promotional materials relating to the use of your product shall clearly and conspicuously state that:

- This test has not been FDA cleared or approved, but has been authorized by FDA under an EUA for use by authorized laboratories;
- This test has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens; and,
- The emergency use of this test 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