4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-N-0126]

Authorizations of Emergency Use of In Vitro Diagnostic Devices for Detection of Ebola Virus; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of three Emergency Use Authorizations (EUAs) (the Authorizations), one of which was amended after initial issuance, for three in vitro diagnostic devices for detection of the Ebola virus in response to the 2014 Ebola virus outbreak in West Africa. FDA is issuing these Authorizations under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as requested by BioFire Defense, LLC (BioFire Defense) and altona Diagnostics GmbH (altona). The Authorizations contain, among other things, conditions on the emergency use of the authorized in vitro diagnostic devices. The Authorizations follow the September 22, 2006, determination by then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, that the Ebola virus presents a material threat against the U.S. population sufficient to affect national security. On the basis of such determination, the Secretary of Health and Human Services (HHS) declared on August 5, 2014, that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of Ebola virus subject to the terms of any authorization issued under the FD&C Act. The Authorizations, which include an explanation of the reasons for issuance, are reprinted in this document.

DATES: The Authorizations for the BioFire FilmArray NGDS BT-E Assay and BioFire FilmArray Biothreat-E test are effective as of October 25, 2014. The Authorization for the altona RealStar® Ebolavirus RT-PCR Kit 1.0, which was amended and reissued on November 26, 2014, is effective as of November 10, 2014.

ADDRESSES: Submit written requests for single copies of the EUAs 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 Authorizations may be sent. See the SUPPLEMENTARY INFORMATION section for electronic access to the Authorizations.

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 (Pub. L. 108-276) and the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (Pub. L. 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 DHS 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 the Department 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; or (4) the identification of a material threat by the Secretary of DHS under section 319F-2 of the Public Health Service (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, 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 CDC (to the extent feasible and appropriate given the applicable circumstances), FDA[1] 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, 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 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.

[1] 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.

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 Requests for In Vitro Diagnostic Devices for Detection of the Ebola Virus

On September 22, 2006, then-Secretary of DHS, Michael Chertoff, determined that the Ebola virus presents a material threat against the U.S. population sufficient to affect national security.[2] On August 5, 2014, 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 Ebola virus, subject to the terms of any authorization issued under section 564 of the FD&C Act. Notice of the declaration of the Secretary was published in the Federal Register on August 12, 2014 (79 FR 47141). On October 22, 2014, BioFire Defense submitted complete EUA requests for both the BioFire FilmArray NGDS BT-E Assay and for the BioFire FilmArray Biothreat-E test, and on October 25, 2014, FDA issued, an EUA for the BioFire FilmArray NGDS BT-E Assay and an EUA for the BioFire FilmArray Biothreat-E test, subject to the terms of these authorizations. On October 29, 2014, altona submitted a complete EUA request for the RealStar® Ebolavirus RT-PCR Kit 1.0, and on November 10, 2014, FDA issued, an EUA for the RealStar® Ebolavirus RT-PCR Kit 1.0, subject to the terms of this authorization. On November 26, 2014, in response to a request from altona on November 18, 2014, FDA amended and reissued in its entirety the EUA to allow, in addition to altona, distributors that are authorized by altona to distribute the RealStar®

[2] Under to section 564(b)(1) of the FD&C Act, the HHS Secretary's declaration that supports EUA issuance must be based on one of four determinations, including the identification by the Secretary of DHS of a material threat under to section 319F-2 of the PHS Act sufficient to affect national security or the health and security of U.S. citizens living abroad (section 564(b)(1)(D) of the FD&C Act).

Ebolavirus RT-PCR Kit 1.0 with certain conditions applicable to such authorized distributor(s), and to allow the use of the assay under the EUA at certain non-U.S. laboratories, with certain conditions. The EUA, as amended and reissued on November 26, 2014, which includes an explanation for its reissuance, is reprinted in this document. Because the November 26, 2014, Authorization for altona's Ebola assay replaces in its entirety the EUA issued on November 10, 2014, the original Authorization issued on November 10, 2014, is not reprinted in this document.

III. 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.

IV. The Authorizations

Having concluded that the criteria for issuance of the Authorizations under section 564(c) of the FD&C Act are met, FDA has authorized the emergency use of certain in vitro diagnostic devices. The Authorization for the BioFire FilmArray NGDS BT-E Assay issued on October 25, 2014, 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:

[PHOTO GRAPHICS]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

October 25, 2014

Cynthia Phillips, Ph.D.
Director, Regulated Products
BioFire Defense, LLC
79 W 4500 S, Suite 14
Salt Lake City, UT 84107

Dear Dr. Phillips:

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 FilmArray NGDS BT-E Assay for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) on the FilmArray Instrument in individuals with signs and symptoms of Ebola virus infection or who are at risk for exposure or may have been exposed to the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in conjunction with epidemiological risk factors, by laboratories designated by the United States Department of Defense (DoD), pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On September 22, 2006, then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, determined, pursuant to section 319F-2 of the Public Health Service (PHS) Act (42 U.S.C. § 247d-6b), that the Ebola virus presents a material threat against the United States population sufficient to affect national security.[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 declared on August 5, 2014, that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection of Ebola 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 FilmArray NGDS BT-E Assay (as described in the Scope of Authorization section of this letter (Section II)) in individuals with signs and symptoms of Ebola virus infection or who are at risk for exposure or may have been exposed to the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in conjunction with epidemiological risk factors (as described in the Scope of Authorization section of this letter (Section II)) for the presumptive detection of Ebola Zaire

[1] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), the HHS Secretary's declaration that supports EUA issuance must be based on one of four determinations, including the identification by the DHS Secretary of a material threat pursuant to section 319F-2 of the PHS Act sufficient to affect national security or the health and security of United States citizens living abroad (section 564(b)(1)(D) of the Act).
[2] U.S. Department of Health and Human Services. *Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus*. 79 Fed. Reg. 47141 (August 12, 2014).

virus (detected in the West Africa outbreak in 2014) by laboratories designated by DoD, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the FilmArray NGDS BT-E Assay for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 Ebola Zaire virus (detected in the West Africa outbreak in 2014) can cause Ebola virus disease, 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 FilmArray NGDS BT-E Assay, when used with the FilmArray Instrument, may be effective in diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection, and that the known and potential benefits of the FilmArray NGDS BT-E Assay, when used with the FilmArray Instrument for diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 FilmArray NGDS BT-E Assay for diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection.[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 FilmArray NGDS BT-E Assay by laboratories designated by DoD for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in individuals with signs and symptoms of Ebola virus infection or who are at risk for exposure or may have been exposed to the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in conjunction with epidemiological risk factors.

The Authorized FilmArray NGDS BT-E Assay:

The FilmArray NGDS BT-E Assay is a real-time reverse transcriptase Polymerase Chain Reaction (rRT-PCR) for the *in vitro* qualitative detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in whole blood specimens from individuals with signs and symptoms of Ebola virus infection or who are at risk for exposure or may have been exposed to the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in conjunction with epidemiological risk factors. The test procedure consists of nucleic acid extraction followed by rRT-PCR on only the FilmArray Instrument.

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

The FilmArray NGDS BT-E Assay consists of the instrument and a self-contained, disposable reagent pouch that includes two internal control assays. It is an automated test system that utilizes a single-use consumable cartridge containing all amplification and detection reagents ("lab-in-a-pouch" system) that performs nucleic acid purification, reverse transcription, nested multiplex PCR amplification, and high resolution melting to analyze samples for the presence of Ebola Zaire virus. Once a whole blood specimen is collected, it takes about 5 minutes to begin the automated test, which produces results in approximately 1 hour.

During a FilmArray run, two stages of PCR are performed. The first stage (PCR1) is a multiplexed, one-step reverse transcriptase (RT) PCR. The PCR1 mixture is diluted and added to the second stage PCR (PCR2) reaction. PCR2 performs specific reactions in triplicate; each reaction contains primer sets that are specific for one of the organisms or controls in the panel. The PCR2 reactions also contain LCGreen Plus™, a double-stranded DNA binding dye whose fluorescence is used to generate real time PCR curves and crossing points (Cp), and melting curves and melting temperatures (Tm). While both the Cp and Tm parameters could be utilized to determine assay results, only the Tms are used to provide qualitative detection results in an automatically generated report.

The above described FilmArray NGDS BT-E Assay, when labeled consistently with the labeling authorized by FDA entitled "FilmArray™ NGDS BT-E Assay Instructions for Use" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by BioFire Defense in consultation with FDA, is authorized to be distributed to and used by laboratories designated by DoD under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described FilmArray NGDS BT-E Assay 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 FilmArray NGDS BT-E Assay Results for Ebola**

- **Fact Sheet for Patients: Understanding Results from the FilmArray NGDS BT-E Test for Ebola**

As described in Section IV below, BioFire Defense is also authorized to make available additional information relating to the emergency use of the authorized FilmArray NGDS BT-E 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 FilmArray NGDS BT-E Assay in the specified population, when used for presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014), 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 FilmArray NGDS BT-E Assay may be effective in the diagnosis of Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed

the scientific information available to FDA including the information supporting the conclusions described in Section I above, and concludes that the authorized FilmArray NGDS BT-E Assay, when used to diagnose Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 FilmArray NGDS BT-E Assay under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the FilmArray NGDS BT-E Assay described above is authorized to diagnose Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection in individuals with signs and symptoms of Ebola virus infection or who are at risk for exposure or may have been exposed to the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in conjunction with epidemiological risk factors.

This EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Waiver of Certain Requirements

I am waiving the following requirements for the FilmArray NGDS BT-E Assay during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the FilmArray NGDS BT-E Assay.

- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 21 CFR 809.30, except for the intended use statement (21 CFR 809.10(a)(2), (b)(2)), adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

IV. Conditions of Authorization

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

BioFire Defense

A. BioFire Defense will distribute the authorized FilmArray NGDS BT-E Assay with the authorized labeling, as may be revised by BioFire Defense in consultation with FDA, only to laboratories designated by DoD.
B. BioFire Defense will provide to laboratories designated by DoD the authorized FilmArray NGDS BT-E Assay Fact Sheet for Health Care Providers and the authorized FilmArray NGDS BT-E Assay Fact Sheet for Patients.

C. BioFire Defense will make available on its website the authorized FilmArray NGDS BT-E Assay Fact Sheet for Health Care Providers and the authorized FilmArray NGDS BT-E Assay Fact Sheet for Patients.

D. BioFire Defense will inform laboratories designated by DoD and relevant public health authority(ies) of this EUA, including the terms and conditions herein.

E. BioFire Defense will ensure that laboratories designated by DoD using the authorized FilmArray NGDS BT-E Assay have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

F. BioFire Defense will track adverse events and report to FDA under 21 CFR Part 803.

G. Through a process of inventory control, BioFire Defense will maintain records of device usage.

H. BioFire Defense 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 BioFire Defense becomes aware.

I. BioFire Defense is authorized to make available additional information relating to the emergency use of the authorized FilmArray NGDS BT-E Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

J. BioFire Defense may request changes to the authorized FilmArray NGDS BT-E Assay Fact Sheet for Health Care Providers or the authorized FilmArray NGDS BT-E Assay Fact Sheet for Patients. Such requests will be made by BioFire Defense in consultation with FDA.

Laboratories Designated by DoD

K. Laboratories designated by DoD will include with reports of the results of the FilmArray NGDS BT-E Assay the authorized Fact Sheet for Health Care Providers and the authorized Fact Sheet for Patients. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

L. Laboratories designated by DoD will perform the FilmArray NGDS BT-E Assay on only the FilmArray Instrument.

M. Laboratories designated by DoD will have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

N. Laboratories designated by DoD will collect information on the performance of the assay, and report to BioFire Defense any suspected occurrence of false positive or false negative results of which they become aware.

O. All laboratory personnel using the assay should be appropriately trained in the NGDS BT-E Assay on the FilmArray platform and use appropriate laboratory and personal protective equipment when handling this kit.

BioFire Defense and Laboratories Designated by DoD

P. BioFire Defense and laboratories designated by DoD will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Advertising and Promotion

Q. All advertising and promotional descriptive printed matter relating to the use of the authorized FilmArray NGDS BT-E Assay shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

R. All advertising and promotional descriptive printed matter relating to the use of the authorized FilmArray NGDS BT-E 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 for use by laboratories designated by DoD;
- This test has been authorized only for the detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) and not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola Zaire virus under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

No advertising or promotional descriptive printed matter relating to the use of the authorized FilmArray NGDS BT-E Assay may represent or suggest that this test is safe or effective for the diagnosis of Ebola Zaire virus (detected in the West Africa outbreak in 2014).

The emergency use of the authorized FilmArray NGDS BT-E Assay as described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

Page 7 – Dr. Phillips, BioFire Defense, LLC

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola virus is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

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

Enclosures

[END PHOTO]

The Authorization for the BioFire FilmArray Biothreat-E test issued October 25, 2014, 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:

[PHOTO GRAPHICS]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

October 25, 2014

Cynthia Phillips, Ph.D.
Director, Regulated Products
BioFire Defense, LLC
79 W 4500 S, Suite 14
Salt Lake City, UT 84107

Dear Dr. Phillips:

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 FilmArray Biothreat-E test for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) on the FilmArray Instrument in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors, 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,[1] pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On September 22, 2006, then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, determined, pursuant to section 319F-2 of the Public Health Service (PHS) Act (42 U.S.C. § 247d-6b), that the Ebola virus presents a material threat against the United States population sufficient to affect national security.[2] 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 declared on August 5, 2014, that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection of Ebola virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).[3]

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 FilmArray Biothreat-E test (as described in the Scope of Authorization section of this letter (Section II)) in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors (as described in the Scope of Authorization section of this letter (Section II)) for the presumptive detection of Ebola Zaire virus (detected in the West Africa

[1] For ease of reference, this letter will refer to these two types of laboratories together as "CLIA Moderate and High Complexity Laboratories."
[2] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), the HHS Secretary's declaration that supports EUA issuance must be based on one of four determinations, including the identification by the DHS Secretary of a material threat pursuant to section 319F-2 of the PHS Act sufficient to affect national security or the health and security of United States citizens living abroad (section 564(b)(1)(D) of the Act).
[3] U.S. Department of Health and Human Services. *Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus*. 79 Fed. Reg. 47141 (August 12, 2014).

outbreak in 2014) by CLIA Moderate and High Complexity Laboratories, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the FilmArray Biothreat-E test for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 Ebola Zaire virus (detected in the West Africa outbreak in 2014) can cause Ebola virus disease, 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 FilmArray Biothreat-E test, when used with the FilmArray Instrument, may be effective in diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection, and that the known and potential benefits of the FilmArray Biothreat-E test, when used with the FilmArray Instrument for diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 FilmArray Biothreat-E test for diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection.[4]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized FilmArray Biothreat-E test by CLIA Moderate and High Complexity Laboratories for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

The Authorized FilmArray Biothreat-E test:

The FilmArray Biothreat-E test is an automated reverse transcriptase Polymerase Chain Reaction (RT-PCR) system for the *in vitro* qualitative detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in whole blood specimens from individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors. The FilmArray Biothreat-E test can also be used with urine specimens when tested in conjunction with a patient-matched whole blood specimen. The test procedure consists of nucleic acid purification followed by reverse transcription, two-stage nested PCR, and high resolution melting to analyze samples for the presence of Ebola Zaire virus on only the FilmArray Instrument.

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

The FilmArray Biothreat-E test consists of the instrument and a self-contained, disposable reagent pouch that includes an internal control assay. The PCR2 reactions also contain LCGreen Plus™, a double-stranded DNA binding dye whose fluorescence is used to generate real time PCR curves, crossing points (Cp), melting curves, and melting temperatures. The melting temperatures (Tm) are used to provide qualitative detection results in an automatically generated report.

Once a clinical specimen is collected, it takes about 5 minutes to begin the automated test, which produces results in approximately 1 hour.

The FilmArray Biothreat-E test includes the following assay control:

- **RNA Process Control** is a positive control carried through all stages of the test process to demonstrate that all steps carried out in the FilmArray BT pouch were successful. The positive control assay targets an RNA transcript from the yeast *Schizosaccharomyces pombe*.

The above described FilmArray Biothreat-E test, when labeled consistently with the labeling authorized by FDA entitled "FilmArray™ Biothreat-E Instructions for Use" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by BioFire Defense in consultation with 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 FilmArray Biothreat-E 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 FilmArray Biothreat-E Test Results for Ebola**

- **Fact Sheet for Patients: Understanding Results from the FilmArray Biothreat-E Test for Ebola**

As described in Section IV below, BioFire Defense is also authorized to make available additional information relating to the emergency use of the authorized FilmArray Biothreat-E 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 FilmArray Biothreat-E test in the specified population, when used for presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014), 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 FilmArray Biothreat-E test may be effective in the diagnosis of Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available to FDA including the information supporting the

conclusions described in Section I above, and concludes that the authorized FilmArray Biothreat-E test, when used to diagnose Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 FilmArray Biothreat-E test under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the FilmArray Biothreat-E test described above is authorized to diagnose Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

This EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Waiver of Certain Requirements

I am waiving the following requirements for the FilmArray Biothreat-E test during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the FilmArray Biothreat-E test.

- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 21 CFR 809.30, except for the intended use statement (21 CFR 809.10(a)(2), (b)(2)), adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

IV. Conditions of Authorization

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

BioFire Defense

A. BioFire Defense will distribute the authorized FilmArray Biothreat-E test with the authorized labeling, as may be revised by BioFire Defense in consultation with FDA, only to CLIA Moderate and High Complexity laboratories.

B. BioFire Defense will provide to CLIA Moderate and High Complexity Laboratories the authorized FilmArray Biothreat-E test Fact Sheet for Health Care Providers and the authorized FilmArray Biothreat-E test Fact Sheet for Patients.

C. BioFire Defense will make available on its website the FilmArray Biothreat-E test Fact Sheet for Health Care Providers and the authorized FilmArray Biothreat-E test Fact Sheet for Patients.

D. BioFire Defense will inform CLIA Moderate and High Complexity Laboratories and relevant public health authority(ies) of this EUA, including the terms and conditions herein.

E. BioFire Defense will ensure that CLIA Moderate and High Complexity Laboratories using the authorized FilmArray Biothreat-E test have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

F. BioFire Defense will track adverse events and report to FDA under 21 CFR Part 803.

G. Through a process of inventory control, BioFire Defense will maintain records of device usage.

H. BioFire Defense 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 BioFire Defense becomes aware.

I. BioFire Defense is authorized to make available additional information relating to the emergency use of the authorized FilmArray Biothreat-E test that is consistent with, and does not exceed, the terms of this letter of authorization.

J. BioFire Defense may request changes to the authorized FilmArray Biothreat-E test Fact Sheet for Health Care Providers or the authorized FilmArray Biothreat-E test Fact Sheet for Patients. Such requests will be made by BioFire Defense in consultation with FDA.

CLIA Moderate and High Complexity Laboratories

K. CLIA Moderate and High Complexity Laboratories will include with reports of the results of the FilmArray Biothreat-E test the authorized Fact Sheet for Health Care Providers and the authorized Fact Sheet for Patients. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

L. CLIA Moderate and High Complexity Laboratories will perform the FilmArray Biothreat-E test on only the FilmArray Instrument.

M. CLIA Moderate and High Complexity Laboratories will have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

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

O. All laboratory personnel using the assay should be appropriately trained in FilmArray Biothreat-E test on the FilmArray platform and use appropriate laboratory and personal protective equipment when handling this kit.

BioFire Defense and CLIA Moderate and High Complexity Laboratories

P. BioFire Defense 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.

Conditions Related to Advertising and Promotion

Q. All advertising and promotional descriptive printed matter relating to the use of the authorized FilmArray Biothreat-E test shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

R. All advertising and promotional descriptive printed matter relating to the use of the authorized FilmArray Biothreat-E 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 for use by CLIA Moderate and High Complexity Laboratories;
- This test has been authorized only for the detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) and not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola Zaire virus under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

No advertising or promotional descriptive printed matter relating to the use of the authorized FilmArray Biothreat-E test may represent or suggest that this test is safe or effective for the diagnosis of Ebola Zaire virus (detected in the West Africa outbreak in 2014).

The emergency use of the authorized FilmArray Biothreat-E test described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola virus is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

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

Enclosures

[END PHOTO]

The Authorization for the RealStar® Ebolavirus RT-PCR Kit 1.0, originally issued on November 10, 2014, as amended and reissued in its entirety on November 26, 2014, (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, and its amendment:

[PHOTO GRAPHIC]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

November 26, 2014

Dr. Sven Cramer
Director, Regulatory Affairs
altona Diagnostics GmbH
Mörkenstraße 12
22767 Hamburg
Germany

Dear Dr. Cramer:

On November 10, 2014, based on a request by altona Diagnostics GmbH, the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the RealStar® Ebolavirus RT-PCR Kit 1.0 for the presumptive detection of RNA from Ebolaviruses[1] on specified instruments in EDTA plasma from individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors, by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests,[2] pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3). On November 18, 2014, FDA received a request from altona Diagnostics GmbH for an amendment to the Emergency Use Authorization (EUA). In response to that request, and having concluded that revising the November 10, 2014, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), the November 10, 2014, letter authorizing the emergency use of the RealStar® Ebolavirus RT-PCR Kit 1.0 is being reissued in its entirety with the amendments incorporated.[3]

On September 22, 2006, then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, determined, pursuant to section 319F-2 of the Public Health Service (PHS) Act (42 U.S.C. § 247d-6b), that the Ebola virus presents a material threat against the United States population sufficient to affect national security.[4] Pursuant to section 564(b)(1) of the Act

[1] This authorization is being issued in response to the epidemic in West Africa involving Zaire ebolavirus. This assay is intended for the qualitative detection of RNA from Ebolaviruses (such as Zaire ebolavirus [including the Zaire ebolavirus strain detected in the West Africa outbreak 2014], Sudan ebolavirus, Tai Forest ebolavirus, Bundibugyo ebolavirus, and Reston ebolavirus); however, it does not distinguish between the different Ebola virus species or strains.

[2] For ease of reference, this letter will refer to this type of laboratory as "CLIA High Complexity Laboratories."

[3] The amendments to the November 10, 2014, letter allow, in addition to altona Diagnostics GmbH, distributors that are authorized by altona Diagnostics GmbH to distribute the RealStar® Ebolavirus RT-PCR Kit 1.0 with certain conditions applicable to such authorized distributor(s). Because this assay may be distributed outside the U.S., the amendments also allow the use of this assay under this EUA, with certain conditions, at non-U.S. laboratories that are similarly qualified as CLIA High Complexity Laboratories. The Instructions for Use and Fact Sheet for Health Care Providers have also been updated to incorporate these amendments.

[4] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), the HHS Secretary's declaration that supports EUA issuance must be based on one of four determinations, including the identification by the DHS

(21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS declared on August 5, 2014, that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection of Ebola virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).[5]

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 RealStar® Ebolavirus RT-PCR Kit 1.0 (as described in the Scope of Authorization section of this letter (Section II)) in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors (as described in the Scope of Authorization section of this letter (Section II)) for the presumptive detection of RNA from Ebolaviruses by CLIA High Complexity Laboratories, or similarly qualified non-U.S. laboratories, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the RealStar® Ebolavirus RT-PCR Kit 1.0 for the presumptive detection of RNA from Ebolaviruses 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. Ebolaviruses can cause Ebola virus disease, 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 RealStar® Ebolavirus RT-PCR Kit 1.0, when used with the specified instruments, may be effective in diagnosing Ebolavirus infection, and that the known and potential benefits of the RealStar® Ebolavirus RT-PCR Kit 1.0, when used with the specified instruments for diagnosing Ebolavirus 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 RealStar® Ebolavirus RT-PCR Kit 1.0 for diagnosing Ebolavirus infection.[6]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 by CLIA High Complexity Laboratories, or similarly qualified non-U.S. laboratories, for the presumptive detection of RNA from Ebolaviruses in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

Secretary of a material threat pursuant to section 319F-2 of the PHS Act sufficient to affect national security or the health and security of United States citizens living abroad (section 564(b)(1)(D) of the Act).

[5] U.S. Department of Health and Human Services. *Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus*. 79 Fed. Reg. 47141 (August 12, 2014).

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

The Authorized RealStar® Ebolavirus RT-PCR Kit 1.0:

The RealStar® Ebolavirus RT-PCR Kit 1.0 is a reverse transcriptase Polymerase Chain Reaction (RT-PCR) system for the *in vitro* qualitative detection of RNA from Ebolaviruses in human EDTA plasma specimens from individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors. RNA is extracted from whole blood collected with EDTA as the anticoagulant using only the QIAamp Viral RNA Mini Kit. The test procedure consists of three processes in a single tube assay: reverse transcription of target RNA and Internal Control RNA to cDNA, PCR amplification of target and Internal Control cDNA, and simultaneous detection of PCR amplicons by fluorescent dye labelled probes to analyze samples for the presence of RNA from Ebola viruses on only the ABI Prism® 7500 SDS instrument, the ABI Prism® 7500 Fast SDS instrument, the LightCycler® 480 Instrument II, and the CFX96™ system/Dx real-time system.

The assay is designed to detect all Ebolavirus species. The reagent system includes a heterologous amplification system (Internal Control) to identify possible RT-PCR inhibition and to confirm the integrity of the reagents of the kit.

The RealStar® Ebolavirus RT-PCR Kit 1.0 includes the following assay control:

> The **Internal Control** contains a defined copy number of an "artificial" RNA molecule with no homologies to any other known sequences. It has to be added to the nucleic acid extraction procedure and is reverse transcribed, amplified and detected in parallel to the Ebolavirus specific RNA. The function of the Internal Control is to ensure the integrity of Ebolavirus specific real-time RT-PCR results by indicating potential RT-PCR inhibition.
>
> The **PCR grade water** is to be used as negative control for the RT-PCR reaction. Its function is to indicate contamination of RT-PCR reagents.
>
> The "**Positive Control Target EBOLA**" consists of an *in vitro* transcript which contains the target sequence used by the RealStar® Ebolavirus RT-PCR Kit 1.0 for the detection of Ebolavirus specific RNA. The "Positive Control Target EBOLA" is used as positive control for the RT-PCR and verifies the functionality of the Ebolavirus RNA specific RT-PCR detection system, which is included in the RealStar® Ebolavirus RT-PCR Kit 1.0.

The above described RealStar® Ebolavirus RT-PCR Kit 1.0, when labeled consistently with the labeling authorized by FDA entitled "RealStar® Ebolavirus RT-PCR Kit 1.0 Instructions for Use" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#ebola), which may be revised only by altona Diagnostics GmbH in consultation with FDA, is authorized to be distributed to and used by CLIA High Complexity Laboratories, or similarly qualified non-U.S. laboratories, under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described RealStar® Ebolavirus RT-PCR Kit 1.0 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 RealStar® Ebolavirus RT-PCR Kit 1.0 Results**

- **Fact Sheet for Patients: Understanding Results from the RealStar® Ebolavirus RT-PCR Kit 1.0**

As described in Section IV below, altona Diagnostics GmbH and its authorized distributor(s) are also authorized to make available additional information relating to the emergency use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 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 RealStar® Ebolavirus RT-PCR Kit 1.0 test in the specified population, when used for presumptive detection of RNA from Ebolaviruses 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 RealStar® Ebolavirus RT-PCR Kit 1.0 may be effective in the diagnosis of infection with Ebolaviruses pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available to FDA including the information supporting the conclusions described in Section I above, and concludes that the authorized RealStar® Ebolavirus RT-PCR Kit 1.0, when used to diagnose infection with Ebolaviruses 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 RealStar® Ebolavirus RT-PCR Kit 1.0 under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the RealStar® Ebolavirus RT-PCR Kit 1.0 described above is authorized to diagnose infection with Ebolaviruses in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

This EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Waiver of Certain Requirements

I am waiving the following requirements for the RealStar® Ebolavirus RT-PCR Kit 1.0 during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the RealStar® Ebolavirus RT-PCR Kit 1.0.

- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 21 CFR 809.30, except for the intended use statement (21 CFR 809.10(a)(2), (b)(2)), adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5), (7), and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

IV. Conditions of Authorization

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

altona Diagnostics GmbH and Its Authorized Distributor(s)

A. altona Diagnostics GmbH and its authorized distributor(s) will distribute the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 with the authorized labeling, as may be revised only by altona Diagnostics GmbH in consultation with FDA, only to CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories.

B. altona Diagnostics GmbH and its authorized distributor(s) will provide to CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 Fact Sheet for Health Care Providers and the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 Fact Sheet for Patients.

C. altona Diagnostics GmbH and its authorized distributor(s) will make available on their websites the RealStar® Ebolavirus RT-PCR Kit 1.0 test Fact Sheet for Health Care Providers and the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 Fact Sheet for Patients.

D. altona Diagnostics GmbH and its authorized distributor(s) will inform CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories and relevant public health authority(ies) of this EUA, including the terms and conditions herein.

E. altona Diagnostics GmbH and its authorized distributor(s) will ensure that CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories using the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

F. Through a process of inventory control, altona Diagnostics GmbH and its authorized distributor(s) will maintain records of device usage.

G. altona Diagnostics GmbH and its authorized distributor(s) 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 altona Diagnostics GmbH and its authorized distributor(s) become aware.

H. altona Diagnostics GmbH and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 that is consistent with, and does not exceed, the terms of this letter of authorization.

altona Diagnostics GmbH

I. altona Diagnostics GmbH will provide its authorized distributor(s) with a copy of this EUA, and communicate to its authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., fact sheets, instructions for use).

J. altona Diagnostics GmbH only may request changes to the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 Fact Sheet for Health Care Providers or the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 Fact Sheet for Patients. Such requests will be made only by altona Diagnostics GmbH in consultation with FDA.

K. altona Diagnostics GmbH will track adverse events and report to FDA under 21 CFR Part 803.

CLIA High Complexity Laboratories and Similarly Qualified Non-U.S. Laboratories

L. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will include with reports of the results of the RealStar® Ebolavirus RT-PCR Kit 1.0 the authorized Fact Sheet for Health Care Providers and the authorized Fact Sheet for Patients. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

M. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will perform the RealStar® Ebolavirus RT-PCR Kit 1.0 on only the ABI Prism® 7500 SDS instrument, the ABI Prism® 7500 Fast SDS instrument, the LightCycler® 480 Instrument II, and the CFX96™ system/Dx real-time system.

N. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

O. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will collect information on the performance of the assay, and report to altona Diagnostics GmbH and its authorized distributor(s) any suspected occurrence of false positive or false negative results of which they become aware.

P. All laboratory personnel using the assay should be appropriately trained in RealStar® Ebolavirus RT-PCR Kit 1.0 on the specified instruments and use appropriate laboratory and personal protective equipment when handling this kit.

altona Diagnostics GmbH, Its Authorized Distributor(s), CLIA High Complexity Laboratories, and Similarly Qualified Non-U.S. Laboratories

Q. altona Diagnostics GmbH, its authorized distributor(s), CLIA High Complexity Laboratories, and similarly qualified non-U.S. laboratories will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

Conditions Related to Advertising and Promotion

R. All advertising and promotional descriptive printed matter relating to the use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

S. All advertising and promotional descriptive printed matter relating to the use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 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 for use by CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories;
- This test has been authorized only for the detection of RNA from Ebolaviruses (such as Zaire ebolavirus, [including the Zaire ebolavirus strain detected in the West Africa outbreak 2014], Sudan ebolavirus, Tai Forest ebolavirus, Bundibugyo ebolavirus, and Reston ebolavirus) and not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola Zaire virus under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

No advertising or promotional descriptive printed matter relating to the use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 may represent or suggest that this test is safe or effective for the diagnosis of infection with Ebolavirus.

The emergency use of the authorized RealStar® Ebolavirus RT-PCR Kit 1.0 described in this letter of authorization must comply with the conditions and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola virus is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

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

Enclosures

[END PHOTO]

Dated: February 2, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015-02467 Filed 02/06/2015 at 8:45 am; Publication Date: 02/09/2015]