March 2, 2015

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

Dear Dr. Phillips:

On October 25, 2014, based on a request by BioFire Defense, LLC, the Food and Drug Administration (FDA) issued a letter authorizing 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) 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).[1] On February 17, 2015, FDA received a request from BioFire Defense, LLC, for an amendment to the Emergency Use Authorization (EUA). In response to that request, and having concluded that revising the October 25, 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 October 25, 2014, letter authorizing the emergency use of the FilmArray NGDS BT-E Assay is being reissued in its entirety with the amendments incorporated.[2]

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.[3] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of the Department 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

[1] U.S. Food and Drug Administration. Authorizations of Emergency Use of In Vitro Diagnostic Devices for Detection of Ebola Virus; Availability. 80 Fed. Reg. 6972 (February 9, 2015).
[2] The amendments to the October 25, 2014, letter authorize use of plasma and serum specimens with the FilmArray NGDS BT-E Assay in addition to whole blood. The Instructions for Use and Fact Sheet for Health Care Providers have also been updated to incorporate this amendment. The amendments also allow the future use of "other specimen types" when requested by BioFire Defense, LLC and concurred with by FDA.
[3] 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).

detection of Ebola virus, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).[4]

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of the 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 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.[5]

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

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

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, plasma, serum and other authorized 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.

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, plasma, serum or other authorized 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. 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 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.

K. BioFire Defense, LLC, may request the addition of other specimen types for use with the authorized FilmArray NGDS BT-E Assay. Such requests will be made by BioFire Defense, LLC, in consultation with, and require concurrence of, FDA.

Laboratories Designated by DoD

L. 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.

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

N. 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.

O. 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.

P. 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

Q. 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

R. 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.

S. 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 EUA 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

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,

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

Enclosures