



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-0670]

Authorization of Emergency Use of an In Vitro Diagnostic Device for Detection of Novel Influenza A (H7N9) Virus; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of an Emergency Use Authorization (EUA) (the Authorization) for an in vitro diagnostic device for detection of the novel influenza A (H7N9) virus (detected in China in 2013). FDA is issuing this Authorization under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as requested by Arbor Vita Corporation. The Authorization contains, among other things, conditions on the emergency use of the authorized in vitro diagnostic device. The Authorization follows the April 19, 2013, determination by the Secretary of Health and Human Services (HHS) that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves the novel influenza A (H7N9) virus. On the basis of such determination, the Secretary of HHS also declared on April 19, 2013, that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of the novel influenza A (H7N9) virus subject to the terms of any authorization issued under the FD&C Act. The Authorization, which includes an explanation of the reasons for issuance, is reprinted in this document.

DATES: The Authorization is effective as of April 25, 2014.

ADDRESSES: Submit written requests for single copies of the EUA to the Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, rm. 4338, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request or include a fax number to which the Authorization may be sent. See the SUPPLEMENTARY INFORMATION section for electronic access to the Authorization.

FOR FURTHER INFORMATION CONTACT: Luciana Borio, Assistant Commissioner for Counterterrorism Policy, Office of Counterterrorism and Emerging Threats, and Acting Deputy Chief Scientist, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, rm. 4340, Silver Spring, MD 20993-0002, 301-796-8510 (this is not a toll free number).

SUPPLEMENTARY INFORMATION:

I. Background

Section 564 of the FD&C Act (21 U.S.C. 360bbb-3) as amended by the Project BioShield Act of 2004 (Public Law 108-276) and the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (Public Law 113-5) allows FDA to strengthen the public health protections against biological, chemical, nuclear, and radiological agents. Among other things, section 564 of the FD&C Act allows FDA to authorize the use of an unapproved medical product or an unapproved use of an approved medical product in certain situations. With this EUA authority, FDA can help assure that medical countermeasures may be used in emergencies to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by biological, chemical, nuclear, or radiological agents when there are no adequate, approved, and available alternatives.

Section 564(b)(1) of the FD&C Act provides that, before an EUA may be issued, the Secretary of HHS must declare that circumstances exist 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 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 U.S. military forces of attack with a biological, chemical, radiological, or nuclear agent or agents; (3) a determination by the Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of U.S. citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such agent or agents;¹ or (4) the identification of a material threat by the Secretary of Homeland Security pursuant to section 319F-2 of the Public Health Service Act (PHS Act) (42 U.S.C. 247d-6b) sufficient to affect national security or the health and security of U.S. citizens living abroad.

Once the Secretary of HHS has declared that circumstances exist justifying an authorization under section 564 of the FD&C 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 FD&C Act, FDA is required to publish in the Federal Register a notice of each authorization, and each termination or revocation of an authorization,

¹ As amended by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (Public Law 113-5), the Secretary of HHS may make a determination of a public health emergency, or a significant potential for a public health emergency, under section 564 of the FD&C Act. The Secretary of HHS is no longer required to make a determination of a public health emergency under section 319 of the PHS Act (42 U.S.C. 247d) to support a determination made under section 564 of the FD&C Act.

and an explanation of the reasons for the action. Section 564 of the FD&C Act permits FDA to authorize the introduction into interstate commerce of a drug, device, or biological product intended for use when the Secretary of HHS has declared that circumstances exist justifying the authorization of emergency use. Products appropriate for emergency use may include products and uses that are not approved, cleared, or licensed under sections 505, 510(k), or 515 of the FD&C Act (21 U.S.C. 355, 360(k), and 360e) or section 351 of the PHS Act (42 U.S.C. 262). FDA may issue an EUA only if, after consultation with the HHS Assistant Secretary for Preparedness and Response, the Director of the National Institutes of Health, and the Director of the Centers for Disease Control and Prevention (to the extent feasible and appropriate given the applicable circumstances), FDA² concludes: (1) That an agent referred to in a declaration of emergency or threat 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: (A) The product may be effective in diagnosing, treating, or preventing (i) such disease or condition; or (ii) a serious or life-threatening disease or condition caused by a product authorized under section 564 of the FD&C Act, approved or cleared under the FD&C 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 (B) 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, taking into consideration the material threat posed by the agent or agents identified in a declaration under section 564(b)(1)(D) of the FD&C Act, if applicable; (3) that there is no adequate, approved, and

² The Secretary of HHS has delegated the authority to issue an EUA under section 564 of the FD&C Act to the Commissioner of Food and Drugs.

available alternative to the product for diagnosing, preventing, or treating such disease or condition; and (4) that such other criteria as may be prescribed by regulation are satisfied.

No other criteria for issuance have been prescribed by regulation under section 564(c)(4) of the FD&C Act. Because the statute is self-executing, regulations or guidance are not required for FDA to implement the EUA authority.

II. EUA Request for an In Vitro Diagnostic Device for Detection of the Novel Influenza A (H7N9) Virus

On April 19, 2013, under section 564(b)(1)(C) of the FD&C Act, the Secretary of HHS determined that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves the novel influenza A (H7N9) virus. Also on April 19, 2013, under section 564(b)(1) of the FD&C Act, and on the basis of such determination, the Secretary of HHS declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of the novel influenza A (H7N9) virus, subject to the terms of any authorization issued under section 564 of the FD&C Act. The Secretary of HHS also specified that this declaration is a declaration of an emergency with respect to in vitro diagnostics as defined under the Public Readiness and Emergency Preparedness (PREP) Act Declaration for Pandemic Influenza Diagnostics, Personal Respiratory Protection Devices, and Respiratory Support Devices signed by then Secretary Michael Leavitt on December 17, 2008 (73 FR 78362, December 22, 2008). Notice of the determination and the declaration of the Secretary were published in the Federal Register on April 30, 2013 (78 FR 25273). On April 9, 2014, Arbor Vita Corporation submitted a complete request for, and on April 25, 2014, FDA issued, an EUA for the A/H7N9 Influenza Rapid Test subject to the terms of this authorization.

III. Electronic Access

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

IV. The Authorization

Having concluded that the criteria for issuance of the Authorization under section 564(c) of the FD&C Act are met, FDA has authorized the emergency use of an in vitro diagnostic device for detection of the novel influenza A (H7N9) virus (detected in China in 2013) subject to the terms of the Authorization. The Authorization in its entirety (not including the authorized versions of the fact sheets and other written materials) follows and provides an explanation of the reasons for its issuance, as required by section 564(h)(1) of the FD&C Act.



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

April 25, 2014

Peter Lu, M.D.
President and CEO
Arbor Vita Corporation
6611 Dumbarton Circle
Fremont, CA 94555

Dear Dr. Lu:

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 Arbor Vita Corporation's A/H7N9 Influenza Rapid Test for the presumptive detection of novel influenza A (H7N9) virus (detected in China in 2013) in patients with signs and symptoms of respiratory infection in conjunction with epidemiological risk factors, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On April 19, 2013, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of Health and Human Services (HHS) determined that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such an agent or agents - in this case, novel influenza A (H7N9) virus.¹ Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for the detection of influenza A (H7N9) virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).²

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 A/H7N9 Influenza Rapid Test (as described in the scope section of this letter (Section II)) by Department of Defense (DoD) network laboratories in the U.S. and outside the U.S. or other U.S. government laboratories outside the U.S. in certain patients (as described in the scope section of this letter (Section II)) or by foreign laboratories for the presumptive detection of influenza A (H7N9) virus (detected in China in 2013), subject to the terms of this authorization.

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

² U.S. Department of Health and Human Services. Determination and Declaration Regarding Emergency Use of *in Vitro* Diagnostics for Detection of the Avian Influenza A (H7N9) Virus. 78 Fed. Reg. 25273 (April 30, 2013).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the A/H7N9 Influenza Rapid Test for the presumptive detection of influenza A (H7N9) virus (detected in China in 2013) in the specified population meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. The influenza A (H7N9) virus (detected in China in 2013) can cause influenza, a serious or life-threatening disease or condition to humans infected with this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the A/H7N9 Influenza Rapid Test may be effective in diagnosing influenza A (H7N9) virus (detected in China in 2013) in the specified population, and that the known and potential benefits of the A/H7N9 Influenza Rapid Test, when used for diagnosing influenza A (H7N9) virus (detected in China in 2013) infection in the specified population, 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 A/H7N9 Influenza Rapid Test for diagnosing influenza A (H7N9) virus (detected in China in 2013) in the specified population.³

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 A/H7N9 Influenza Rapid Test for the presumptive detection of influenza A (H7N9) virus (detected in China in 2013) in patients with signs and symptoms of respiratory infection in conjunction with epidemiological risk factors. This test is intended for use by DoD network laboratories in the U.S. and outside the U.S. or other U.S. government laboratories outside the U.S. for testing U.S. citizens living and traveling abroad in China and other affected areas and for U.S. military, Department of State, and other U.S. governmental agency personnel stationed and working in China and other affected areas who may potentially be exposed to influenza A (H7N9) virus (detected in China in 2013) or be exposed to individuals who may carry the influenza A (H7N9) virus (detected in China in 2013), or by foreign laboratories.

The Authorized A/H7N9 Influenza Rapid Test:

The A/H7N9 Influenza Rapid Test is an immunoassay in a lateral flow device configuration for the *in vitro* qualitative detection of A (H7N9) influenza virus (detected in China in 2013) in nasal swab specimens from patients presenting influenza-like illness (ILI) of respiratory infection in conjunction with epidemiological risk factors. The test detects the nonstructural protein 1 (NS1) of influenza A (H7N9) virus (detected in China in 2013). The test may react with NS1 protein antigen of other Asian avian influenza viruses, such as A/H9N2, A/H5N1, and A/H10N8.

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

The A/H7N9 Influenza Rapid Test has three components: Test Cassette, External Positive Control, and Lysis Buffer. The Test Cassette is a lateral flow device in which the input sample is lysed and applied to the Test Cassette to produce a red line that is read visually.

The A/H7N9 Influenza Rapid Test includes the following assay controls:

- **Built-in Controls**
 1. **Internal control line (C)** that functions as a run control to ensure proper functioning of the buffer reagents, capillary flow, and functional integrity of the test strip within the cassette.
 2. **A second control, Line 1** contains monoclonal antibodies that detect NS1 protein from all influenza A strains (Pan-influenza A).
- **External Controls**
 1. **Positive Control:** recombinant influenza A (H7N9) NS1 protein in dried form (non-pathogenic)
 2. **Negative Controls:** Lysis Buffer

The above described A/H7N9 Influenza Rapid Test, when labeled consistently with the labeling authorized by FDA, entitled "A/H7N9 Influenza Rapid Test Instructions for Use" (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), which may be revised with written permission of FDA, is authorized to be distributed to and used by the DoD network laboratories in the U.S. and outside the U.S. or other U.S. government laboratories outside the U.S. under this EUA for testing U.S. citizens living and traveling abroad in China and other affected areas and U.S. military, Department of State, and other U.S. governmental agency personnel stationed and working in China and other affected areas who may potentially be exposed to influenza A (H7N9) virus (detected in China in 2013) or be exposed to individuals who may carry the influenza A (H7N9) virus (detected in China in 2013), or distributed to and used by foreign laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described A/H7N9 Influenza Rapid Test is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to health care professionals and patients:

- **Fact Sheet for Health Care Providers: Interpreting A/H7N9 Influenza Rapid Test Results**
- **Fact Sheet for Patients: Understanding Results from the A/H7N9 Influenza Rapid Test**

As described in section IV below, Arbor Vita Corporation is also authorized to make available additional information relating to the emergency use of the authorized A/H7N9 Influenza Rapid 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 A/H7N9 Influenza Rapid Test in the specified

population, when used for presumptive detection of influenza A (H7N9) virus (detected in China in 2013), 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 A/H7N9 Influenza Rapid Test may be effective in the diagnosis of influenza A (H7N9) virus (detected in China in 2013) 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 A/H7N9 Influenza Rapid Test, when used to diagnose influenza A (H7N9) virus (detected in China in 2013) infection in the specified population, meets the criteria set forth in section 564(e) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized A/H7N9 Influenza Rapid 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's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the A/H7N9 Influenza Rapid Test described above is authorized to diagnose influenza A (H7N9) virus (detected in China in 2013) infection in the specified population in conjunction with epidemiological risk factors.

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 A/H7N9 Influenza Rapid 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 A/H7N9 Influenza Rapid 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), (7), and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

IV. Conditions of Authorization

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

Arbor Vita Corporation

- A. Arbor Vita Corporation will distribute the authorized A/H7N9 Influenza Rapid Test with the authorized labeling, as may be revised with written permission of FDA, only to DoD network laboratories in the U.S. and outside the U.S., other U.S. government laboratories outside the U.S., or foreign laboratories.
- B. Arbor Vita Corporation will provide to the appropriate DoD network laboratories in the U.S. and outside the U.S. and other U.S. government laboratories outside the U.S. the authorized A/H7N9 Influenza Rapid Test Fact Sheet for Health Care Providers and the authorized A/H7N9 Influenza Rapid Test Fact Sheet for Patients.
- C. Arbor Vita Corporation will make available on its website the authorized A/H7N9 Influenza Rapid Test Fact Sheet for Health Care Providers and the authorized A/H7N9 Influenza Rapid Test Fact Sheet for Patients.
- D. Arbor Vita Corporation 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 A/H7N9 Influenza Rapid 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 for use only by DoD network laboratories in the U.S. and outside the U.S., other U.S. government laboratories outside the U.S., or foreign laboratories;
 - This test has been authorized only for the detection of influenza A (H7N9) virus (detected in China in 2013) and not for any other viruses or pathogens; and
 - This test is only authorized for the duration of the HHS declaration of emergency that justifies this authorization, unless the authorization is revoked sooner.
- F. No advertising or promotional descriptive printed matter relating to the use of the authorized A/H7N9 Influenza Rapid Test may represent or suggest that this test is safe or effective for the diagnosis of influenza A (H7N9) virus (detected in China in 2013).
- G. Arbor Vita Corporation will ensure that appropriate DoD network laboratories in the U.S. and outside the U.S. or other U.S. government laboratories outside the U.S. using the authorized A/H7N9 Influenza Rapid Test have a process in place for reporting test results to health care professionals and U.S. federal, state, and/or local public health authorities, as appropriate.
- H. Arbor Vita Corporation will track adverse events and report to FDA as required under 21 CFR Part 803.

- I. Through a process of inventory control, Arbor Vita Corporation will maintain records of device usage.
- J. Arbor Vita Corporation 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 Arbor Vita Corporation becomes aware.
- K. Arbor Vita Corporation is authorized to make available additional information relating to the emergency use of the authorized A/H7N9 Influenza Rapid Test that is consistent with, and does not exceed, the terms of this letter of authorization.
- L. Only Arbor Vita Corporation may request changes to the authorized A/H7N9 Influenza Rapid Test Fact Sheet for Health Care Providers or the authorized A/H7N9 Influenza Rapid Test Fact Sheet for Patients. Such requests will be made by contacting FDA concerning FDA review and approval.

DoD Network Laboratories in the U.S. and outside the U.S. and Other U.S. Government Laboratories outside the U.S.

- M. DoD network laboratories in the U.S. and outside the U.S. and other U.S. government laboratories outside the U.S. will include with reports of the results of the A/H7N9 Influenza Rapid Test the authorized Fact Sheet for Health Care Providers and the authorized Fact Sheet for Patients.
- N. DoD network laboratories in the U.S. and outside the U.S. and other U.S. government laboratories outside the U.S. will have a process in place for reporting test results to health care professionals and federal, state, and/or local public health authorities, as appropriate.
- O. DoD network laboratories in the U.S. and outside the U.S. and other U.S. government laboratories outside the U.S. will collect information on the performance of the assay, and report to Arbor Vita Corporation any suspected occurrence of false positive or false negative results of which they become aware.
- P. DoD network laboratories in the U.S. and outside the U.S. and other U.S. government laboratories outside the U.S. will clearly and conspicuously state on reports of the results of the A/H7N9 Influenza Rapid Test that this test is only authorized for the diagnosis of influenza A (H7N9) virus (detected in China in 2013) and not for seasonal influenza A, B, or any other pathogen.

Arbor Vita Corporation, DoD Network Laboratories in the U.S. and outside the U.S., and Other U.S. Government Laboratories outside the U.S.

- Q. Arbor Vita Corporation, DoD network laboratories in the U.S. and outside the U.S., and other U.S. government laboratories outside the U.S. 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 A/H7N9 Influenza Rapid 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

Enclosures

Dated: June 16, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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