



March 27, 2018

Anne Schuchat, MD (RADM, USPHS)
Acting Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
Atlanta, GA 30333

Dear Dr. Schuchat:

On April 22, 2013, based on a request by the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay¹ for the presumptive detection of novel influenza A(H7N9) virus in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in real-time reverse transcriptase PCR (rRT-PCR) assays in patients with signs and symptoms of respiratory infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3), by public health and other qualified laboratories.

On March 5, 2018, FDA received a request from CDC to amend the Emergency Use Authorization (EUA). In response to that request, and having concluded that revising the April 22, 2013, 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)), the April 22, 2013, letter authorizing the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay is being reissued in its entirety with the amendments incorporated.²

On April 19, 2013, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that there is a significant potential for 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

¹ U.S. Food and Drug Administration. *Authorization of Emergency Use of an In Vitro Diagnostic for Detection of the Novel Avian Influenza A (H7N9) Virus; Availability*. 78 FR 38044 (June 25, 2013).

² The amendments to the April 22, 2013, letter authorize the use of additional extraction methods for use with the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay, additional guidance on reporting/referring presumptive positive results to CDC, and a minor name change. The amendments also include revisions to the Instructions for Use and Fact Sheets for Healthcare Providers and Patients to address these additions. The amendments also allow the future use of “other authorized instruments,” of “other authorized extraction methods,” of “other authorized control materials,” of “other authorized ancillary reagents and materials,” and of “other authorized specimen types,” when requested by CDC and concurred with by the Division of Microbiology Devices/Office of In Vitro Diagnostics and Radiological Health/Center for Devices and Radiological Health (DMD/OIR/CDRH).

that involves the avian influenza A (H7N9) virus.³ Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for the detection of avian influenza A (H7N9) virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).⁴

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay (as described in the scope section of this letter (Section II)) used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel (#K172091) in rRT-PCR assays in individuals with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors for the presumptive detection of avian influenza A (H7N9) virus by authorized laboratories⁵, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays for the presumptive detection of avian influenza A (H7N9) virus in individuals with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The avian influenza A (H7N9) virus can cause influenza, a serious or life threatening disease or condition to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay may be effective in diagnosing avian influenza A (H7N9) virus, and that the known and potential benefits of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays, when used for diagnosing avian influenza A (H7N9) virus infection, outweigh the known and potential risks of such product; and

³ As amended by the Pandemic and All Hazards Preparedness Reauthorization Act, Pub. L. No. 113-5, under section 564(b)(1)(C) of the Act, the Secretary may make a determination of a public health emergency, or of a significant potential for a public health emergency.

⁴ U.S. Department of Health and Human Services. *Determination and Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of the Avian Influenza A (H7N9) Virus*. 78 Fed. Reg. 25273 (April 30, 2013).

⁵ Authorized laboratories are laboratories designated by CDC and, in the U.S, certified either under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, or the Department of Defense Clinical Laboratory Improvement Program (CLIP) to perform high complexity tests, or by similarly qualified non-U.S. laboratories.

3. There is no adequate, approved, and available alternative to the emergency use of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays for diagnosing avian influenza A (H7N9) virus.⁶

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 use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays for the presumptive detection of avian influenza A (H7N9) virus in individuals with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors.

The Authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays is for the *in vitro* qualitative detection and differentiation of A(H7) [Eurasian Lineage] influenza viral RNA in upper respiratory tract specimens, such as nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), nasal aspirates (NA), nasal washes (NW), and dual nasopharyngeal/throat swabs (NPS/TS) and lower respiratory tract specimens (including bronchoalveolar lavage (BAL), bronchial wash (BW), tracheal aspirate (TA), sputum, lung tissue, and other authorized specimens from individuals with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors. The testing procedure consists of nucleic acid extraction and purification from the human specimen using authorized extraction methods/instruments followed by rRT-PCR, where the RNA is reverse transcribed into cDNA and then amplified using the primer set and detected using the specific probe. The rRT-PCR is performed on the FDA cleared Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument, or other authorized instruments.

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay includes the following materials or other authorized materials:

- EuH7-F, EuH7-R and EuH7-P vials containing primers and probes that target the gene encoding the HA protein to detect influenza A (H7) [Eurasian Lineage] virus strains
- EuH7PC vial containing the influenza A(H7) [Eurasian Lineage] virus positive control used in the assay

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay also requires the use of additional authorized materials and authorized ancillary reagents that are not included with the test but are commonly used in clinical

⁶ No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

laboratories and are described in the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Instructions for Use.

The CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel requires the following control materials, or other authorized control materials; all controls listed below must generate expected results in order for a test to be considered valid, as outlined in the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Instructions for Use:

- Human Specimen Control (HSC): A human cell culture preparation used as an extraction control and positive control for the RNase P primer and probe set that is extracted and tested concurrently with the test specimens.
- Positive Control for influenza A(H7) [Eurasian Lineage] virus: Run with each batch of specimens. Monitors for failures of rRT-PCR reagents and reaction conditions.
- No Template Control (NTC): Nuclease-free water included in each run. Monitors for reagent and system contamination.
- RNase P control in clinical samples: All clinical samples and HSC are tested for human RNase P, using the RP primer and probe set, to control for specimen quality and as an indicator that nucleic acid resulted from the extraction process.

The above described CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay, when labeled consistently with the labeling authorized by FDA, entitled “CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Instructions for Use” (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), which may be revised by CDC in consultation with, and with concurrence of, the Division of Microbiology Devices (DMD)/Office of In Vitro Diagnostics and Radiological Health (OIR)/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 federal law.

The above described CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Interpreting CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Test Results
- Fact Sheet for Patients: Understanding Results from the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay

As described in Section IV below, CDC is also authorized to make available additional information relating to the emergency use of the authorized CDC Human Influenza Virus Real-

Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

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 the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays in the specified population, when used for presumptive detection avian influenza A (H7N9) virus and used consistently with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of such a 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 the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays may be effective in the presumptive detection of avian influenza A (H7N9) virus, 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 the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays, when used for detection of the avian influenza A (H7N9) virus in the specified population (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 the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay used in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays 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), the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay described above is authorized to detect the avian influenza A (H7N9) virus in individuals with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors.

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 the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay 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 the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 21 CFR 809.30, except for 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).

IV. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

Centers for Disease Control and Prevention (CDC)

- A. CDC will distribute the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay with the authorized labeling only to authorized laboratories. Changes to the authorized labeling will be made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.
- B. CDC will provide to authorized laboratories the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Fact Sheet for Healthcare Providers and the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Fact Sheet for Patients.
- C. CDC will make available on its website the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Fact Sheet for Healthcare Providers and the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Fact Sheet for Patients.
- D. CDC will inform authorized laboratories and relevant public health authority(ies) of this EUA, including the terms and conditions herein.

- E. CDC will ensure that the authorized laboratories using the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- F. Through a process of inventory control, CDC will maintain records of device usage.
- G. CDC will collect information on the performance of the test. CDC will report to FDA any suspected occurrence of false positive and false negative results and significant deviations from the established performance characteristics of the test of which CDC becomes aware.
- H. CDC is authorized to make available additional information relating to the emergency use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay that is consistent with, and does not exceed, the terms of this letter of authorization.
- I. CDC may request changes to the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Fact Sheet for Healthcare Providers and the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay Fact Sheet for Patients. Such requests will be made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.
- J. CDC may request the addition of other instruments for use with the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay. Such requests will be made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.
- K. CDC may request the addition of other extraction methods for use with the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay. Such requests will be made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.
- L. CDC may request the addition of other specimen types for use with the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay. Such requests will be made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.
- M. CDC may request the addition and/or substitution of other control materials for use with the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay. Such requests will be made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.
- N. CDC may request the addition and/or substitution of other ancillary reagents and materials for use with the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay. Such requests will be

made by CDC in consultation with, and require concurrence of, DMD/OIR/CDRH.

- O. CDC will track adverse events and report to FDA under 21 CFR Part 803.

Authorized Laboratories

- P. Authorized laboratories will include with reports of the results of the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Q. Authorized laboratories will perform the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay in conjunction with the FDA cleared CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel in rRT-PCR assays.
- R. Authorized laboratories will perform the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay as outlined in the manufacturer's Instructions for Use. Deviations from the authorized procedures, including the authorized RT-PCR instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to perform the CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay are not permitted.
- S. Authorized laboratories will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- T. Authorized laboratories will collect information on the performance of the test and report to DMD/OIR/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and CDC any suspected occurrence of false positive or false negative results of which they become aware.
- U. All laboratory personnel using the test should be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.

CDC and Authorized Laboratories

- V. CDC and authorized laboratories, will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Advertising and Promotion

- W. All advertising and promotional descriptive printed matter relating to the use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay 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.
- X. All advertising and promotional descriptive printed matter relating to the use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay 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 detection of RNA from avian influenza A (H7N9) virus, 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 the emergency use of *in vitro* diagnostic tests for detection of avian influenza A (H7N9) virus 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 the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay may represent or suggest that this test is safe or effective for the detection of avian influenza A (H7N9) virus.

The emergency use of the authorized CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay 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* diagnostic tests for detection of avian influenza A (H7N9) virus is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

Rachel Sherman, M.D., M.P.H.
Principal Deputy Commissioner

Enclosures