

- (iii) the clinician judges IV therapy is appropriate due to other circumstances.
- b. Pediatric patients for whom an IV agent is clinically appropriate because:
  - (i) patient not responding to either oral or inhaled antiviral therapy, or
  - (ii) drug delivery by a route other than IV (e.g., enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible.

C.5. Health Care Providers will ensure that patients with known or suspected renal insufficiency have creatinine clearance determined prior to peramivir dose calculation and first administration. (See Fact Sheet For Health Care Providers; Dosage and Administration for Impaired Renal Function Dosing).

C.6. Health Care Providers prescribing and/or administering authorized peramivir will ensure that patients with history of severe allergic reaction to any other neuraminidase inhibitor (zanamivir or oseltamivir) or any ingredient of peramivir will not receive authorized peramivir. (See Fact Sheet for Health Care Providers; Product Description.)

C.7. Health Care Providers will only make available additional written information relating to the emergency use of authorized peramivir to the extent that it is consistent with and does not exceed the terms of this letter of authorization (including the facts sheets referenced in Section II of this letter).

C.8. Health Care Providers will make available to FDA and/or CDC upon request any records maintained in connection with this letter. Upon request, Health Care Providers will report to FDA and/or CDC information with respect to the emergency use of authorized peramivir.

#### D. BioCryst

D.1. BioCryst will post on its website the following statement: "For information about the FDA-authorized emergency use of peramivir, please see [www.cdc.gov/h1n1flu/eua](http://www.cdc.gov/h1n1flu/eua)."

D.2. BioCryst will distribute authorized peramivir only to CDC and/or its designees subject to the terms and conditions of this letter.

D.3. BioCryst will contact FDA concerning the need for any FDA review and approval before any changes are made to the manufacturing, packaging, and labeling processes authorized as of the date of this letter.

D.4. BioCryst (or anyone acting on behalf of BioCryst) will not represent authorized peramivir in a promotional context or otherwise promote authorized peramivir.

D.5. BioCryst will make available to FDA and (as reasonably appropriate) CDC upon request any records maintained in connection with this letter. Upon request, BioCryst will report to FDA and/or (as reasonably appropriate) CDC information with respect to the emergency use of authorized peramivir.

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

#### V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Joshua M. Sharfstein, M.D.  
Principal Deputy Commissioner  
Food and Drugs

<sup>1</sup> FDA is authorizing the emergency use of peramivir administered intravenously for treatment of 2009 H1N1 in certain adult and pediatric patients as described in the scope section of this letter (Section II of this letter). For ease of reference, this letter of authorization will also use the term "authorized peramivir."

<sup>2</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

<sup>3</sup> The activities with respect to authorized peramivir refer to requesting, preparing, prescribing, and/or administering authorized peramivir, unless otherwise specified.

Dated: April 9, 2010.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2010-8604 Filed 4-16-10; 8:45 am]

BILLING CODE 4160-01-S

#### DEPARTMENT OF HEALTH AND HUMAN SERVICES

#### Food and Drug Administration

[Docket No. FDA-2009-N-0277]

#### Authorization of Emergency Use of Certain In Vitro Diagnostic Devices; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the issuance of 10 Emergency Use

Authorizations (EUAs) (the Authorizations) several of which were amended after initial issuance, for certain in vitro diagnostic devices. FDA also is announcing an amendment to the EUA for the Centers for Disease Control and Prevention (CDC) Swine Influenza Virus Real-time RT-PCR Detection Panel authorized on April 27, 2009. FDA is issuing the Authorizations and amendments thereto under the Federal Food, Drug, and Cosmetic Act (the act). The Authorizations contain, among other things, conditions on the emergency use of the authorized in vitro diagnostics. The Authorizations follow

the determination by the Acting Secretary of the U.S. Department of Health and Human Services, Charles E. Johnson (the Acting Secretary), that a public health emergency exists involving Swine Influenza A (now known as 2009 H1N1 Influenza A, or 2009 H1N1 flu) that affects, or has the significant potential to affect, national security. On the basis of such determination, the Acting Secretary declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics, accompanied by emergency use information subject to the terms of any authorization issued under the Federal Food, Drug, and Cosmetic Act (the act). The Authorizations, which include explanations of the reasons for their issuance or reissuance, are reprinted in this document.

**DATES:** See the **SUPPLEMENTARY INFORMATION** section of this document for effective dates of the Authorizations.

**ADDRESSES:** Submit written requests for single copies of the EUAs to the Office of Counterterrorism and Emerging Threats (HF-29), Food and Drug Administration, 5600 Fishers Lane, rm. 14C-26, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your request or include a fax number to which the Authorization(s) may be sent. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the Authorizations.

**FOR FURTHER INFORMATION CONTACT:** RADM Boris Lushniak, Office of Counterterrorism and Emerging Threats (HF-29), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4067.

#### **SUPPLEMENTARY INFORMATION:**

##### **I. Background**

Section 564 of the act (21 U.S.C. 360bbb-3), as amended by the Project BioShield Act of 2004 (Public Law 108-276), allows FDA to strengthen the public health protections against biological, chemical, nuclear, and radiological agents. Among other things, section 564 of the act allows FDA to authorize the use of an unapproved medical product or an unapproved use of an approved medical product during a public health emergency that affects, or has a significant potential to affect, national security, and that involves biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents. With this EUA authority, FDA can help assure that medical countermeasures may be used in an emergency to diagnose, treat, or prevent serious or

life-threatening diseases or conditions caused by such agents, when there are no adequate, approved, and available alternatives.

Section 564(b)(1) of the act provides that, before an EUA may be issued, the Secretary must declare an emergency justifying the authorization based on one of the following grounds:

(1) a determination by the Secretary of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiological, or nuclear agent or agents;

(2) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents; or

(3) a determination by the Secretary of a public health emergency under section 319 of the Public Health Service Act (PHS Act) (42 U.S.C. 247d) that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents.

Once the Secretary has declared an emergency justifying an authorization under section 564 of the act, FDA may authorize the emergency use of a drug, device, or biological product if the agency concludes that the statutory criteria are satisfied. Under section 564(h)(1) of the act, FDA is required to publish in the **Federal Register** a notice of each authorization, and each termination or revocation of an authorization, and an explanation of the reasons for the action. Section 564 of the act permits FDA to authorize the introduction into interstate commerce of a drug, device, or biological product intended for use in a declared emergency. Products appropriate for emergency use may include products and uses that are not approved, cleared, or licensed under sections 505, 510(k), and 515 of the act (21 U.S.C. 355, 360(k), and 360e, respectively) or section 351 of the PHS Act (42 U.S.C. 262). FDA may issue an EUA only if, after consultation with the National Institutes of Health (NIH) and the CDC (to the extent feasible and appropriate given the circumstances of the emergency), FDA<sup>1</sup> concludes:

(1) that an agent specified in a declaration of emergency can cause a serious or life-threatening disease or condition;

(2) that, based on the totality of scientific evidence available to FDA, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that:

- the product may be effective in diagnosing, treating, or preventing—
  - such disease or condition; or
  - a serious or life-threatening disease or condition caused by a product authorized under section 564 of the act, approved or cleared under the act, or licensed under Section 351 of the PHS Act, for diagnosing, treating, or preventing such a disease or condition caused by such an agent; and
- the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product;
  - that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such disease or condition; and
  - that such other criteria as the Secretary may by regulation prescribe are satisfied.

No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the act. Because the statute is self-executing, FDA does not require regulations or guidance to implement the EUA authority. However, FDA published guidance in July 2007 entitled “Emergency Use Authorization of Medical Products” to provide more information for stakeholders and the public about the EUA authority and the agency’s process for the consideration of EUA requests.

##### **II. EUA Request for Certain In Vitro Diagnostic Products**

On April 26, 2009, under section 564(b)(1)(C) of the act, the Acting Secretary determined that a public health emergency exists involving Swine Influenza A (now known as 2009 H1N1 Influenza A, or 2009 H1N1 flu) that affects, or has the significant potential to affect, national security. The determination has been renewed. On April 26, 2009, under section 564(b) of the act, and on the basis of such determination, the Acting Secretary declared an emergency justifying the authorization of certain in vitro diagnostics for detection of Swine Influenza A (2009 H1N1 flu), accompanied by emergency use information subject to the terms of any authorization issued under section

<sup>1</sup> The Secretary has delegated his authority to issue an EUA under section 564 of the act to the Commissioner of Food and Drugs.

564(a) of the act. Notice of the determination and the declaration of the Acting Secretary was published in the **Federal Register** on August 4, 2009 (74 FR 38628).

(1) On July 23, 2009, in response to a request from Focus Diagnostics, Inc., FDA issued an EUA for the Focus Diagnostics Influenza A H1N1 (2009) Real-Time RT-PCR IVD device with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. In response to requests from Focus Diagnostics, Inc., FDA amended the Authorization letter and reissued the Authorization letter in its entirety two times. On August 14, 2009, FDA amended the Authorization letter to authorize certain changes to the authorized labeling and permit future changes to the authorized labeling with written permission from FDA. On December 18, 2009, FDA amended the Authorization letter to authorize use of additional upper respiratory tract samples and lower respiratory tract specimens, and for other reasons. The Authorization letter, as amended and reissued on December 18, 2009, which includes an explanation for its reissuance, is reprinted in this document. Because the December 2009 amendment incorporated both the July 2009 Authorization letter and the August 2009 amendment to the Authorization letter in their entirety, the original July 2009 Authorization letter and the August 2009 amendment to the Authorization letter are not reprinted in this document.

(2) On August 24, 2009, in response to a request from the Department of Defense (DOD), FDA issued an EUA for the CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel on JBAIDS with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. On December 18, 2009, in response to a request from DOD, FDA amended the Authorization letter to authorize use of additional upper respiratory tract samples and lower respiratory tract specimens, and for other reasons, and reissued the Authorization letter in its entirety. The Authorization letter, as amended and reissued on December 18, 2009, which includes an explanation for its reissuance, is reprinted in this document. The original August 2009 Authorization letter is not reprinted in this document.

(3) On October 9, 2009, in response to a request from Diatherix Laboratories, Inc., FDA issued an EUA for the

Diatherix H1N1-09 Influenza Test with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

(4) On October 16, 2009, in response to a request from Focus Diagnostics, Inc., FDA issued an EUA for the Focus Diagnostics Simplexa Influenza A H1N1 (2009) with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. On December 18, 2009, in response to a request from Focus Diagnostics, Inc., FDA amended the Authorization letter to authorize use of additional upper respiratory tract samples and lower respiratory tract specimens, and for other reasons, and reissued the Authorization letter in its entirety. The Authorization letter, as amended and reissued on December 18, 2009, which includes an explanation for its reissuance, is reprinted in this document. The original October 2009 Authorization letter is not reprinted in this document.

(5) On October 27, 2009, in response to a request from Prodesse, Inc., FDA issued an EUA for the Prodesse ProFlu-ST Influenza A Subtyping Assay with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

(6) On November 13, 2009, in response to a request from Epoch BioSciences, FDA issued an EUA for the ELITech Molecular Diagnostics 2009-H1N1 Influenza A Virus Real Time RT-PCR test with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

(7) On November 13, 2009, in response to a request from Roche Diagnostics GmbH, FDA issued an EUA for the Roche RealTime ready Influenza A/H1N1 Detection Set with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

(8) On December 9, 2009, in response to a request from DxNA, LLC, FDA

issued an EUA for the GeneSTAT 2009 A/H1N1 Influenza Test with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

(9) On December 16, 2009, in response to a request from TessArae, LLC, FDA issued an EUA for the TessArray Resequencing Influenza A Microarray Detection Panel with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

(10) On April 27, 2009, in response to a request from CDC, FDA issued an EUA for the CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel. On May 2, 2009, in response to a request from CDC, FDA amended the Authorization letter to authorize the use of different sample types and reagents, and on August 4, 2009, notice of the initial Authorization and the amended Authorization was published in the **Federal Register** (74 FR 38636, August 4, 2009). On December 18, 2009, in response to a request from CDC, FDA amended the Authorization letter again to authorize the use of an additional upper respiratory tract specimen and use of lower respiratory tract specimens, to remove the word "presumptive" from the Intended Use, to allow the use of the CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel as a stand alone test, and for other reasons. FDA reissued the Authorization letter in its entirety. The Authorization letter, as amended and reissued on December 18, 2009, which includes an explanation for its reissuance, is reprinted in this document.

(11) On December 24, 2009, in response to a request from Cepheid, FDA issued an EUA for the Cepheid Xpert Flu A Panel with certain written information, including fact sheets for healthcare providers and patients and adequate directions for use, which are authorized under the EUA. The Authorization letter, which includes an explanation for its issuance, is reprinted in this document.

### III. Effective Dates of the Authorizations

The Authorizations are effective as follows:

(1) The Authorization for Focus Diagnostics Influenza A H1N1 (2009)

Real-Time RT-PCR IVD device is effective as of July 23, 2009;

(2) The Authorization for CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel on the Joint Biological Agent Identification and Diagnostic System Instrument (CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel JBAIDS) is effective as of August 24, 2009;

(3) The Authorization for Diatherix H1N1-09 Influenza Test is effective as of October 9, 2009;

(4) The Authorization for Focus Diagnostics Simplexa Influenza A H1N1 (2009) is effective as of October 16, 2009;

(5) The Authorization for Prodesse ProFlu-ST Influenza A Subtyping Assay is effective as of October 27, 2009;

(6) The Authorization for ELITech Molecular Diagnostics 2009-H1N1

Influenza A virus Real-Time RT-PCR test by Associated Regional and University Pathologists Laboratories is effective as of November 13, 2009;

(7) The Authorization for Roche RealTime ready Influenza A/H1N1 Detection Set is effective as of November 13, 2009;

(8) The Authorization for GeneSTAT 2009 A/H1N1 Influenza Test is effective as of December 9, 2009;

(9) The Authorization for TessArray Resequencing Influenza A Microarray Detection Panel is effective as of December 16, 2009;

(10) The amendment to the EUA for the CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel is effective as of December 18, 2009; and

(11) The Authorization for Cepheid Xpert Flu A Panel is effective as of December 24, 2009.

#### IV. Electronic Access

An electronic version of this document and the full text of the Authorizations are available on the Internet at <http://www.regulations.gov>.

#### V. The Authorizations

Having concluded that the criteria for issuance of the Authorizations, one as amended, under section 564(c) of the act are met, FDA has authorized the emergency use of certain in vitro diagnostic devices.

(1) The Authorization for Focus Diagnostics Influenza A H1N1 (2009) Real-Time RT-PCR IVD device issued on July 23, 2009, as amended and reissued in its entirety on December 18, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

John G. R. Hurrell, Ph.D.  
Vice President and General Manager  
Focus Diagnostics, Inc.  
11331 Valley View Street  
Cypress, CA 90630

Dear Dr. Hurrell:

On July 23, 2009 FDA issued a letter authorizing the emergency use of the Focus Diagnostics Influenza A H1N1 (2009) Real-Time RT-PCR (Flu A H1N1 (2009) rRT-PCR) for the diagnosis of 2009 H1N1 influenza virus infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests (CLIA High Complexity Laboratories). On November 20, 2009, Focus submitted a request for an amendment to the Emergency Use Authorization. In response to that request, the letter authorizing emergency use of the Flu A H1N1 (2009) rRT-PCR is being reissued in its entirety with the amendments incorporated.<sup>1</sup>

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>2</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 Flu A H1N1 (2009) rRT-PCR for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Flu A H1N1 (2009) rRT-PCR for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) The 2009 H1N1 influenza 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 Flu A H1N1 (2009) rRT-PCR may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the Flu A H1N1 (2009) rRT-PCR, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
- (3) There is no adequate, approved, and available alternative to the emergency use of the Flu A H1N1 (2009) rRT-PCR for the diagnosis of 2009 H1N1 influenza virus infection.<sup>3</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 use of the authorized Flu A H1N1 (2009) rRT-PCR for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

#### **The Authorized Flu A H1N1 (2009) rRT-PCR:**

The Focus Diagnostics Influenza A H1N1 (2009) Real Time RT-PCR test is a real-time RT-PCR assay that utilizes fluorogenic hydrolysis (Taqman®) probes for use on the ABI 7500 Real-Time PCR instrument for the *in vitro* qualitative detection of 2009 H1N1 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 (such as bronchoalveolar lavage (BAL), bronchial aspirate (BA); bronchial wash (BW); endotracheal aspirate (EA); endotracheal wash (EW); tracheal aspirate (TA), and lung tissue) from patients with signs and symptoms of respiratory infection. The assay is composed of two principal steps: (1) extraction of RNA from patient specimens, (2) one-step reverse transcription and PCR amplification with human influenza A virus and the 2009 H1N1 influenza virus-specific primers and real-time detection with influenza A and 2009 H1N1 influenza virus-specific probes.

The Flu A H1N1 (2009) rRT-PCR includes the following primer and probe sets:

- **FLU A** detects a well-conserved region of the matrix gene from influenza A viruses in both human influenza A virus and 2009 H1N1 influenza virus.
- **SWINE 1 and SWINE 2** specifically detect two separate regions of the 2009 H1N1 influenza virus strain's HA gene. The SWINE 1 and SWINE 2 reactions are not multiplexed and are performed in parallel in separate wells.

The Flu A H1N1 (2009) rRT-PCR also includes control materials:

- **Internal Positive Amplification Control (IPC):** Exogenous IPC Reagent available separately from Applied Biosystems (Catalog No. 4308323). An internal positive control is included to confirm the absence of PCR inhibition.
- **External Positive Control:** Swine influenza virus stock (ATCC VR-897) diluted at 1:800.
- **External Negative Control:** Nuclease free water.

The above described Flu A H1N1 (2009) rRT-PCR test, when labeled consistently with the labeling authorized by FDA, entitled Influenza A H1N1 (2009) Real-Time RT-PCR Package Insert, (see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to and used by CLIA High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described Flu A H1N1 (2009) rRT-PCR test 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 Focus Diagnostics Influenza A H1N1 (2009) Real-Time RT-PCR Test Results**
- **Fact Sheet For Patients: Understanding The Focus Diagnostics Influenza A H1N1 (2009) Real-Time RT-PCR Test Results**

As described in section IV below, Focus Diagnostics and CLIA High Complexity Laboratories are also authorized to make available additional information relating to the emergency use of the authorized Flu A H1N1 (2009) rRT-PCR 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 Flu A H1N1 (2009) rRT-PCR in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 Flu A H1N1 (2009) rRT-PCR may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized Flu A H1N1 (2009) rRT-PCR when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Flu A H1N1 (2009) rRT-PCR under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. 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 Flu A H1N1 (2009) rRT-PCR described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 Flu A H1N1 (2009) rRT-PCR during the duration of this emergency use authorization:

- 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 Flu A H1N1 (2009) rRT-PCR.

- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

##### **Focus Diagnostics**

- A. Focus Diagnostics will distribute the Flu A H1N1 (2009) rRT-PCR with the authorized labeling, as may be revised with written permission of FDA, only to CLIA High Complexity Laboratories.
- B. Focus Diagnostics will provide to the CLIA High Complexity Laboratories the authorized Flu A H1N1 (2009) rRT-PCR Fact Sheet for Healthcare Providers and the authorized Flu A H1N1 (2009) rRT-PCR Fact Sheet for Patients.
- C. Focus Diagnostics will make available on its website the authorized Flu A H1N1 (2009) rRT-PCR Fact Sheet for Healthcare Providers and the authorized Flu A H1N1 (2009) rRT-PCR Fact Sheet for Patients.
- D. Focus Diagnostics will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. All advertising and promotional descriptive printed matter relating to the use of the authorized Flu A H1N1 (2009) rRT-PCR shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. All advertising and promotional descriptive printed matter relating to the use of the Flu A H1N1 (2009) rRT-PCR shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the authorized Flu A H1N1 (2009) rRT-PCR may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- H. Focus Diagnostics will ensure CLIA High Complexity Laboratories using the authorized Flu A H1N1 (2009) rRT-PCR have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. Focus Diagnostics will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, Focus Diagnostics will maintain records of device usage.
- K. Focus Diagnostics will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which Focus Diagnostics becomes aware.

##### **CLIA High Complexity Laboratories**

- L. CLIA High Complexity Laboratories will include with reports of the results of the Flu A H1N1 (2009) rRT-PCR the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients.
- M. CLIA High Complexity Laboratories will perform the assay on an Applied Biosystems 7500 Fast Dx Real-time PCR instrument or the RUO marketed Applied Biosystems 7500 Real-time PCR instrument.
- N. CLIA High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- O. CLIA High Complexity Laboratories will collect information on the performance of the assay, and report to Focus Diagnostics any suspected occurrence of false positive or false negative results of which CLIA High Complexity Laboratories become aware.

##### **Focus Diagnostics and CLIA High Complexity Laboratories**

- P. Focus Diagnostics is authorized to make available additional information relating to the emergency use of the authorized Flu A H1N1 (2009) rRT-PCR that is consistent with, and does not exceed, the terms of this letter of authorization.

Q. Only Focus Diagnostics may request changes to the authorized Fact Sheet for Healthcare Providers or the authorized Flu A H1N1 (2009) rRT-PCR Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

R. Focus Diagnostics 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.

The emergency use of the authorized Flu A H1N1 (2009) rRT-PCR as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

#### V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> The amendments to the July 23, 2009 letter authorize use of additional upper respiratory tract samples, such as nasal swabs (NS), throat swabs (TS), nasal aspirates (NA), nasal washes (NW), and dual nasopharyngeal / throat swabs (NPS/TS), and lower respiratory tract specimens, such as bronchoalveolar lavage (BAL), bronchial aspirate (BA), bronchial wash (BW), endotracheal aspirate (EA), endotracheal wash (EW), tracheal aspirate (TA), and lung tissue. There are also corrections to the waiver section and minor wording changes made to be consistent with more recently issued Emergency Use Authorizations for in vitro diagnostic devices.

<sup>2</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>3</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

(2) The Authorization for the CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel on JBAIDS issued	on August 24, 2009, as amended and reissued in its entirety on December 18, 2009, follows and provides an	explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:
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Robert E. Miller, Ph.D., RAC  
Director  
United States Army Medical Material Development Activity  
1430 Veterans Drive  
Ft. Detrick, Maryland 21702-9232

Dear Dr. Miller:

On August 24, 2009, FDA issued a letter authorizing the emergency use of the CDC swH1N1 (swine) Influenza Virus Real-time RT-PCR Detection Panel on the Joint Biological Agent Identification and Diagnostic System (JBAIDS)<sup>1</sup> Instrument (rRT-PCR Swine Flu Panel on JBAIDS) for the diagnosis of 2009 H1N1 influenza virus infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3) by qualified Department of Defense (DoD) laboratories that are equipped with the JBAIDS instruments. On November 16, 2009, the Office of the Surgeon General, Department of the Army submitted a request for an amendment to the Emergency Use Authorization. In response to that request, the letter authorizing emergency use of the rRT-PCR Swine Flu Panel on JBAIDS is being reissued in its entirety with the amendments, as requested by the Office of the Surgeon General, Department of the Army, incorporated.<sup>2</sup>

On April 26, 2009, 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 public health emergency under 42 U.S.C. § 247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>3</sup> Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).

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 rRT-PCR Swine Flu Panel on JBAIDS (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the rRT-PCR Swine Flu Panel on JBAIDS for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) The 2009 H1N1 influenza 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 rRT-PCR Swine Flu Panel on JBAIDS may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the rRT-PCR Swine Flu Panel on JBAIDS, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such products; and

- (3) There is no adequate, approved, and available alternative to the emergency use of the rRT-PCR Swine Flu Panel on JBAIDS for the diagnosis of 2009 H1N1 influenza virus infection.<sup>4</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 use of the authorized rRT-PCR Swine Flu Panel on JBAIDS for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

### The authorized rRT-PCR Swine Flu Panel on JBAIDS:

rRT-PCR Swine Flu Panel on JBAIDS is a panel of oligonucleotide primers and dual-labeled hydrolysis (Taqman®) probes for use in the real-time RT-PCR assay on the Joint Biological Agent Identification and Diagnostic System (JBAIDS) instrument for the *in vitro* qualitative detection of 2009 H1N1 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 (LRTS), such as bronchoalveolar lavage (BAL), bronchial aspirate (BA), bronchial wash (BW), endotracheal aspirate (EA), endotracheal wash (EW), tracheal aspirate (TA), and lung tissue, from patients with signs and symptoms of respiratory infection and in viral culture.

The rRT-PCR Swine Flu Panel on JBAIDS includes the following primer and probe sets:

- **InfA** detects universal influenza A strains
- **swInfA** specifically detects swine influenza A strains (NP gene)
- **swH1** is specific for swine influenza A, subtype H1 (HA gene)

The rRT-PCR Swine Flu Panel on JBAIDS also includes control materials:

- **RNase P (RP)** detects human RNase P and is used as a positive control with human clinical specimens to indicate that adequate isolation of nucleic acid resulted from the extraction of the clinical specimen.
- **Swine Influenza Panel Real-Time RT-PCR Positive Control (SIPC)** is a positive control designed to react with all the primer and probe sets including RNase P.

The rRT-PCR Swine Flu Panel on JBAIDS requires the following hardware and software:

- **JBAIDS Instrument** is a real-time polymerase chain reaction (PCR) instrument developed as part of a biothreat detection system for the Department of Defense (DoD). It comes with a ruggedized laptop computer loaded with specific, user-friendly system software.
- **JBAIDS Influenza Specific Macro** is a compact disc (CD) provided by the JBAIDS Training Facility that contains the Influenza specific macro with Operating Instructions.

The rRT-PCR Swine Flu Panel on JBAIDS requires the use of the following nucleic acid extraction kit:

- **Qiagen QIAamp Viral RNA Mini kit and protocol**

The above described rRT-PCR Swine Flu Panel on JBAIDS, when labeled consistently with the labeling authorized by FDA, entitled CDC swH1N1 (swine) Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) on JBAIDS (see <http://www.fda.gov/medicaldevices/Safety/emergencysituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to and used by qualified Department of Defense (DoD) laboratories<sup>5</sup> that are equipped with the JBAIDS instruments under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described rRT-PCR Swine Flu Panel on JBAIDS 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 Test Results Obtained with the CDC swH1N1 (swine) Influenza Virus Real-time RT-PCR Detection Panel on the Joint Biological Agent Identification and Diagnostic System (JBAIDS) Instrument
- Fact Sheet For Patients: Understanding Test Results Obtained with the CDC swH1N1 (swine) Influenza Virus Real-time RT-PCR Detection Panel on the Joint Biological Agent Identification and Diagnostic System (JBAIDS) Instrument

As described in section IV below, DoD and JBAIDS are also authorized to make available additional information relating to the emergency use of the authorized rRT-PCR Swine Flu Panel on JBAIDS 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 rRT-PCR Swine Flu Panel on JBAIDS in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 rRT-PCR Swine Flu Panel on JBAIDS may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized rRT-PCR Swine Flu Panel on JBAIDS, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized rRT-PCR Swine Flu Panel on JBAIDS under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. 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 rRT-PCR Swine Flu Panel on JBAIDS described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.



This EUA will cease to be effective when the declaration of emergency 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 rRT-PCR Swine Flu Panel on JBAIDS during the duration of this emergency use authorization:

- 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 rRT-PCR Swine Flu Panel on JBAIDS
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

#### DoD/ Joint Project Management Office (JPMO), Chemical Biological Medical Systems (CBMS)

- DoD/JPMO,CBMS will distribute the rRT-PCR Swine Flu Panel on JBAIDS with the authorized labeling, as may be revised with written permission of FDA, only to qualified DoD laboratories that are equipped with the JBAIDS instruments.
- DoD/JPMO,CBMS will provide to the qualified DoD laboratories the authorized rRT-PCR Swine Flu Panel on JBAIDS Fact Sheets for Healthcare Providers, and the authorized rRT-PCR Swine Flu Panel on JBAIDS Fact Sheets for Patients.
- DoD/JPMO,CBMS will make available on its website the authorized rRT-PCR Swine Flu Panel on JBAIDS Fact Sheets for Healthcare Providers, and the authorized rRT-PCR Swine Flu Panel on JBAIDS Fact Sheets for Patients.
- DoD/JPMO,CBMS will ensure that the state and/or local public health authority(ies) are informed of this EUA, including the terms and conditions herein.
- DoD/JPMO,CBMS will ensure that qualified DoD laboratories using the authorized rRT-PCR Swine Flu Panel on BAIDS have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.
- DoD/JPMO,CBMS will track adverse events and report to FDA as required under 21 CFT part 803..
- Through a process of inventory control, DoD/JPMO,CBMS will maintain records of device usage.
- DoD/JPMO,CBMS will collect information on the performance of the assay, to include the incidence of false positive and negative results.

#### Qualified DoD Laboratories

- Qualified DoD laboratories will include with reports of the results of the rRT-PCR Swine Flu Panel on JBAIDS, the authorized Fact Sheets for Healthcare Providers and the authorized Fact Sheet for Patients.
- Qualified DoD laboratories will perform the assay on a JBAIDS instrument.
- Qualified DoD laboratories will have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.
- Qualified DoD laboratories will collect information on the performance of the assay, and report to DoD/JPMO,CBMS any suspected occurrence of false positive or false negative results of which Qualified DoD laboratories become aware.

#### DoD/ Joint Project Management Office (JPMO), Chemical Biological Medical Systems (CBMS) and Qualified DoD Laboratories

- DoD/JPMO,CBMS is authorized to make available additional information relating to the emergency use of the authorized rRT-PCR Swine Flu Panel on JBAIDS that is consistent with, and does not exceed, the terms of this letter of authorization.
- Only DoD/JPMO,CBMS may request changes to the authorized rRT-PCR Swine Flu Panel on JBAIDS Fact Sheet for Healthcare Providers or the authorized rRT-PCR Swine Flu Panel on JBAIDS Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.
- DoD/JPMO,CBMS and the qualified DoD 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.

The emergency use of the authorized rRT-PCR Swine Flu Panel on JBAIDS as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

## V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> For ease of reference, this letter will use the term the "rRT-PCR Swine Flu Panel on JBAIDS."

<sup>2</sup> The amendments to the August 24, 2009 letter authorize use of additional upper respiratory tract samples, such as nasal swabs (NS), throat swabs (TS), nasal aspirates (NA), nasal washes (NW), and dual nasopharyngeal / throat swabs (NPS/TS), and lower respiratory tract specimens, such as bronchoalveolar lavage (BAL), bronchial aspirate (BA), bronchial wash (BW), endotracheal aspirate (EA), endotracheal wash (EW), tracheal aspirate (TA), and lung tissue. There are also corrections to the waiver section, an additional condition for DoD Laboratories, and minor wording changes made to be consistent with more recently issued Emergency Use Authorizations for in vitro diagnostic devices.

<sup>3</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

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

<sup>5</sup> All users, analysts, and any person reporting diagnostic results from use of this device should be trained to perform and interpret the results from this procedure by JBAIDS instructors or designees prior to use. Use of this device is limited to qualified Department of Defense (DoD) laboratories equipped with the JBAIDS instruments. See "Conditions of Authorization" below.

(3) The Authorization for Diatherix H1N1-09 Influenza Test issued on October 9, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

Dennis L. Grimaud  
Chairman and Chief Executive Officer  
DIATHERIX Laboratories, Inc.  
601 Genome Way, Suite 4208  
Huntsville, AL 35806

Dear Mr. Grimaud:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the DIATHERIX H1N1-09 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3), by DIATHERIX Laboratories, Inc., a CLIA High Complexity Laboratory certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests.

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>1</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 DIATHERIX H1N1-09 Influenza Test (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the DIATHERIX H1N1-09 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The recently isolated 2009 H1N1 influenza 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 DIATHERIX H1N1-09 Influenza Test may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the DIATHERIX H1N1-09 Influenza Test, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the DIATHERIX H1N1-09 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection.<sup>2</sup>

Therefore, I have concluded that the emergency use of the DIATHERIX H1N1-09 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the above criteria for issuance of an authorization.

### 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 DIATHERIX H1N1-09 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

**The Authorized DIATHERIX H1N1-09 Influenza Test:**

The DIATHERIX H1N1-09 Influenza Test is a multiplexed molecular diagnostic assay that performs target enriched multiplex PCR nucleic acid amplification on the ABI 9700 thermocycler followed by probe hybridization and subsequent detection on the Qiagen Luminex LiquiChip 100 platform for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in nasopharyngeal swabs, nasal swabs, throat swabs, nasal aspirates, and nasopharyngeal aspirates specimens from patients with signs and symptoms of respiratory infection.

The DIATHERIX H1N1-09 Influenza Test includes the following primer and probe sets:

- **H1 (H109C):** a total of 4 primers designed for nested PCR to detect the presence of the hemagglutinin gene specifically found in the 2009 H1N1 influenza A virus.
- **N1 (N109B):** a total of 4 primers designed for nested PCR to detect the presence of the neuraminidase gene specifically found in the 2009 H1N1 influenza A virus.
- **Probes:** each amplicon is hybridized to complementary capture probes (H109C De and N109B De, respectively), which are covalently coupled to color coded beads detectable by the Luminex technology.

The DIATHERIX H1N1-09 Influenza Test also includes the following control materials:

- **ABM, extraction positive control:** *Acinetobacter baumannii*, ATCC strain 19606, will be used as a culture stock diluted and subjected to extraction as an additional sample during each batch of patient specimen extractions to demonstrate the effectiveness of the extraction method (rule out false negatives due to extraction failure and false positives due to carryover contamination).
- **PCR Blank, negative control:** A water blank will be run as an additional PCR sample during each batch of patient specimen testing to demonstrate that no carryover contamination has occurred during the PCR process (rule out false positives).
- **PCR positive control:** Nucleic acid from *Haemophilus influenzae*, ATCC strain 10211, will be run as a separate PCR sample with each batch run of patient specimens. The PCR positive control demonstrates the effectiveness of the PCR reaction to amplify targets in the assay (rule out PCR false negatives).
- **PCR positive internal control:** DNA from *Acinetobacter baumannii* ATCC strain 19606 will be added to each PCR to act as an internal amplification control. For each sample, if either the ABM target or any other target is positive, the PCR passes. If both ABM and all other targets fail to produce a positive signal, the PCR has failed and must be repeated.

The DIATHERIX H1N1-09 Influenza Test requires the following hardware with corresponding software:

- **Thermo Fisher Kingfisher 96, software version 2.6.2:** nucleic acid extraction instrument.
- **ABI 9700 Thermocycler, software version 3.09:** PCR amplification instrument.
- **Qiagen Luminex LiquiChip 100, software version 2.3.182:** bead detection instrumentation.

The DIATHERIX H1N1-09 Influenza Test requires the use of the following additional reagent kits:

- **Starplex Collection Kit** (tube, swab, medium, biohazard bag and shipping box) (Catalog number: SP132-FL75).
- **Scigenix MagnetX Extraction Kit** (Catalog number: R2-2400-DTX-I0).
- **Qiagen OneStep RT-PCR Kit** (Catalog number: 210212).
- **BioRad Luminex beads** (Catalog number: 171506xx).

The above described DIATHERIX H1N1-09 Influenza Test, when labeled consistently with the labeling authorized by FDA, entitled Diatherix Laboratories H1N1-09 Influenza Test Package Insert, as may be revised with written permission of FDA, is authorized to be used by DIATHERIX Laboratories, Inc.,<sup>3</sup> under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described DIATHERIX H1N1-09 Influenza Test is authorized to be accompanied by the following information pertaining to the emergency use, which are authorized to be made available to healthcare providers and patients:**

- Fact Sheet for Healthcare Providers: Interpretation of the DIATHERIX H1N1-09 Influenza Virus Test Results
- Fact Sheet for Patients: Understanding the DIATHERIX H1N1-09 Influenza Virus Test Results

As described in section IV below, DIATHERIX Laboratories, Inc., is also authorized to make available additional information relating to the emergency use of the authorized DIATHERIX H1N1-09 Influenza Test 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 DIATHERIX H1N1-09 Influenza Test in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 DIATHERIX H1N1-09 Influenza Test may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized DIATHERIX H1N1-09 Influenza Test, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized DIATHERIX H1N1-09 Influenza Test under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS' determination under section 564(b)(1)(C) described above and the Secretary of HHS' corresponding declaration under section 564(b)(1), the DIATHERIX H1N1-09 Influenza Test described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 DIATHERIX H1N1-09 Influenza Test during the duration of this emergency use authorization:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, and storage of the DIATHERIX H1N1-09 Influenza Test.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

#### DIATHERIX Laboratories, Inc.

- DIATHERIX Laboratories, Inc., will not sell or distribute the DIATHERIX H1N1-09 Influenza Test to other laboratories.
- DIATHERIX Laboratories, Inc., will include with reports of the results of the DIATHERIX H1N1-09 Influenza Test the authorized DIATHERIX H1N1-09 Influenza Test Fact Sheets for Healthcare Providers and the authorized DIATHERIX H1N1-09 Influenza Test Fact Sheets for Patients.
- DIATHERIX Laboratories, Inc., will make available on its Web site the authorized DIATHERIX H1N1-09 Influenza Test Fact Sheets for Healthcare Providers and the authorized DIATHERIX H1N1-09 Influenza Test Fact Sheets for Patients.
- DIATHERIX Laboratories, Inc., will clearly and conspicuously state on reports of the results of the DIATHERIX H1N1-09 Influenza Test that this test is only authorized for the diagnosis of 2009 H1N1 influenza virus and not for seasonal influenza A, B, or any other pathogen.
- DIATHERIX Laboratories, Inc., will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- All advertising and promotional descriptive printed matter relating to the use of the DIATHERIX H1N1-09 Influenza Test shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- All advertising and promotional descriptive printed matter relating to the use of the DIATHERIX H1N1-09 Influenza Test shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.

- H. No advertising or promotional descriptive printed matter relating to the use of the DIATHERIX H1N1-09 Influenza Test assay may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- I. DIATHERIX Laboratories, Inc., will have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.
- J. DIATHERIX Laboratories, Inc., will track adverse events and report to FDA as required under 21 CFR part 803.
- K. Through a process of inventory control, DIATHERIX Laboratories, Inc., will maintain records of device usage.
- L. DIATHERIX Laboratories, Inc., will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or negative results of which DIATHERIX Laboratories, Inc., becomes aware.
- M. DIATHERIX Laboratories, Inc., is authorized to make available additional information relating to the emergency use of the authorized DIATHERIX H1N1-09 Influenza Test that is consistent with, and does not exceed, the terms of this letter of authorization.
- N. Only DIATHERIX Laboratories, Inc., may request changes to the authorized DIATHERIX H1N1-09 Influenza Test Fact Sheet for Healthcare Providers or the authorized DIATHERIX H1N1-09 Influenza Test Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.
- O. DIATHERIX Laboratories, Inc., will perform the assay on the Applied Biosystems 9700 Thermocycler, coupled to the Qiagen Luminex LiquiChip 100 detection platform.
- P. DIATHERIX Laboratories, Inc., 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.

The emergency use of the authorized DIATHERIX H1N1-09 Influenza Test as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

#### V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

<sup>3</sup> This EUA does not authorize the DIATHERIX H1N1-09 Influenza Test to be sold or distributed to or used by other laboratories.

(4) The Authorization for the Focus Diagnostics Simplexa Influenza A H1N1 (2009) issued on October 16, 2009, as amended and reissued in its entirety on December 18, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

John G. R. Hurrell, Ph.D.  
Vice President and General Manager  
Focus Diagnostics, Inc.  
11331 Valley View Street  
Cypress, CA 90630

Dear Dr. Hurrell:

On October 16, 2009 FDA issued a letter authorizing the emergency use of the Focus Diagnostics Simplexa™ Influenza A H1N1 (2009) (Simplexa™ Inf A H1N1-09) for the diagnosis of 2009 H1N1 influenza virus infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests (CLIA High Complexity Laboratories). On November 20, 2009, Focus submitted a request for an amendment to the Emergency Use Authorization. In response to that request, the letter authorizing emergency use of the Focus Diagnostics Simplexa™ Inf A H1N1-09) is being reissued in its entirety with the amendments incorporated.<sup>1</sup>

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>2</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 Simplexa™ Inf A H1N1-09 for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

## I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Simplexa™ Inf A H1N1-09 for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) The 2009 H1N1 influenza 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 Simplexa™ Inf A H1N1-09 may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the Simplexa™ Inf A H1N1-09, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
- (3) There is no adequate, approved, and available alternative to the emergency use of the Simplexa™ Inf A H1N1-09 for the diagnosis of 2009 H1N1 influenza virus infection.<sup>3</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 use of the authorized Simplexa™ Inf A H1N1-09 for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

### The Authorized Simplexa™ Inf A H1N1-09

The Focus Diagnostics Simplexa™ Inf A H1N1-09 is a real-time RT-PCR assay that utilizes a fluorescent probe-primer for use on the 3M Integrated Cycler for the *in vitro* qualitative detection of 2009 H1N1 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 (such as bronchoalveolar lavage (BAL), bronchial aspirate (BA), bronchial wash (BW), endotracheal aspirate (EA), endotracheal wash (EW), tracheal aspirate (TA), and lung tissue) from patients with signs and symptoms of respiratory infection. The assay is composed of two principal steps: (1) extraction of RNA from patient specimens, (2) a bi-functional fluorescent probe-primer is used together with a reverse primer to amplify a specific target (for each analyte and internal control).

The Simplexa™ Inf A H1N1-09 kit includes the following primer sets:

- **FLUA** detects a well-conserved region of the matrix gene from influenza A viruses in both human influenza A virus and 2009 H1N1 influenza virus.
- **H1N1** specifically detects the 2009 H1N1 influenza virus strain's hemagglutinin gene. The FLUA and H1N1 reactions are multiplexed and are performed in the same well.

The Simplexa™ Inf A H1N1-09 kit also includes control materials:

- **Armored RNA Internal Control (AR IC):** An internal positive control is included to confirm the absence of PCR inhibition.
- **External Positive Control:** Inactivated 2009 H1N1 Virus.
- **External Negative Control:** Nuclease free water.

The Simplexa™ Inf A H1N1-09 requires the following hardware with corresponding software:

- Roche MagNA Pure LC: Nucleic acid extraction instrument.
- 3M Integrated Cycler: PCR amplification instrument.

The Simplexa™ Inf A H1N1-09 requires the use of the following additional reagent kit:

- MagNA Pure LC Total Nucleic Acid Isolation Kit (Roche Cat. No 3038505001)

The above described Simplexa™ Inf A H1N1-09, when labeled consistently with the labeling authorized by FDA, entitled Simplexa™ Influenza A H1N1 (2009) Package Insert, (see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to and used by CLIA High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described Simplexa™ Inf A H1N1-09 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 Focus Diagnostics Simplexa™ Influenza A H1N1 (2009) Test Results**
- **Fact Sheet For Patients: Understanding The Focus Diagnostics Simplexa™ Influenza A H1N1 (2009) Test Results**

As described in section IV below, Focus Diagnostics and CLIA High Complexity Laboratories are also authorized to make available additional information relating to the emergency use of the authorized Simplexa™ Inf A H1N1-09 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 Simplexa™ Inf A H1N1-09 in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 Simplexa™ Inf A H1N1-09 may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized Simplexa™ Inf A H1N1-09 when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Simplexa™ Inf A H1N1-09 under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. 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 Simplexa™ Inf A H1N1-09 described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 Simplexa™ Inf A H1N1-09 during the duration of this emergency use authorization:

- 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 Simplexa™ Inf A H1N1-09.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

#### Focus Diagnostics

- A. Focus Diagnostics will distribute the Simplexa™ Inf A H1N1-09 with the authorized labeling, as may be revised with written permission of FDA, only to CLIA High Complexity Laboratories.
- B. Focus Diagnostics will provide to the CLIA High Complexity Laboratories the authorized Simplexa™ Inf A H1N1-09 Fact Sheet for Healthcare Providers and the authorized Simplexa™ Inf A H1N1-09 Fact Sheet for Patients.
- C. Focus Diagnostics will make available on its website the authorized Simplexa™ Inf A H1N1-09 Fact Sheet for Healthcare Providers and the authorized Simplexa™ Inf A H1N1-09 Fact Sheet for Patients.
- D. Focus Diagnostics will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. All advertising and promotional descriptive printed matter relating to the use of the authorized Focus Diagnostics Simplexa™ Inf A H1N1-09 shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. All advertising and promotional descriptive printed matter relating to the use of the Focus Diagnostics Simplexa™ Inf A H1N1-09 shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the authorized Simplexa™ Inf A H1N1-09 may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- H. Focus Diagnostics will ensure CLIA High Complexity Laboratories using the authorized Simplexa™ Inf A H1N1-09 have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. Focus Diagnostics will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, Focus Diagnostics will maintain records of device usage.

K. Focus Diagnostics will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which Focus Diagnostics becomes aware.

#### **CLIA High Complexity Laboratories**

L. CLIA High Complexity Laboratories will include with reports of the results of the Simplexa™ Inf A H1N1-09 the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients.

M. CLIA High Complexity Laboratories will perform the assay on a 3M Integrated Cyclor as part of the Microfluidic Molecular System.

N. CLIA High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.

O. CLIA High Complexity Laboratories will collect information on the performance of the assay, and report to Focus Diagnostics any suspected occurrence of false positive or false negative results of which CLIA High Complexity Laboratories become aware.

#### **Focus Diagnostics and CLIA High Complexity Laboratories**

P. Focus Diagnostics is authorized to make available additional information relating to the emergency use of the authorized Simplexa™ Inf A H1N1-09 that is consistent with, and does not exceed, the terms of this letter of authorization.

Q. Only Focus Diagnostics may request changes to the authorized Fact Sheet for Healthcare Providers or the authorized Simplexa™ Inf A H1N1-09 Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

R. Focus Diagnostics 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.

The emergency use of the authorized Simplexa™ Inf A H1N1-09 as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

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

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> The amendments to the October 16, 2009 letter authorize use of additional upper respiratory tract samples, such as nasal swabs (NS), throat swabs (TS), nasal aspirates (NA), nasal washes (NW), and dual nasopharyngeal / throat swabs (NPS/TS), and lower respiratory tract specimens, such as bronchoalveolar lavage (BAL), bronchial aspirate (BA), bronchial wash (BW), endotracheal aspirate (EA), endotracheal wash (EW), tracheal aspirate (TA), and lung tissue. There are also minor wording changes made to be consistent with more recently issued Emergency Use Authorizations for in vitro diagnostic devices.

<sup>2</sup> Memorandum, Determination Pursuant to §564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>3</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

(5) The Authorization for Prodesse ProFlu-ST Influenza A Subtyping Assay issued on October 27, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

Thomas M. Shannon  
President and Chief Executive Officer  
Prodesse, Inc.  
W229 N1870 Westwood Drive  
Waukesha, WI 53186

Dear Mr. Shannon:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the Prodesse ProFlu-ST Influenza A Subtyping Assay for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3) by CLIA High Complexity Laboratories, which are laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. § 263a, to perform high complexity tests.



On April 26, 2009, 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 public health emergency under 42 U.S.C. § 247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>1</sup> Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of the Department of Health and Human Services then declared an emergency justifying the authorization of the emergency use of certain *in vitro* diagnostics for the detection of Swine Influenza A (2009 H1N1 influenza virus), subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).

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 Prodesse ProFlu-ST Influenza A Subtyping Assay (Prodesse ProFlu-ST Assay)<sup>2</sup> for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Prodesse ProFlu-ST Assay for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices, meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

- (1) The 2009 H1N1 influenza 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 Prodesse ProFlu-ST Assay may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the Prodesse ProFlu-ST Assay, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
- (3) There is no adequate, approved, and available alternative to the emergency use of the Prodesse ProFlu-ST Assay for the diagnosis of 2009 H1N1 influenza virus infection.<sup>3,4</sup>

Therefore, I have concluded that the emergency use of the Prodesse ProFlu-ST Assay for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices meets the above criteria for issuance of an authorization.

#### 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 Prodesse ProFlu-ST Assay for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices

##### The Authorized Prodesse ProFlu-ST Assay:

The Prodesse ProFlu-ST Assay is a multiplex real-time RT-PCR assay that utilizes fluorogenic hydrolysis (Taqman) probes for use on the Cepheid SmartCycler II instrument for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in nasopharyngeal swabs (NPS) from patients who are diagnosed with influenza A by currently available FDA-cleared or authorized devices. The assay is composed of two principal steps: (1) extraction of RNA from patient specimens, (2) one-step multiplex reverse transcription and PCR amplification with human seasonal influenza A virus subtypes and the 2009 H1N1 influenza virus specific primers, and real-time detection with seasonal influenza A virus subtypes and the 2009 H1N1 influenza virus specific probes.

The Prodesse ProFlu-ST Assay kit includes:

- ProFlu-ST Supermix that contains buffer, MgCl<sub>2</sub>, nucleotides (dNTPs), Fast Start Taq polymerase, 4 pairs of oligonucleotide primers and 4 probes (4 sets)
- M-MLV Reverse Transcriptase
- RNase Inhibitor
- Influenza A subtyping RNA Control (pooled RNA control for all three detections)
- Internal Control

The Prodesse ProFlu-ST Assay includes the following primer and probe sets:

- **Seasonal H1** detects a conserved area of the seasonal influenza A/H1 Hemagglutinin (HA) gene.
- **Seasonal H3** detects a conserved area of the seasonal influenza A/H3 Hemagglutinin (HA) gene.
- **2009 H1N1 Influenza (S-OIV)** detects a conserved area of the 2009 H1N1 Influenza Nucleoprotein (NP) gene.
- **Internal RNA Control III** detects an 1158 base-long RNA transcript (MS2 Bacteriophage sequence) that is noncompetitive with the other targets of the ProFlu-ST Assay.

Control materials to be used with the Prodesse ProFlu-ST Assay include:

- **Internal RNA Control III (IC)** is a non-infectious *in vitro* transcribed 1158 base-long RNA (MS2 Bacteriophage sequence). The IC is incorporated into every sample and is carried through all steps of the procedure from nucleic acid isolation and purification through amplification to monitor for inhibitors present in the specimen or reaction tube. The IC also serves as a general process control ensuring that each step of the procedure is performed correctly, assay and instrument parameters are set correctly, and that general reagents are working.

- **Influenza A Subtyping RNA Control (PC)** is a pooled control containing three RNA transcripts, one each for the A/H1, A/H3, and A/2009 H1N1 detections targeted by the ProFlu-ST Assay. The PC does not go through nucleic acid isolation and purification, but is included during set-up of the RT-PCR reaction. The PC is required for each ProFlu-ST assay run. The PC in conjunction with the IC is used to verify reagent and system performance.
- **Negative Control (NC)** is blank viral transport medium used to monitor reagent and/or environmental contamination.
- **Extraction Control (EC)** is a previously characterized positive seasonal influenza A (H1 or H3) sample, positive 2009 H1N1 influenza sample, or a negative sample spiked with a well characterized seasonal influenza (H1 or H3) strain or 2009 H1N1 influenza strain. Good laboratory practice recommends including a positive extraction control in each nucleic acid isolation run. The extraction control should be treated like a sample during assay performance and analysis.

The Prodesse ProFlu-ST Assay requires the following instruments with corresponding software:

- The ProFlu-ST Assay utilizes the **Roche MagNA Pure LC System with software version 3.0.11** or the **bioMérieux NucliSENS easyMAG System with software version 1.0.1 or 2.0** for nucleic acid extraction.
- The ProFlu-ST Assay utilizes the **Cepheid SmartCycler II system with Dx software versions 1.7b, 3.0a, or 3.0b** for amplification and detection.

The above Prodesse ProFlu-ST Assay, when labeled consistently with the labeling agreed to by FDA and titled Prodesse ProFlu-ST Assay Instructions for Use, as may be revised with written permission of FDA, is authorized to be distributed to CLIA High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described Prodesse ProFlu-ST 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 the Prodesse ProFlu-ST Assay Results
- Fact Sheet For Patients: Understanding the Prodesse ProFlu-ST Assay Results

As described in section IV below, Prodesse Inc. CLIA High Complexity Laboratories are also authorized to make available additional information relating to the emergency use of the authorized Prodesse ProFlu-ST 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 Prodesse ProFlu-ST Assay in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, outweigh the known and potential risks of such 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 Prodesse ProFlu-ST Assay may be effective in the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results pursuant to section 564(c)(2)(A) of the Act. FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized Prodesse ProFlu-ST Assay, when used to diagnose 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Prodesse ProFlu-ST Assay under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. 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 Prodesse ProFlu-ST Assay described above is authorized to diagnose 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices.

This EUA will cease to be effective when the declaration of emergency 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 Prodesse ProFlu-ST Assay during the duration of this emergency use authorization:

- 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 Prodesse ProFlu-ST Assay.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

**Prodesse Inc.**

- A. Prodesse, Inc. will distribute the Prodesse ProFlu-ST Assay with the labeling agreed to by FDA and titled Prodesse ProFlu-ST Assay Instructions for Use, as may be revised with written permission of FDA, only to CLIA High Complexity Laboratories.
- B. Prodesse, Inc. will provide to the CLIA High Complexity Laboratories the authorized Prodesse ProFlu-ST Assay Fact Sheet for Healthcare Providers and the authorized Prodesse ProFlu-ST Assay Fact Sheet for Patients.
- C. Prodesse, Inc. will make available on its website the authorized Prodesse ProFlu-ST Assay Fact Sheet for Healthcare Providers and the authorized Prodesse ProFlu-ST Assay Fact Sheet for Patients.
- D. Prodesse, Inc. will ensure that the state and/or local public health authority(ies) are informed of this EUA, including the terms and conditions herein.
- E. As a condition of this EUA, all advertising and promotional descriptive printed matter relating to the use of the Prodesse ProFlu-ST Assay shall be consistent with the Fact Sheets and labeling agreed to by FDA and titled Prodesse ProFlu-ST Assay Instructions for Use, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. As a condition of this EUA, all advertising and promotional descriptive printed matter relating to the use of the Prodesse ProFlu-ST 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 Emergency Use Authorization;
  - This test has been authorized only for the diagnosis of 2009 H1N1 influenza virus infection in patients who have already been diagnosed with influenza A by currently available FDA-cleared or authorized devices;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the Prodesse ProFlu-ST Assay may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus, seasonal influenza A/H1 virus, or seasonal influenza A/H3 virus.
- H. Prodesse, Inc. will ensure CLIA High Complexity Laboratories have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. Prodesse, Inc. will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, Prodesse, Inc. will maintain records of device usage.
- K. Prodesse, Inc. will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which Prodesse, Inc becomes aware.

#### **CLIA High Complexity Laboratories**

- L. CLIA High Complexity Laboratories will test a patient sample using the Prodesse ProFlu - ST Assay only when the patient sample has already been tested positive for Influenza A by a currently available FDA-cleared nucleic acid amplification technologies (NAAT)-based Influenza A device with high performance<sup>5</sup>.
- M. CLIA High Complexity Laboratories will include with reports of the results of the Prodesse ProFlu-ST Assay the authorized fact sheets for health care providers and the authorized fact sheets for patients.
- N. CLIA High Complexity Laboratories will use the Roche MagNA Pure LC System or the bioMérieux NucliSENS easyMAG System for nucleic acid extraction, and perform the assay on the Cepheid SmartCycler II Real-time PCR instrument.
- O. CLIA High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- P. CLIA High Complexity Laboratories will collect information on the performance of the assay, and report to Prodesse, Inc. any suspected occurrence of false positive or false negative results of which CLIA High Complexity Laboratories become aware.

#### **Prodesse, Inc. and CLIA High Complexity Laboratories**

- Q. Prodesse, Inc. is authorized to make available additional information relating to the emergency use of the authorized Prodesse ProFlu-ST Assay that is consistent with, and does not exceed, the terms of this letter of authorization.
- R. Only Prodesse, Inc. may request changes to the authorized Prodesse ProFlu-AT Assay Fact Sheet for Healthcare Providers or the authorized Prodesse ProFlu-AT Assay Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.
- S. Prodesse, Inc. and CLIA High Complexity 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.

The emergency use of the authorized Prodesse ProFlu-ST Assay as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

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

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> FDA is authorizing the emergency use of the Prodesse ProFlu-ST Assay as described in the scope section of this letter (Section II).

<sup>3</sup> Although there are no approved or cleared tests for the diagnosis of 2009 H1N1 influenza virus, to date, several devices have been FDA authorized under EUA to help address diagnostic needs. The information on the authorized devices is available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>.

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

<sup>5</sup> An FDA-cleared NAAT-based Influenza A device with high performance is an FDA cleared NAAT-based IVD device detecting Influenza A that demonstrates sensitivity (compared to viral culture) of at least 95% and specificity of at least 92% with a lower bound of 95% (two-sided) confidence interval exceeding 90% and that does not require culture confirmation for negative results.

(6) The Authorization for the ELITech Molecular Diagnostics 2009-H1N1 Influenza A Virus Real Time RT-PCR test issued on November 13, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

Dr. Walt Mahoney  
VP R&D and Operations  
Managing Director  
Epoch BioSciences  
21720 23<sup>rd</sup> Drive S.E. Suite 150  
Bothell, WA 98021

Dear Dr. Mahoney:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test by Associated Regional and University Pathologists (ARUP) Laboratories for the diagnosis of 2009 H1N1 influenza virus infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3). ARUP Laboratories is a CLIA High Complexity Laboratory, certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests.

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>1</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The 2009 H1N1 influenza 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 ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test for the diagnosis of 2009 H1N1 influenza virus infection.<sup>2</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 use of the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

**The Authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR Test:**

The ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test is a real-time reverse-transcription PCR for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in nasopharyngeal swabs, nasal swabs, throat swabs, and nasal aspirates from patients with signs and symptoms of respiratory infection. Amplification and detection are accomplished using PCR primers and Pleiades hybridization probes manufactured by Epoch BioSciences, a Division of Wescor, Inc. The testing procedure consists of nucleic acid extraction on the Qiagen BioRobot 9604 instrument followed by real-time reverse-transcription PCR on the Applied Biosystems 7900HT Real-Time PCR System.

The ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test includes the following primer and probe sets:

- **2009H1:** detects the presence of the hemagglutinin (HA) gene specifically found in the 2009 H1N1 influenza A virus.
- **M1:** detects a conserved region of the Matrix Protein 1 (M1) gene that is present in seasonal and 2009-H1N1 influenza A viruses.
- **Bacteriophage MS2 Internal Control:** detects RNA sequence in whole bacteriophage MS2 that is noncompetitive with the 2009-H1N1 and M1 targets.

The ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test also includes the following control materials:

- **Bacteriophage MS2 Internal Control (IC)** is added to every patient sample and is carried through all steps of the procedure from nucleic acid isolation and purification through amplification to monitor for inhibitors present in the specimen or reaction tube. The IC also serves as a general process control ensuring that each step of the procedure was performed correctly, assay and instrument parameters were set correctly, and that general reagents were working.
- **Negative Control** consists of IC diluted with water and is taken through both nucleic acid extraction and PCR processes to demonstrate that no carryover contamination has occurred during the test process (rule out false positives caused by contamination). The Negative Control is incorporated into each batch of patient specimen processing.
- **Positive Controls** consists of separate RNA templates containing targets recognized by the 2009H1 and M1 detection systems. Each Positive Control is taken through both nucleic acid extraction and PCR processes to demonstrate that nucleic acid extraction and PCR are effective (rule out false negatives caused by test failure). The Positive Controls are incorporated into each batch of patient specimen processing.

The ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test requires the following hardware with corresponding software:

- Applied Biosystems 7900HT Real-Time PCR System with ABI Software: SDS 7900HT, v2.2.2.
- Qiagen BioRobot 9604 with QIAsoft 3.0 PLUS software.

The ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test requires the use of the following additional reagents/materials:

- Qiagen QuantiTect Probe RT-PCR Master mix (Qiagen Cat. No 204443)
- Consumables for Qiagen BioRobot 9604
- QIAamp Virus Biorobot 9604 Kit (Qiagen Cat. No 965662)
- RNase Inhibitor (Applied Biosystems Cat. No N8080119)
- Heat-labile Uracil N-Glycosylase (Roche Cat No 11775367001)
- MasterAmp 10X PCR Enhancer (Epicentre Cat No ME81210)

The above described ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test, when labeled consistently with the labeling authorized by FDA, entitled ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Package Insert (see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to and used by ARUP Laboratories,<sup>3</sup> under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test is authorized to be accompanied by the following information pertaining to the emergency use, which are authorized to be made available to healthcare providers and patients:**

- Fact Sheet for Healthcare Providers: Interpretation of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR Test Results
- Fact Sheet for Patients: Understanding the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR Test Results

As described in section IV below, Epoch Biosciences, is also authorized to make available additional information relating to the emergency use of the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test 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 ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS' determination under section 564(b)(1)(C) described above and the Secretary of HHS' corresponding declaration under section 564(b)(1), the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test during the duration of this emergency use authorization:

- 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 ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

#### Epoch Biosciences

- Epoch Biosciences will distribute the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test with the authorized labeling, as may be revised with written permission of FDA, only to ARUP Laboratories.
- Epoch Biosciences will provide to ARUP Laboratories the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Healthcare Providers and the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Patients.
- Epoch Biosciences will make available on its website the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Healthcare Providers and the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Patients.
- Epoch Biosciences will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- Epoch Biosciences will ensure ARUP Laboratories has a process in place for reporting test results to health care providers and federal, state, and/or local public health authorities, as appropriate.
- Epoch Biosciences will track adverse events and report to FDA as required under 21 CFR part 803.
- Through a process of inventory control, Epoch Biosciences will maintain records of device usage.
- Epoch Biosciences will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which Epoch Biosciences becomes aware.
- Epoch Biosciences is authorized to make available additional information relating to the emergency use of the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test that is consistent with, and does not exceed, the terms of this letter of authorization.

- J. Only Epoch Biosciences may request changes to the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheet for Healthcare Providers or the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

#### **ARUP Laboratories**

- K. ARUP Laboratories will include with reports of the results of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Healthcare Providers and the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Patients.
- L. ARUP Laboratories will clearly and conspicuously state on reports of the results of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test that this test is only authorized for the diagnosis of 2009 H1N1 influenza virus and not for seasonal influenza A, B, respiratory syncytial virus (RSV) or any other pathogen.
- M. ARUP Laboratories will use the Qiagen BioRobot 9604 for nucleic acid extraction and perform the assay on the Applied Biosystems 7900HT Real-time PCR instrument.
- N. ARUP Laboratories will have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.
- O. ARUP Laboratories will collect information on the performance of the assay, and report to Epoch Biosciences any suspected occurrence of false positive or false negative results of which ARUP Laboratories becomes aware.

#### **Epoch Biosciences and ARUP Laboratories**

- P. Epoch Biosciences and ARUP Laboratories will make available on their Web sites the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Healthcare Providers and the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test Fact Sheets for Patients.
- Q. Epoch Biosciences and ARUP 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.
- R. All advertising and promotional descriptive printed matter relating to the use of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- S. All advertising and promotional descriptive printed matter relating to the use of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test shall clearly and conspicuously state that:
- This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- T. No advertising or promotional descriptive printed matter relating to the use of the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.

The emergency use of the authorized ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

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

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> Memorandum, Determination Pursuant to §564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

<sup>3</sup> This EUA does not authorize the ELITech Molecular Diagnostics 2009-H1N1 Influenza A virus Real-Time RT-PCR test to be sold or distributed to or used by other laboratories.

(7) The Authorization for the Roche RealTime ready Influenza A/H1N1 Detection Set issued on November 13,

2009, follows and provides an explanation of the reasons for its

issuance, as required by section 564(h)(1) of the act:

Dr. Bernd Schmidt  
Head of RAS Global Quality Management & Regulatory Affairs  
Roche Diagnostics GmbH  
Roche Applied Science  
Nonnenwald 2  
82377 Penzberg / Germany

Dear Dr. Schmidt:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the Roche RealTime ready Influenza A/H1N1 Detection Set for the diagnosis of 2009 H1N1 influenza virus infection, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3), by CLIA High Complexity Laboratories, which are laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests.

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>1</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain *in vitro* diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 Roche RealTime ready Influenza A/H1N1 Detection Set (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Roche RealTime ready Influenza A/H1N1 Detection Set for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The 2009 H1N1 influenza 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 Roche RealTime ready Influenza A/H1N1 Detection Set may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the Roche RealTime ready Influenza A/H1N1 Detection Set, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the Roche RealTime ready Influenza A/H1N1 Detection Set for the diagnosis of 2009 H1N1 influenza virus infection.<sup>2</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 use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

#### The Authorized Roche RealTime ready Influenza A/H1N1 Detection Set:

The Roche RealTime ready Influenza A/H1N1 Detection Set is a real-time reverse-transcription PCR for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in nasal swabs, nasopharyngeal swabs, nasal washes, or nasal aspirates from patients with signs and symptoms of respiratory infection. The Roche RealTime ready Influenza A/H1N1 Detection Set is to be used in combination with the Roche RealTime ready RNA Virus Master kit which is a reaction mix for one-step RT-PCR using the LightCycler® system. The assay is composed of two principal steps: (1) extraction of RNA from patient specimens, (2) one-step reverse transcription and PCR amplification using fluorogenic hydrolysis (Taqman) probes for detection.

The Roche RealTime ready Influenza A/H1N1 Detection Set includes the following primer and probe sets:

- **Inf A/M2:** detects a well-conserved region of the Matrix Protein 2 (M2) gene from influenza A viruses in both seasonal human influenza A virus and 2009 H1N1 virus.
- **Inf A/H1:** detects the presence of the hemagglutinin (HA) gene specifically found in the 2009 H1N1 virus. Detection with Inf A/M2 and Inf A/H1 systems are carried out in separate reactions.
- **Internal Control:** detects the human Myostatin gene as a common nucleic acid in patient samples and verifies adequacy of sample and reaction. The primers and probes for Inf A/M2 and Internal Control are combined by the user and the reactions are performed in the same capillary.



The Roche RealTime ready Influenza A/H1N1 Detection Set also includes the following control materials:

- **External Positive Control for Inf A/M2** consists of lyophilized plasmid DNA containing the cloned target sequence of the M2 gene. The Inf A/M2 Positive Control is incorporated into each batch of patient specimen testing for the Inf A/M2 target.
- **External Positive Control for Inf A/H1** consists of lyophilized plasmid DNA containing the cloned target sequence of the hemagglutinin gene of the 2009 H1N1 virus. The Inf A/H1 Positive Control is incorporated into each batch of patient specimen testing for the Inf A/H1 target.
- **Negative Control** consists of nuclease free water and is taken through both nucleic acid extraction and PCR processes to demonstrate that no carryover contamination has occurred during the test process. The Negative Control is incorporated into each batch of patient specimen processing.

The Roche RealTime ready Influenza A/H1N1 Detection Set requires the following hardware with corresponding software:

- MagNA Pure LC 1.0 Instrument or
- MagNA Pure LC 2.0 Instrument
- LightCycler® 2.0 Instrument
- LightCycler® Software Version 4
- LightCycler® Capillaries (20 ml)
- LightCycler® Centrifuge Adapters
- LightCycler® Capping Tool

Optional hardware:

- LC Carousel Centrifuge 2.0 including rotor buckets or
- LC Carousel Centrifuge and LC Carousel Centrifuge 2.0 Rotor Set

The Roche RealTime ready Influenza A/H1N1 Detection Set requires the use of the following additional reagents/materials:

- MagNA Pure LC Total Nucleic Acid Isolation Kit - High Performance
- RealTime ready RNA Virus Master

The above described Roche RealTime ready Influenza A/H1N1 Detection Set, when labeled consistently with the labeling authorized by FDA, entitled RealTime ready Influenza A/H1N1 Detection Set Package Insert, (see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to CLIA High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described Roche RealTime ready Influenza A/H1N1 Detection Set is authorized to be accompanied by the following information pertaining to the emergency use, which are authorized to be made available to healthcare providers and patients:**

- Fact Sheet for Healthcare Providers: Interpreting the Roche RealTime ready Influenza A/H1N1 Detection Set Test Results
- Fact Sheet for Patients: Understanding the Roche RealTime ready Influenza A/H1N1 Detection Set Test Results

As described in section IV below, Roche Diagnostics GmbH, is also authorized to make available additional information relating to the emergency use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set 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 Roche RealTime ready Influenza A/H1N1 Detection Set in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 Roche RealTime ready Influenza A/H1N1 Detection Set may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized Roche RealTime ready Influenza A/H1N1 Detection Set, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS' determination under section 564(b)(1)(C) described above and the Secretary of HHS' corresponding declaration under section 564(b)(1), the Roche RealTime ready Influenza A/H1N1 Detection Set described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 Roche RealTime ready Influenza A/H1N1 Detection Set during the duration of this emergency use authorization:

- 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 Roche RealTime ready Influenza A/H1N1 Detection Set.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

##### Roche Diagnostics GmbH

- A. Roche Diagnostics GmbH will distribute the authorized Roche RealTime ready Influenza A/H1N1 Detection Set with the authorized labeling, as may be revised with written permission of FDA, only to CLIA High Complexity Laboratories.
- B. Roche Diagnostics GmbH will provide to the CLIA High Complexity Laboratories the authorized Roche RealTime ready Influenza A/H1N1 Detection Set Fact Sheets for Healthcare Providers and the authorized Roche RealTime ready Influenza A/H1N1 Detection Set Fact Sheets for Patients.
- C. Roche Diagnostics GmbH will make available on its website the authorized Roche RealTime ready Influenza A/H1N1 Detection Set Fact Sheets for Healthcare Providers and the authorized Roche RealTime ready Influenza A/H1N1 Detection Set Fact Sheets for Patients.
- D. Roche Diagnostics GmbH will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. All advertising and promotional descriptive printed matter relating to the use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. All advertising and promotional descriptive printed matter relating to the use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- H. Roche Diagnostics GmbH will ensure that CLIA High Complexity Laboratories using the authorized Roche RealTime ready Influenza A/H1N1 Detection Set have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. Roche Diagnostics GmbH will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, Roche Diagnostics GmbH will maintain records of device usage.
- K. Roche Diagnostics GmbH will collect information on the performance of the assay and report to FDA any suspected occurrence of false positive or negative results of which Roche Diagnostics GmbH becomes aware.

##### CLIA High Complexity Laboratories

- L. CLIA High Complexity Laboratories will include with reports of the results of the Roche RealTime ready Influenza A/H1N1 Detection Set the authorized Fact Sheets for Healthcare Providers and the authorized Fact Sheets for Patients.
- M. CLIA High Complexity Laboratories will use the MagNA Pure LC Instrument and the MagNA Pure LC Total Nucleic Acid Isolation Kit - High Performance for nucleic acid extraction and perform the assay on the LightCycler® V2.0 instrument.
- N. CLIA High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate

O. CLIA High Complexity Laboratories will collect information on the performance of the assay, and report to Roche Diagnostics GmbH any suspected occurrence of false positive or false negative results of which CLIA High Complexity Laboratories become aware.

#### Roche Diagnostics GmbH and CLIA High Complexity Laboratories

P. Roche Diagnostics GmbH is authorized to make available additional information relating to the emergency use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set that is consistent with, and does not exceed, the terms of this letter of authorization.

Q. Only Roche Diagnostics GmbH may request changes to the authorized Roche RealTime ready Influenza A/H1N1 Detection Set Fact Sheet for Healthcare Providers or the authorized Roche RealTime ready Influenza A/H1N1 Detection Set Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

R. Roche Diagnostics GmbH 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.

The emergency use of the authorized Roche RealTime ready Influenza A/H1N1 Detection Set as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

#### V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

(8) The Authorization for the GeneSTAT 2009 A/H1N1 Influenza Test issued on December 9, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

Mark J. Rosenfeld, M.S., Ph.D.  
Chief Science Advisor, DxNA, LLC  
3879 S. River Road, Bldg. A  
St. George, UT 84790

Dear Dr. Rosenfeld:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the GeneSTAT 2009 A/H1N1 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection 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 CLIA High Complexity Laboratories, which are laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests.

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>1</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 GeneSTAT 2009 A/H1N1 Influenza Test (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the GeneSTAT 2009 A/H1N1 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The 2009 H1N1 influenza 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 GeneSTAT 2009 A/H1N1 Influenza Test may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the GeneSTAT 2009 A/H1N1 Influenza Test, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative to the emergency use of the GeneSTAT 2009 A/H1N1 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection.<sup>2</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 use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

### The Authorized GeneSTAT 2009 A/H1N1 Influenza Test:

The GeneSTAT 2009 A/H1N1 Influenza Test is a reverse-transcription polymerase chain reaction assay for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in nasopharyngeal swabs or nasal swabs from patients with signs and symptoms of respiratory infection. The GeneSTAT 2009 A/H1N1 Influenza Test is to be used in combination with the Roche High Pure RNA Isolation Kit and the GeneSTAT Analytical Platform. The assay is composed of two principal steps: (1) extraction of RNA from patient specimens, (2) one-step reverse transcription and PCR amplification using fluorogenic probes for detection.

The GeneSTAT 2009 A/H1N1 Influenza Test includes the following primer and probe sets:

- **H1:** a primer-probe set designed to detect the presence of the hemagglutinin gene specifically found in the 2009 H1N1 influenza A virus.
- **N1:** a primer-probe set designed to detect the presence of the neuraminidase gene specifically found in the 2009 H1N1 influenza A virus.
- **MA:** a primer-probe set designed to detect the presence of a well conserved region of the matrix gene found in both, seasonal human influenza A virus and 2009 H1N1 influenza A virus.
- **P28:** a primer-probe set designed to detect the presence of the Caprine Arthritis-Encephalitis Virus core polypeptide p28 gene (Exogenous Reaction Control).

The GeneSTAT 2009 A/H1N1 Influenza Test also includes the following control materials:

- **Influenza A Matrix-Positive Control Swab.**
- **H1-Positive Control Swab (2009 H1N1 specific).**

The GeneSTAT 2009 A/H1N1 Influenza Test requires the following hardware with corresponding software:

- GeneSTAT Analytical Platform.

The GeneSTAT 2009 A/H1N1 Influenza Test requires the use of the following additional reagents/materials:

- GeneSTAT H1N1 Test Module.
- GeneSTAT Sample Prep Vial.
- Roche High Pure RNA Isolation Kit.

The above described GeneSTAT 2009 A/H1N1 Influenza Test, when labeled consistently with the labeling authorized by FDA, entitled GeneSTAT™ 2009 A/H1N1 Influenza Test Package Insert, (see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to CLIA High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described GeneSTAT 2009 A/H1N1 Influenza Test 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 GeneSTAT 2009 A/H1N1 Influenza Test Results**
- **Fact Sheet for Patients: Understanding the GeneSTAT 2009 A/H1N1 Influenza Test Results**

As described in section IV below, DxNA, LLC, is also authorized to make available additional information relating to the emergency use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test 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 GeneSTAT 2009 A/H1N1 Influenza Test in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 GeneSTAT 2009 A/H1N1 Influenza Test may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized GeneSTAT 2009 A/H1N1 Influenza Test, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS' determination under section 564(b)(1)(C) described above and the Secretary of HHS' corresponding declaration under section 564(b)(1), the GeneSTAT 2009 A/H1N1 Influenza Test described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 GeneSTAT 2009 A/H1N1 Influenza Test during the duration of this emergency use authorization:

- 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 GeneSTAT 2009 A/H1N1 Influenza Test.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

#### **DxNA, LLC**

- A. DxNA, LLC will distribute the authorized GeneSTAT 2009 A/H1N1 Influenza Test with the authorized labeling, as may be revised with written permission of FDA, only to CLIA High Complexity Laboratories.
- B. DxNA, LLC will provide to the CLIA High Complexity Laboratories the authorized GeneSTAT 2009 A/H1N1 Influenza Test Fact Sheets for Healthcare Providers and the authorized GeneSTAT 2009 A/H1N1 Influenza Test Fact Sheets for Patients.
- C. DxNA, LLC will make available on its website the authorized GeneSTAT 2009 A/H1N1 Influenza Test Fact Sheets for Healthcare Providers and the authorized GeneSTAT 2009 A/H1N1 Influenza Test Fact Sheets for Patients.
- D. DxNA, LLC will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. All advertising and promotional descriptive printed matter relating to the use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. All advertising and promotional descriptive printed matter relating to the use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- H. DxNA, LLC will ensure that CLIA High Complexity Laboratories using the authorized GeneSTAT 2009 A/H1N1 Influenza Test have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. DxNA, LLC will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, DxNA, LLC will maintain records of device usage.
- K. DxNA, LLC will collect information on the performance of the assay and report to FDA any suspected occurrence of false positive or negative results of which DxNA, LLC becomes aware.

#### **CLIA High Complexity Laboratories**

- L. CLIA High Complexity Laboratories will include with reports of the results of the GeneSTAT 2009 A/H1N1 Influenza Test the authorized Fact Sheets for Healthcare Providers and the authorized Fact Sheets for Patients.
- M. CLIA High Complexity Laboratories will use the Roche High Pure RNA Isolation Kit for nucleic acid extraction and perform the assay on the GeneSTAT Analytical Platform, ensuring that at least once per day that specimens are to be tested, a known sample (2009 H1N1 positive or influenza A positive specimen) is tested as a positive control for RNA extraction and subsequent protocol steps.
- N. CLIA High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- O. CLIA High Complexity Laboratories will collect information on the performance of the assay, and report to DxNA, LLC any suspected occurrence of false positive or false negative results of which CLIA High Complexity Laboratories become aware.

#### **DxNA, LLC and CLIA High Complexity Laboratories**

- P. DxNA, LLC is authorized to make available additional information relating to the emergency use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test that is consistent with, and does not exceed, the terms of this letter of authorization.
- Q. Only DxNA, LLC may request changes to the authorized GeneSTAT 2009 A/H1N1 Influenza Test Fact Sheet for Healthcare Providers or the authorized GeneSTAT 2009 A/H1N1 Influenza Test Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.
- R. DxNA, LLC 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.

The emergency use of the authorized GeneSTAT 2009 A/H1N1 Influenza Test as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

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

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

(9) The Authorization for the  
TessArray Resequencing Influenza A  
Microarray Detection Panel issued on

December 16, 2009, follows and  
provides an explanation of the reasons

for its issuance, as required by section  
564(h)(1) of the act:

Clark Tibbetts, PhD  
Executive Vice President  
TessArae, LLC  
46090 Lake Center Plaza  
Suite 304  
Sterling, VA 20165

Dear Dr. Tibbetts:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) for emergency use of the TessArray® Resequencing Influenza A Microarray Detection Panel (TessArray RM-Flu) for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, in patients with signs and symptoms of respiratory infection, by CLIA High Complexity Laboratories, which are laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, 42 U.S.C. §263a, to perform high complexity tests.

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>1</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 TessArray RM-Flu (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the TessArray RM-Flu for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The 2009 H1N1 influenza 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 TessArray RM-Flu may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the TessArray RM-Flu, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the TessArray RM-Flu for the diagnosis of 2009 H1N1 influenza virus infection.<sup>2</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 use of the authorized TessArray RM-Flu for the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, in individuals with signs and symptoms of respiratory infection.

#### The Authorized TessArray RM-Flu:

The TessArray RM-Flu is a resequencing microarray assay for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in throat swabs from patients with signs and symptoms of respiratory infection. The TessArray RM-Flu is to be used in combination with the EPICENTRE Masterpure™ Complete DNA and RNA Purification Kit and the Affymetrix® GeneChip® Microarray Instrumentation System. The assay protocol follows a number of steps, starting from RNA extraction from patient specimens, through reverse transcription and amplification by multiplex PCR, followed by labeling of fragmented DNA and hybridization to a microarray. After washing, the array is stained with fluorescent dye and subsequently scanned. The image analysis readout sequence from the detector tiles in the array is scored and also submitted for BLAST homology determination, to define the most similar homology with any known flu virus sequence.

The gene resequencing detector tiles of the TessArray RM-Flu assay represent:

- *2009 H1N1 influenza virus*
  - **NA1av** an avian type A influenza virus neuraminidase gene sequence
  - **NSav** an avian type A influenza virus non-structural gene sequence
  - **M1hu** a representative matrix gene sequence from seasonal A/H1N1
  - **M3hu** a representative matrix gene sequence from seasonal A/H3N2
  - **M5Av** an avian type A influenza virus matrix gene sequence
- *Seasonal A/H1N1*
  - **HA1hu** a representative hemagglutinin gene sequence from A/H1N1
  - **NA1hu** a representative neuraminidase gene sequence from A/H1N1
  - **M1hu** a representative matrix gene sequence from seasonal A/H1N1
  - **M3hu** a representative matrix gene sequence from seasonal A/H3N2
  - **M5Av** an avian type A influenza virus matrix gene sequence
- *Seasonal A/H3N2*
  - **HA3hu** a representative hemagglutinin gene sequence from A/H1N1
  - **NA2hu** a representative neuraminidase gene sequence from A/H1N1
  - **M1hu** a representative matrix gene sequence from seasonal A/H1N1
  - **M3hu** a representative matrix gene sequence from seasonal A/H3N2
  - **M5Av** an avian type A influenza virus matrix gene sequence

The TessArray RM-Flu assay also includes the following control detector tiles:

**Negative/Background Controls:** 25 non-analyte resequencing detector tiles as background control detector tiles representing a variety of different type A influenza virus HA and NA genes, from subtypes that rarely infect humans. They are used to set a threshold for detection of the assay's targeted influenza viruses and to monitor resequencing data quality of the assay.

**Positive/Protocol Controls:** Each batch of specimens to be tested should include a known sample, such as that of a seasonal influenza virus vaccine, as a positive control for RNA extraction and subsequent protocol steps. Two additional resequencing detector tiles represent over 1,000 nucleotides of sequences of the TIM and NAC1 genes from *Arabidopsis thaliana* (wild mustard weed). Template controls are included in each specimen. Positive scoring of these controls provides assurance of successful execution of the different steps in the sample processing.

The TessArray RM-Flu assay requires the following hardware with corresponding software:

- **Thermal Cyclers** that were tested with the RM-Flu Multiplex PCR:
  - Bio-Rad MJ Mini
  - Bio-Rad MyCycler
  - Bio-Rad Peltier DNA Engine Tetrad
- **Affymetrix® GeneChip® Microarray Instrumentation Systems** tested:
  - GCS 3000 7G (RUO)
  - GCS 3000Dx (IVD)
  - GCS 3000Dx2 (IVD)
- **Workstation and Software:**
  - GCOS/GSEQ
  - AGCC/GSEQ
  - AGCC-Dx or AGCC-Dx2

The TessArray RM-Flu assay requires the use of the following additional reagents/materials:

- EPICENTRE® Biotechnologies Masterpure™ Complete DNA and RNA Purification Kit
- Life Technologies™ Superscript™ III Reverse Transcriptase
- Life Technologies™ RNaseOUT™ Recombinant Ribonuclease Inhibitor
- Promega®, GoTaq® Flexi DNA Polymerase
- USB (Affymetrix®) Uracil-DNA Glycosylase (UDG), Heat-Labile
- Qiagen® QIAquick® PCR Purification Kit
- Affymetrix® GeneChip® Resequencing Assay Kit

The above described TessArray RM-Flu test, when labeled consistently with the labeling authorized by FDA, entitled TessArray RM-Flu Package Insert, (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to and used by CLIA High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described TessArray RM-Flu 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 TessArray® Resequencing Influenza A Microarray Detection Panel (TessArray RM-Flu) Test Results**
- **Fact Sheet for Patients: Understanding the TessArray® Resequencing Influenza A Microarray Detection Panel (TessArray RM-Flu) Test Results**

As described in section IV below, TessArae, LLC, is also authorized to make available additional information relating to the emergency use of the authorized TessArray RM-Flu 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 TessArray RM-Flu in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, 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 TessArray RM-Flu may be effective in the diagnosis of 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized TessArray RM-Flu, when used to diagnose 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized TessArray RM-Flu under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. 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 TessArray RM-Flu described above is authorized to diagnose 2009 H1N1 influenza virus infection aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results, in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 TessArray RM-Flu during the duration of this emergency use authorization:

- 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 TessArray RM-Flu.



- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

##### **TessArae, LLC**

- A. TessArae, LLC will distribute the authorized TessArray RM-Flu with the authorized labeling, as may be revised with written permission of FDA, only to CLIA High Complexity Laboratories.
- B. TessArae, LLC will provide to the CLIA High Complexity Laboratories the authorized TessArray RM-Flu Fact Sheet for Healthcare Providers and the authorized TessArray RM-Flu Fact Sheet for Patients.
- C. TessArae, LLC will make available on its website the authorized TessArray RM-Flu Fact Sheet for Healthcare Providers and the authorized TessArray RM-Flu Fact Sheet for Patients.
- D. TessArae, LLC will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. All advertising and promotional descriptive printed matter relating to the use of the authorized TessArray RM-Flu shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. All advertising and promotional descriptive printed matter relating to the use of the authorized TessArray RM-Flu shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Act, 21 U.S.C. §360bbb-3(b)(1); and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated or revoked sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the authorized TessArray RM-Flu may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- H. TessArae, LLC will ensure that CLIA High Complexity Laboratories using the authorized TessArray RM-Flu have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. TessArae, LLC will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, TessArae, LLC will maintain records of device usage.
- K. TessArae, LLC will collect information on the performance of the assay and report to FDA any suspected occurrence of false positive or false negative results of which TessArae, LLC becomes aware.
- L. TessArae, LLC is authorized to make available additional information relating to the emergency use of the authorized TessArray RM-Flu that is consistent with, and does not exceed, the terms of this letter of authorization.
- M. Only TessArae, LLC may request changes to the authorized TessArray RM-Flu Fact Sheet for Healthcare Providers or the authorized TessArray RM-Flu Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

##### **CLIA High Complexity Laboratories**

- N. CLIA High Complexity Laboratories will include with reports of the results of the TessArray RM-Flu the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients.
- O. CLIA High Complexity Laboratories will use the EPICENTRE Masterpure™ Complete DNA and RNA Purification Kit for nucleic acid extraction and perform the assay on the Affymetrix® GeneChip® Microarray Instrumentation System, ensuring that at least once per day specimens are tested, a known sample (such as that of a seasonal influenza virus vaccine) is tested as a positive control for RNA extraction, and is processed through all subsequent protocol steps.
- P. CLIA High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.

Q. CLIA High Complexity Laboratories will collect information on the performance of the assay, and report to TessArae, LLC any suspected occurrence of false positive or false negative results of which CLIA High Complexity Laboratories become aware.

R. CLIA High Complexity Laboratories will clearly and conspicuously state on reports of the results of the TessArray RM-Flu that this test is only authorized for the diagnosis of 2009 H1N1 influenza virus and not for seasonal influenza A, B, or any other pathogen.

#### **TessArae, LLC and CLIA High Complexity Laboratories**

S. TessArae, LLC, and CLIA High Complexity 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.

The emergency use of the authorized TessArray RM-Flu test as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

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

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>2</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

(10) The Authorization for the CDC Swine Influenza Virus Real-time rRT-PCR Detection Panel issued on April 27, 2009, amended on May 2, 2009, and as amended again and reissued in its entirety on December 18, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

Thomas R. Frieden, MD, MPH  
Director  
Centers for Disease Control and Prevention  
1600 Clifton Rd, MS D-14  
Atlanta, GA 30333

Dear Dr. Frieden:

On April 27, 2009, FDA issued a letter authorizing the emergency use of the Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) assay for the presumptive diagnosis of 2009 H1N1 influenza virus 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 May 1, 2009, CDC submitted a request for an amendment to the Emergency Use Authorization.<sup>1</sup> On August 31, 2009 CDC submitted a request for a second amendment<sup>2</sup> and on November 30, 2009 CDC submitted a request for a third amendment<sup>3</sup> to the Emergency Use Authorization G090072. In response to those requests, the letter authorizing emergency use of the rRT-PCR Swine Flu Panel is being reissued in its entirety with the amendments, as requested by CDC.

On April 26, 2009, 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 public health emergency under 42 U.S.C. § 247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents -- in this case, 2009 H1N1 influenza virus.<sup>4</sup> Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).

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 Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

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

I have concluded that the emergency use of the rRT-PCR Swine Flu Panel for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The 2009 H1N1 influenza 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 rRT-PCR Swine Flu Panel may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the rRT-PCR Swine Flu Panel, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such products; and

3. There is no adequate, approved, and available alternative to the emergency use of the rRT-PCR Swine Flu Panel for the diagnosis of 2009 H1N1 influenza virus infection.<sup>5</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 use of the authorized rRT-PCR Swine Flu Panel for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

### The Authorized rRT-PCR Swine Flu Panel:

The Swine Influenza Virus Real-time RT-PCR Detection Panel is a panel of oligonucleotide primers and dual-labeled hydrolysis (Taqman®) probes for use in the real-time RT-PCR assay on the Roche LightCycler® 2.0, and the Applied Biosystems (ABI) 7500 Fast Dx Real-time PCR, and the RUO marketed 7500 Fast Real-time PCR instruments for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in upper respiratory tract specimens (such as nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), dual NPS/TS swabs, or nasal aspirates (NA)) and the lower respiratory tract specimens (such as bronchoalveolar lavage (BAL), bronchial aspirate (BA); bronchial washes (BW), endotracheal aspirates (EA) and endotracheal wash (EW), tracheal aspirates (TA), and lung tissue) from patients with signs and symptoms of respiratory infection and from viral culture. The universal influenza A (Matrix gene), 2009 H1N1 influenza swInfA (NP gene), and swH1 (HA gene) primer and probe sets are designed for detection of 2009 H1N1 influenza viruses.

The rRT-PCR Swine Flu Panel includes the following primer and probe sets:

- **InfA** detects a well-conserved region of the Matrix Protein (M) gene from influenza A viruses in both seasonal human influenza A virus and 2009 H1N1 virus.
- **swInfA** specifically detects the 2009 H1N1 influenza strains (NP gene).
- **swH1** is specific for the 2009 H1N1 influenza and detects the presence of the hemagglutinin (HA) gene specifically found in the 2009 H1N1 virus.

The rRT-PCR Swine Flu Panel also includes control materials:

- **RNase P (RP)** detects human RNase P and is used as a positive control with human clinical specimens to indicate that adequate isolation of nucleic acid resulted from the extraction of the clinical specimen.
- **Swine Influenza Panel Real-Time RT-PCR Positive Control (SIPC)** is a positive control designed to react with all the primer and probe sets including RNase P.

The above rRT-PCR Swine Flu Panel, when labeled consistently with the labeling authorized by FDA, entitled the Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) (see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to public health and other qualified laboratories<sup>6</sup> under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described rRT-PCR Swine Flu Panel is authorized to be accompanied by the following information pertaining to the emergency use, which are authorized to be made available to health care providers and patients:**

- **Fact Sheet For Healthcare Providers: Interpreting the Swine Influenza Virus Real-time RT-PCR Detection Panel Test Results**
- **Fact Sheet For Patients: Understanding rRT-PCR Swine Influenza Detection Panel Test Results**

As described in section IV below, CDC and the appropriate state and/or local public health authority(ies) are also authorized to make available additional information relating to the emergency use of the authorized rRT-PCR Swine Flu Panel 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 rRT-PCR Swine Flu Panel in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such 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 rRT-PCR Swine Flu Panel may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized rRT-PCR Swine Flu Panel, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized rRT-PCR Swine Flu Panel under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS' determination under section 564(b)(1)(C) described above and the Secretary of HHS' corresponding declaration under section 564(b)(1), the rRT-PCR Swine Flu Panel described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 rRT-PCR Swine Flu Panel during the duration of this emergency use authorization:

- 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 rRT-PCR Swine Flu Panel;
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

##### **CDC**

- A. CDC will distribute the rRT-PCR Swine Flu Panel with the authorized labeling, as may be revised with written permission of FDA only to qualified laboratories.
- B. CDC will provide to the qualified laboratories and state and/or local public health authority(ies) the authorized rRT-PCR Swine Flu Panel Fact Sheets for Health Care Providers, and the authorized rRT-PCR Swine Flu Panel Fact Sheets for Patients.
- C. CDC will make available on its website the authorized rRT-PCR Swine Flu Panel Fact Sheets for Health Care Providers, and the authorized rRT-PCR Swine Flu Panel Fact Sheets for Patients.
- D. CDC will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. CDC will ensure that qualified laboratories using the rRT-PCR Swine Flu Panel have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.
- F. CDC will track adverse events and report to FDA as required under 21 CFR part 803.
- G. Through a process of inventory control, CDC will maintain records of device usage.
- H. CDC will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive and negative results of which CDC becomes aware.

##### **Public Health and Other Qualified Laboratories**

- I. Public health and other qualified laboratories will include with reports of the results of the rRT-PCR Swine Flu Panel, the authorized Fact Sheets for Health Care Providers and the authorized Fact Sheet for Patients.
- J. Qualified laboratories will perform the assay on the Roche LightCycler® 2.0 Real-time PCR system, or an Applied Biosystems 7500 Fast Dx Real-time PCR instrument, or the RUO marketed Applied Biosystems 7500 Real-time PCR instrument that is validated by Applied Biosystems with regard to the updated software but only partially qualified regarding its laboratory performance (proficiency testing with the CDC sample panel not performed).
- K. Qualified laboratories will have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.
- L. Qualified laboratories will collect information on the performance of the assay, and report to CDC any suspected occurrence of false positive or false negative results of which qualified laboratories become aware.

##### **CDC and State and/or Local Public Health Authority(ies)**

- M. CDC and the appropriate state and/or local public health authority(ies) are authorized to make available additional information relating to the emergency use of the authorized rRT-PCR Swine Flu Panel that is consistent with, and does not exceed, the terms of this letter of authorization.
- N. Only CDC may request changes to the authorized Fact Sheet for Health Care Providers or the authorized rRT-PCR Swine Flu Panel Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.
- O. CDC and the appropriate state and/or local public health authority(ies) 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.

The emergency use of the authorized rRT-PCR Swine Flu Panel as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

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

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

<sup>1</sup> The amendment to the April 27, 2009 letter allow use of different sample types (throat swabs (TS), dual NPS/TS swab, or nasal aspirate (NA) specimens) and different reagents.

<sup>2</sup> The amendment to the May 2, 2009 letter allow use of the LightCycler® 2.0 Real-time PCR system, in addition to the ABI 7500 Fast Dx system, with the CDC rRT-PCR Swine Flu Panel.

<sup>3</sup> The amendment to the May 2, 2009 letter authorize use of nasal washes as additional upper respiratory tract specimen and use of lower respiratory tract specimens (such as bronchoalveolar lavage (BAL), bronchial aspirate (BA); bronchial wash (BW); endotracheal aspirate (EA); endotracheal wash (EW); tracheal aspirate (TA), and lung tissue) as acceptable clinical specimens with the CDC rRT-PCR Swine Flu Panel; to remove the word "presumptive" from the Intended Use; to allow the use of the CDC rRT-PCR Swine Flu Panel as a stand alone test; to include Human Specimen Control (HSC) that was previously included in the CDC rRT-PCR Flu Panel (IVD, K080570); and to update packaging by removing product from foam envelopes and segregating into boxes. There are also minor wording changes made to be consistent with more recently issued Emergency Use Authorizations for in vitro diagnostic devices.

<sup>4</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>5</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

<sup>4</sup> All users, analysts, and any person reporting diagnostic results from use of this device should be trained to perform and interpret the results from this procedure by a CDC instructor or designee prior to use. CDC Influenza Division will limit the distribution of this device to those users who have successfully completed training provided by CDC instructors or designees. Use is limited to designated laboratories that are qualified to receive and use the CDC rRT-PCR Flu Panel (IVD) 510(K) 080570. See "Conditions of Authorization" below.

(11) The Authorization for the Cepheid Xpert Flu A Panel issued on December 24, 2009, follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the act:

Russel K. Enns, Ph.D.  
Senior Vice President  
Regulatory, Clinical & Government Affairs and Quality Systems  
Cepheid  
904 Caribbean Drive  
Sunnyvale, CA 94089

Dear Dr. Enns:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the Cepheid Xpert® Flu A Panel for the diagnosis of 2009 H1N1 influenza virus infection 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 laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate complexity tests and by laboratories certified under CLIA to perform high complexity tests.<sup>1</sup>

On April 26, 2009, 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 public health emergency under 42 U.S.C. §247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents - in this case, 2009 H1N1 influenza virus.<sup>2</sup> Pursuant to section 564(b) of the Act (21 U.S.C. §360bbb-3(b)), and on the basis of such determination, the Secretary of HHS then declared an emergency justifying the authorization of the emergency use of certain in vitro diagnostics for the detection of 2009 H1N1 influenza virus, subject to the terms of any authorization issued under 21 U.S.C. §360bbb-3(a).

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 Xpert® Flu A Panel (as described in the scope section of this letter (Section II)) for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection, subject to the terms of this authorization.

#### I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Xpert® Flu A Panel for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The 2009 H1N1 influenza 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 Xpert® Flu A Panel may be effective for the diagnosis of 2009 H1N1 influenza virus infection, and that the known and potential benefits of the Xpert® Flu A Panel, when used in the diagnosis of 2009 H1N1 influenza virus infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the Xpert® Flu A Panel for the diagnosis of 2009 H1N1 influenza virus infection.<sup>3</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 use of the authorized Xpert® Flu A Panel for the diagnosis of 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

**The Authorized Xpert® Flu A Panel:**

The Cepheid Xpert Flu A Panel is a rapid, automated *in vitro* diagnostic test for qualitative detection and differentiation of 2009 H1N1 influenza virus RNA. The assay is performed on the Cepheid GeneXpert Dx System. The system automates and integrates sample purification, nucleic acid amplification, and detection of the target viral RNA sequences using real-time reverse transcriptase polymerase chain reaction (rRT-PCR). The system consists of an instrument, personal computer, and preloaded software for running tests and viewing the results.

The assay detects specific viral gene sequences for the Flu A matrix (Flu A target), and the hemagglutinin gene of 2009 H1N1 influenza virus (2009 H1N1 target). The specimen types for which analytical and method comparison in clinical samples performance data are provided include nasal aspirates/washes (NA/W) and nasopharyngeal (NP) swab specimens in viral transport media (VTM) or universal transport media (UTM) collected from patients suspected of having influenza.

**Components of the Test:**

The Xpert Flu A Panel includes the following assays:

- Flu A Matrix: four forward primer sequences, three reverse primers and one probe sequence for detecting the matrix gene in Flu A
- 2009 H1: two forward primer sequences, one reverse primer and one probe sequence for detecting the hemagglutinin gene in 2009 Flu A H1.

The Xpert Flu A Panel also includes the following controls:

- SPC: Armored RNA in the form of a dry bead that is included in each cartridge to verify adequate processing of the sample virus.
- PCC: The Probe Check Control PCC indicates that the probes and dyes are present and intact

The Xpert Flu A Panel requires the following hardware with corresponding software:

- Cepheid GeneXpert Dx System and software package

The above described Xpert Flu A Panel, when labeled consistently with the labeling authorized by FDA, entitled Xpert Flu A Panel Assay Package Insert, (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), as may be revised with written permission of FDA, is authorized to be distributed to and used by CLIA Moderate and High Complexity Laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

**The above described Xpert® Flu A Panel 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 Cepheid® Xpert® Flu A Panel Test Results**
- **Fact Sheet For Patients: Understanding Cepheid® Xpert® Flu A Panel Test Results**

As described in section IV below, Cepheid is also authorized to make available additional information relating to the emergency use of the authorized Xpert® Flu A Panel 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 Xpert® Flu A Panel in the specified population, when used for diagnosis of 2009 H1N1 influenza virus infection, 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 Xpert® Flu A Panel may be effective in the diagnosis of 2009 H1N1 influenza virus infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized Xpert® Flu A Panel, when used to diagnose 2009 H1N1 influenza virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Xpert® Flu A Panel under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. 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 Xpert® Flu A Panel described above is authorized to diagnose 2009 H1N1 influenza virus infection in individuals with signs and symptoms of respiratory infection.

This EUA will cease to be effective when the declaration of emergency 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 Xpert® Flu A Panel during the duration of this emergency use authorization:

- 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 Xpert® Flu A Panel.

- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 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) 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:

##### **Cepheid**

- A. Cepheid will distribute the authorized Xpert® Flu A Panel with the authorized labeling, as may be revised with written permission of FDA, only to CLIA Moderate and High Complexity Laboratories.
- B. Cepheid will provide to the CLIA Moderate and High Complexity Laboratories the authorized Xpert® Flu A Panel Fact Sheet for Healthcare Providers and the authorized Xpert® Flu A Panel Fact Sheet for Patients.
- C. Cepheid will make available on its website the authorized Xpert® Flu A Panel Fact Sheet for Healthcare Providers and the authorized Xpert® Flu A Panel Fact Sheet for Patients.
- D. Cepheid will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. All advertising and promotional descriptive printed matter relating to the use of the authorized Xpert® Flu A Panel shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- F. All advertising and promotional descriptive printed matter relating to the use of the authorized Xpert® Flu A Panel shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;
  - FDA has not determined that this test may be performed in settings with certificates of waiver under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a;
  - This test has been authorized by FDA under an Emergency Use Authorization;
  - This test has been authorized only for the detection of 2009 H1N1 influenza virus and not for any other viruses or pathogens;
  - This test is only authorized for the duration of the declaration of emergency under section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is revoked sooner; and
  - The declaration of emergency will expire on April 26, 2010, unless it is terminated sooner or renewed.
- G. No advertising or promotional descriptive printed matter relating to the use of the authorized Xpert® Flu A Panel may represent or suggest that this test is safe or effective for the diagnosis of 2009 H1N1 influenza virus.
- H. Cepheid will ensure that CLIA Moderate and High Complexity Laboratories using the authorized Xpert® Flu A Panel have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.
- I. Cepheid will track adverse events and report to FDA as required under 21 CFR part 803.
- J. Through a process of inventory control, Cepheid will maintain records of device usage.
- K. Cepheid will collect information on the performance of the assay and report to FDA any suspected occurrence of false positive or false negative results of which Cepheid becomes aware.
- L. Cepheid is authorized to make available additional information relating to the emergency use of the authorized Xpert® Flu A Panel that is consistent with, and does not exceed, the terms of this letter of authorization.
- M. Only Cepheid may request changes to the authorized Xpert® Flu A Panel Fact Sheet for Healthcare Providers or the authorized Xpert® Flu A Panel Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

##### **CLIA Moderate and High Complexity Laboratories**

- N. CLIA Moderate and High Complexity Laboratories will include with reports of the results of the Xpert® Flu A Panel the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients.
- O. CLIA Moderate and High Complexity Laboratories will perform the assay on the Cepheid GeneXpert Dx System.
- P. CLIA Moderate and High Complexity Laboratories will have a process in place for reporting test results to healthcare providers and federal, state and/or local public health authorities, as appropriate.

Q. CLIA Moderate and High Complexity Laboratories will collect information on the performance of the assay, and report to Cepheid any suspected occurrence of false positive or false negative results of which CLIA Moderate and High Complexity Laboratories become aware.

R. CLIA Moderate and High Complexity Laboratories will clearly and conspicuously state on reports of the results of the Xpert Flu A that this test is only authorized for the diagnosis of 2009 H1N1 influenza virus and not for seasonal influenza A, B, or any other pathogen.

**Cepheid and CLIA Moderate and High Complexity Laboratories**

S. Cepheid and CLIA Moderate and High Complexity 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.

The emergency use of the authorized Xpert® Flu A Panel as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

**V. Duration of Authorization**

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Joshua M. Sharfstein, M.D.  
Principal Deputy Commissioner of Food and Drugs

<sup>1</sup> For ease of reference this letter will refer to these two types of laboratories together as “CLIA Moderate and High Complexity Laboratories.”

<sup>2</sup> Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).

<sup>3</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

Dated: April 9, 2010.

**Leslie Kux,**

*Acting Assistant Commissioner for Policy.*

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