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.

[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