

April 14, 2020

Marlene A. Hanna, RAC
Director, Regulatory Affairs
Ortho-Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, NY 14626

Device: VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator.

Company: Ortho-Clinical Diagnostics, Inc.

Indication: Qualitative detection of total antibodies (including IgG and IgM) to SARS-CoV-2 in human serum and plasma (K2 EDTA) specimens from individuals suspected of COVID-19 by a 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, to perform moderate and high complexity tests.

Dear Ms. Hanna:

This letter is in response to your¹ request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of your product,² pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

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

¹ For ease of reference, this letter will use the term “you” and related terms to refer to Ortho-Clinical Diagnostics, Inc.

² For ease of reference, this letter will use the term “your product” to refer to the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator 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.³

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 Section 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.⁴

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 total antibodies (including IgG and IgM) to SARS-CoV-2 in human serum and plasma (K2 EDTA) specimens from individuals suspected of COVID-19 by a healthcare provider. Results are for the detection of SARS-CoV-2 total antibodies that are generated as part of the human immune response to the virus. Positive results for total antibodies could occur after infection and can be indicative of acute or recent infection.

The test is performed using the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack and the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator on the VITROS ECi/ECiQ/3600 Immunodiagnostic System and the VITROS 5600/XT 7600 Integrated Systems. An immunometric technique is used; this involves a two stage reaction. In the first stage antibodies to SARS-CoV-2 present in the specimen bind with SARS-CoV-2 antigen coated on the well. Unbound specimen is removed by washing. In the second stage horseradish peroxidase (HRP)-labeled recombinant SARS-CoV-2 antigen is added in the

³ 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. FR 7316 February 7, 2020.

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

conjugate reagent. The conjugate binds specifically to any anti-SARS-CoV-2 captured on the well in the first stage. Unbound conjugate is removed by the subsequent wash step. The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent is added 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 its emission. The light signals are read by the system. The amount of HRP conjugate bound is indicative of the amount of SARS-CoV-2 antibody present.

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, (e.g., quality control materials such as VITROS Immunodiagnostic Products VITROS Anti-SARS-CoV-2 Total Controls).

The above described product, when labeled consistently with the labeling authorized by FDA, entitled “VITROS Immunodiagnostic Products Instructions for Use CoV2T” (available at <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations>), which may be revised in consultation with, and with concurrence of, the Division of Microbiology Devices (DMD)/Office of Health Technology 7 Office of In Vitro Diagnostics and Radiological Health (OHT7-OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH), 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.

Your product is authorized to be accompanied by the following product-specific information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack
- Fact Sheet for Patients: VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack

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 total antibodies against SARS-CoV-2 and used consistently 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 for the indication above, 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 (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) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), your product is authorized for the indication above.

This EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under Section 564(b)(2) of the Act or when the EUA is revoked under Section 564(g) of the Act.

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:

Ortho-Clinical Diagnostics, Inc. (You) and Authorized Distributor(s)⁵

- 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)); any 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) will make your product available with the authorized labeling to authorized laboratories. You may request changes to the authorized labeling. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- C. You and authorized distributor(s) will provide to authorized laboratories the Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients. You may request changes to the authorized Fact Sheets. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

⁵ "Authorized Distributor(s)" are identified by you, Ortho-Clinical Diagnostics, Inc., in your EUA submission as an entity allowed to distribute your device.

- D. You and authorized distributor(s) will make available on your website(s) the Fact Sheet for Healthcare Providers and the Fact Sheet for Patients.
- E. You and authorized distributor(s) will inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product, authorized labeling and authorized Fact Sheets.
- F. Through a process of inventory control, you and authorized distributor(s) will maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.
- G. You and authorized distributor(s) will collect information on the performance of your product. You will report to FDA 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.
- I. You and authorized distributor(s) will make available the control material or other authorized control materials for purchase at the same time as your product.

Ortho-Clinical Diagnostics, Inc. (You)

- J. You will notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).
- K. You will 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).
- L. You may request changes to the Scope of Authorization (Section II in this letter) of your product. Such requests will be made in consultation with DMD/OHT7-OIR/OPEQ/CDRH, and require concurrence of, Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and DMD/OHT7-OIR/OPEQ/CDRH.
- M. You may request the addition of other ancillary methods for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- N. You may request the addition of other specimen types for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

- O. You may request the addition and/or substitution of control materials for use with your product. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- P. You may request substitution for or changes to the authorized materials used in the detection process of human antibodies against SARS-CoV-2. Such requests will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- Q. You will evaluate the performance and assess traceability⁶ of your product with any FDA-recommended reference material(s) or established panel(s) of characterized clinical specimens. After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, 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.
- R. You will track adverse events, including any occurrence of false results and report to FDA under 21 CFR Part 803.
- S. You will complete the agreed upon supplemental interference study. After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, you will update your product labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- T. You will complete the agreed upon real-time stability study for your product. After submission to FDA and DMD/OHT7-OIR/CDRH's review of and concurrence with the data, you will update your product labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

Authorized Laboratories

- U. Authorized laboratories using your product will 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.
- V. Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- W. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.

⁶ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

- X. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Y. Authorized laboratories will 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 (OrthoCOVID19Test@orthoclinicaldiagnostics.com) 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.
- Z. All laboratory personnel using your product must be appropriately trained in automated immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.

Ortho-Clinical Diagnostics, Inc. (You), Authorized Distributors and Authorized Laboratories

- AA. You, authorized distributors, and authorized laboratories using your product will 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 Advertising and Promotion

- BB. All advertising and promotional descriptive printed matter relating to the use of your product shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.
- CC. All advertising and promotional descriptive printed matter relating to the use of your product shall clearly and conspicuously state that:
 - This test has not been FDA cleared or approved;
 - This test has been authorized by FDA under an EUA for use by authorized laboratories;
 - This test has been authorized only for the presence of total antibodies against SARS-CoV-2, not for any other viruses or pathogens; and
 - 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 Act, 21

U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

No advertising or promotional descriptive printed matter 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.

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

Enclosures