

May 11, 2021

James A. Hayward, Ph.D.  
Chairman, President & CEO  
Applied DNA Sciences, Inc.  
50 Health Sciences Drive  
Stony Brook, NY 11790

Device: Linea COVID-19 Assay Kit

EUA Number: EUA200474

Company: Applied DNA Sciences, Inc.

Indication: Qualitative detection of nucleic acid from SARS-CoV-2 in upper respiratory specimens including anterior nasal swabs, self-collected at a healthcare location or collected by a healthcare worker, and nasopharyngeal swabs and oropharyngeal swabs, nasopharyngeal wash/aspirate or nasal aspirates, and bronchoalveolar lavage (BAL) specimens collected by a healthcare worker from individuals who are suspected of COVID-19 by their healthcare provider (HCP). The test is also intended for use with anterior nasal swab specimens that are self-collected in the presence of an HCP from individuals without symptoms or other reasons to suspect COVID-19 when tested at least weekly and with no more than 168 hours between serially collected specimens. Emergency use of this test is limited to authorized laboratories.

Authorized Laboratories: Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity tests.

Dear Dr. Hayward:

On May 13, 2020, based on your<sup>1</sup> request the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the Linea COVID-19 Assay Kit, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3), for the qualitative detection of nucleic acid from SARS-CoV-2 in upper respiratory specimens including nasal swabs, self-collected at a healthcare location or collected by a healthcare worker, and nasopharyngeal swabs and oropharyngeal swabs, nasopharyngeal wash/aspirate or nasal aspirates collected by a healthcare worker from individuals who are suspected of COVID-19 by their healthcare provider. Testing was limited to laboratories certified under CLIA that

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<sup>1</sup> For ease of reference, this letter will use the term “you” and related terms to refer to Applied DNA Sciences, Inc.

meet requirements to perform high complexity tests. Based on your requests, FDA has also granted updates to the authorized labeling on July 8, 2020,<sup>2</sup> July 30, 2020,<sup>3</sup> September 25, 2020<sup>4</sup> and November 21, 2020.<sup>5</sup>

On April 9, 2021, you requested to amend your Emergency Use Authorization (EUA). Based on that request and having concluded that revising the May 13, 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 May 13, 2020, letter in its entirety with the revisions incorporated.<sup>6</sup> 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<sup>7</sup> is now intended for the indication described above.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of in

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<sup>2</sup> On July 8, 2020, your request was granted to update the Instructions for Use (IFU) to: (1) include use of the manual RNA extraction kit, Omega Bio-Tek Mag-Bind Viral RNA Xpress Kit, and (2) include minor edits in the IFU for clarification. FDA also updated the “Intended Use”, “Warnings and Precautions”, and “Limitations” sections of the IFU to reflect language used in more recent authorizations. FDA also updated the Healthcare Provider and Patient Fact Sheets accordingly.

<sup>3</sup> On July 30, 2020, your request was granted to update the Instructions for Use (IFU) to include: (1) use of the Omega Bio-Tek Mag-Bind Viral RNA Xpress Kit on the Hamilton Company Microlab STARlet Liquid Handling System, (2) use of the Thermo Fisher Scientific (Applied Biosystems) QuantStudio 5 Real-Time PCR System equipped with QuantStudio Design and Analysis software v1.4, and (3) updates to the IFU to incorporate the additional, validated extraction method and real-time PCR instrument.

<sup>4</sup> On September 25, 2020, your supplement was acknowledged to update the IFU with results from testing with the FDA Reference Panel.

<sup>5</sup> On November 21, 2020, your request was granted to update the Instructions for Use (IFU) to include the Applied Biosystems 7500 Fast Dx Real-Time PCR System (ABI 7500) as an additional PCR instrument. FDA also updated the Intended Use and the Healthcare Provider and Patient Fact Sheets to reflect language used in more recent authorizations.

<sup>6</sup> The revisions to the May 13, 2020, letter and authorized labeling include: (1) revisions to the intended use and authorized labeling documents, including the Fact Sheet for Healthcare Providers and Fact Sheet for Patients to reflect current information known about serial testing as outlined in the March 16, 2021, FDA “Supplemental Template for Developers of Molecular and Antigen Diagnostic COVID-19 Tests for Screening with Serial Testing” (<https://www.fda.gov/media/146695/download>), which includes testing of individuals without symptoms or other epidemiological reasons to suspect COVID-19, (2) updates to the Conditions of Authorization to require post-authorization studies; (a) clinical study to support the serial testing claim, and (b) analytical performance study using material representing agreed upon SARS-CoV-2 sequence variant(s), (3) updates to the authorized extraction methodologies, including removal of the TRIzol RNA Extraction Kit and addition of the Omega Bio-Tek Mag-Bind Viral RNA Xpress Kit and the Applied Biosystems MagMAX Viral/Pathogen II Nucleic Acid Isolation Kit both performed on the KingFisher Flex Purification System, (4) addition of an Emergency Use Only (EUO) label for the QuantStudio 5 Real-Time PCR System, (5) updates to the IFU, Conditions of Authorization (including consolidation of several conditions in new condition K), Fact Sheet for Healthcare Providers and Fact Sheet for Patients to reflect language used in more recent authorizations and (6) revisions to include use of a product information card.

<sup>7</sup> For ease of reference, this letter will use the term “your product” to refer to the Linea COVID-19 Assay Kit 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.<sup>8</sup>

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

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

## **I. Criteria for Issuance of Authorization**

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.<sup>9</sup>

## **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 upper respiratory specimens including anterior nasal swabs, self-collected at a healthcare location or collected by a healthcare worker, and nasopharyngeal swabs and oropharyngeal swabs, nasopharyngeal wash/aspirate or nasal aspirates, and bronchoalveolar lavage (BAL) specimens collected by a healthcare worker from individuals who are suspected of COVID-19 by their healthcare provider (HCP). Your product is also intended for use with anterior nasal swab specimens that are self-collected in the presence of an HCP from individuals without symptoms or other reasons to suspect COVID-19 when tested at least weekly and with no more than 168 hours between serially collected specimens. The SARS-CoV-2 nucleic acid is generally

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<sup>8</sup> 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).

<sup>9</sup> No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

detectable in respiratory 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. The agent detected may not be the definite cause of disease. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

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

To use your product, SARS-CoV-2 nucleic acid is first extracted, isolated and purified from nasal, nasopharyngeal and oropharyngeal swabs, and nasopharyngeal wash/aspirate or nasal aspirates. The purified nucleic acid is then reverse transcribed into cDNA followed by PCR amplification and detection using an authorized real-time (RT) PCR instrument. The Linea COVID-19 Assay Kit includes the following materials or other authorized materials: S1 and S2 Primers and Probes, Positive Control (concentrated), Positive Control Dilution Buffer, Master Mix, Nuclease Free Water, RNase P Control.

Your product requires the following control materials, or other authorized control materials (as may be requested under Condition K. below), that are processed in the same way as the specimens and are required to be included with each batch of specimens tested with your product. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Instructions for Use:

- Internal Control - RNase P (RP) control in clinical samples: The RP primer and probe set is included in each run to test for human RP, which controls for specimen quality and demonstrates that nucleic acid was generated by the extraction process.
- Positive Template Control - contains genomic regions targeted by the kit. The positive control is used to monitor for failures of PCR reagents and reaction conditions.
- No Template Control - Nuclease-free, molecular-grade water used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents.

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

The labeling entitled “Linea COVID-19 Real-Time PCR Assay Kit Instructions for Use” (available at <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas>), the “Linea COVID-19 Real-Time PCR Assay Kit” Product Information Card, and the following fact sheets pertaining to the emergency use, is required to be made available as set forth in the Conditions of Authorization (Section IV), and are collectively referred to as “authorized labeling”:

- Fact Sheet for Healthcare Providers: Linea COVID-19 Assay Kit
- Fact Sheet for Patients: Linea COVID-19 Assay Kit

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

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of your authorized product, when used for the qualitative detection of SARS-CoV-2 and used 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 for in diagnosing COVID-19, when used consistently with the Scope of Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

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

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

### **III. Waiver of Certain Requirements**

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

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

### **IV. Conditions of Authorization**

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

#### **Applied DNA Sciences, Inc. (You) and Authorized Distributor(s)<sup>10</sup>**

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<sup>10</sup> “Authorized Distributor(s)” are identified by you, Applied DNA Sciences, Inc., in your EUA submission as an

- 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) 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 distributor(s) must include a physical copy of the “Linea COVID-19 Real-Time PCR Assay Kit” Product Information Card with each shipped product to authorized laboratories, and will make the authorized “Linea COVID-19 Real-Time PCR Assay Kit Instructions for Use” electronically available with the opportunity to request a copy in paper form, and after such request, you must promptly provide the requested information without additional cost.
- E. You and authorized distributor(s) must inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.
- F. Through a process of inventory control, you and authorized distributor(s) must maintain records of the authorized laboratories to which they distribute the test and number of tests they distribute.
- G. You and authorized distributor(s) must collect information on the performance of your product. You must report to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) (via email: CDRH-EUA- Reporting@fda.hhs.gov) any suspected occurrence of false positive 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.

**Applied DNA Sciences, Inc. (You)**

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entity allowed to distribute your product.

- I. You must notify FDA of any authorized distributor(s) of your product, including the name, address, and phone number of any authorized distributor(s).
- J. You must provide authorized distributor(s) with a copy of this EUA and communicate to authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets).
- K. You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling, including requests to make available additional authorized labeling specific to an authorized distributor. Such additional labeling may use another name for the product but otherwise must be consistent with the authorized labeling, and not exceed the terms of authorization of this letter. Any request for changes to this EUA should be submitted to DMD/OHT7-OIR/OPEQ/CDRH and require appropriate authorization from FDA prior to implementation.
- L. You must comply with the following requirements under FDA regulations: 21 CFR 820 Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).
- M. You must have lot release procedures and the lot release procedures, including the study design and statistical power, must ensure that your product released for distribution has the clinical and analytical performance claimed in the authorized labeling.
- N. If requested by FDA, you must submit lot release procedures to FDA, including sampling protocols, testing protocols, and acceptance criteria, that you use to release lots of your product for distribution in the U.S. If such lot release procedures are requested by FDA, you must provide it within 48 hours of the request.
- O. You must evaluate the analytical limit of detection and assess traceability<sup>11</sup> of your product with any FDA-recommended reference material(s). After submission to and concurrence with the data by FDA you will update your labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.
- P. You must evaluate the clinical performance of your product to support the screening claim in an FDA agreed upon post authorization clinical evaluation study within 6 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you must update the authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

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<sup>11</sup> Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material.

- Q. You must further evaluate the analytical performance of your product using material representing SARS-CoV-2 sequence variant(s) in an FDA agreed upon post authorization study within 2 months of the date of this letter (unless otherwise agreed to with DMD/OHT7-OIR/OPEQ/CDRH). After submission to FDA and DMD/OHT7-OIR/OPEQ/CDRH's review of the data, FDA will consider whether additional action is appropriate. If the data are acceptable, you must update your authorized 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 must have a process in place to track adverse events, including any occurrence of false results and report to FDA in accordance with 21 CFR Part 803.

### **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 these Fact Sheets may be used, which may include mass media.
- T. Authorized laboratories using your product must use your product as outlined in the authorized labeling. 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.
- 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](mailto:CDRH-EUA-Reporting@fda.hhs.gov)) and you (via email: [dxccovid@adnas.com](mailto:dxccovid@adnas.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.
- X. All laboratory personnel using your product must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling.

### **Applied DNA Sciences, Inc. (You), Authorized Distributors and Authorized Laboratories**

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

### **Conditions Related to Printed Materials, Advertising and Promotion**



- Z. All descriptive printed matter, advertising and promotional materials relating to the use of your product shall be consistent with the Fact Sheets and 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, including advertising and promotional materials relating to the use of your product shall clearly and conspicuously state that:
- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
  - This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and
  - The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

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

#### **V. Duration of Authorization**

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

Sincerely,

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RADM Denise M. Hinton  
Chief Scientist  
Food and Drug Administration

Enclosure