



July 9, 2021

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

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

EUA Number: EUA210322

Company: Ortho-Clinical Diagnostics, Inc.

Indication: Qualitative and quantitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma (dipotassium EDTA, tripotassium EDTA, and lithium heparin). For use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. For use on samples from individuals that are 15 days or more post symptom onset. 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 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).

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 IgG Quantitative Reagent Pack used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator. You also refer to your product as the “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative test.”

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.³

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 “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack/VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator” 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 recent or prior infection with SARS-CoV-2 by aiding in identifying individuals with an adaptive immune response to the virus that causes COVID-19, and that the known and potential benefits of your product when used for such use, 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

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. 85 FR 7316 (February 7, 2020).

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

Your product is a chemiluminescent immunoassay test intended for the qualitative and quantitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma (dipotassium EDTA, tripotassium EDTA and lithium heparin). Your product is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. Testing is limited to laboratories certified under CLIA that meet requirements to perform moderate or high complexity tests. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. Quantitative results from your product should not be interpreted as an indication or degree of immunity or protection from reinfection. The test is to be used on samples from individuals that are 15 days or more post symptom onset.

The test is performed using the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack and the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator on the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems (includes “Operating Instructions”). An immunometric technique is used; this involves a two stage reaction. In the first stage, antibodies to SARS-CoV-2 present in the sample bind with SARS-CoV-2 antigen coated on the well. Unbound sample is removed by washing. In the second stage, horseradish peroxidase (HRP)-labeled murine monoclonal anti-human IgG antibodies are added in the conjugate reagent. The conjugate binds specifically to any anti-SARS-CoV-2 antibody 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. Results are traceable to the certified reference material First WHO International Standard Anti-SARS-CoV-2 Immunoglobulin (Human), NIBSC 20/136 (CRM). Results are interpreted as below:

Numerical Result (BAU/mL)*	Result	Test Result Interpretation
$X < 17.8$	Non-reactive (Negative); Numerical result is not reported outside the laboratory	IgG Antibodies for SARS-CoV-2 are not detected.
$200 \geq X \geq 17.8$	Reactive (Positive); Numerical result is reported outside the laboratory	IgG Antibodies for SARS-Cov-2 are detected.
> 200	Reactive (Positive); Report outside the laboratory indicates that the result is above 200 BAU/mL (ULMI**)	

*BAU/mL – Binding Antibody Units/mL

**ULMI – Upper limit of measuring interval

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack used in combination with the VITROS Immunodiagnostic Products Anti- SARS-CoV-2 IgG Quantitative Calibrator includes the following materials or other authorized materials: Qualitative Reagent Pack with coated wells, assay reagent and conjugate reagent and Quantitative Calibrator pack with calibrators, lot calibration card, protocol card and calibrator bar code labels.

Your product also requires use of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls or other authorized controls (as may be requested under Condition M below) which are not included with your product but are available from you with the “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls” product insert to be run as outlined in the “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack/VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator” Instructions for Use:

- Negative Control, SC1: Negative - approximately 4 BAU/mL Human SARS-CoV-2 Spike S1 reactive Antibody.
- Positive Control, SC2: Positive Near Cutoff – approximately 30 BAU/mL Human SARS-CoV-2 Spike S1 reactive Antibody.
- Positive Control, SC3: Moderately Positive – approximately 100 BAU/mL Human SARS-CoV-2 Spike S1 reactive Antibody.

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 “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack/VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator” Instructions for Use and “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls” product insert (available at <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>), the two product information cards (PICs) and the following product-specific information 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: Ortho-Clinical Diagnostics, Inc. - VITROS Anti-SARS-CoV-2 IgG Quantitative Reagent Pack used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator
- Fact Sheet for Recipients: Ortho-Clinical Diagnostics, Inc. - VITROS Anti-SARS-CoV-2 IgG Quantitative Reagent Pack used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator

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 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 recent or prior infection with SARS-CoV-2 by aiding in identifying individuals with an adaptive immune response to the virus that causes 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)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

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

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 Fact Sheet for Healthcare Providers and the Fact Sheet for Recipients.
- D. You and authorized distributor(s) must include a physical copy of the relevant authorized PIC card with each shipped product of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack/VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator and VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls to authorized laboratories, and will make the “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Reagent Pack/VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Calibrator” Instructions for Use and the “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls” product insert electronically available with the opportunity to request copies 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 your product and number 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.
- I. You and authorized distributor(s) must make available the control material (VITROS

Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls) with the “VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Quantitative Controls” product insert (refer to Condition D above), or other authorized control materials (as may be requested under Condition M 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 amendments 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: 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 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.
- N. You must 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 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.
- O. 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.
- P. 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.

⁶ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material. FDA may request, for example, that you perform this study in the event that we receive reports of adverse events concerning your product.

- Q. 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.
- R. If requested by FDA, you must participate in a National Cancer Institute study on the evaluation of your product. After submission to and concurrence with the data by FDA 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.
- S. If requested by FDA, you must periodically submit new lots for testing at the National Cancer Institute, or by another government agency designated by FDA, to confirm continued performance characteristics across lots. In addition, FDA may request records regarding lot release data for tests to be distributed or already distributed. If such lot release data are requested by FDA, you must provide it within 48 hours of the request.
- T. You must complete the agreed upon real-time stability studies for your product. 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.
- U. You must further complete the agreed upon interference study for your product. After submission to and concurrence with the data by FDA, you must update your labeling to reflect the additional testing within 30 calendar days of the date of this letter. Such labeling updates must be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- V. 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.
- W. 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

- X. 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.

- Y. Authorized laboratories must use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instrument, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- Z. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- AA. 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.
- BB. 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 to you (OrthoCareTechnicalSolutions@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.
- CC. 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 Distributor(s) and Authorized Laboratories

- DD. 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 will be made available to FDA for inspection upon request.

Conditions Related to Printed Materials, Advertising and Promotion

- EE. 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.
- FF. 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.
- GG. 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 detecting IgG antibodies to 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