



December 23, 2014

Jintao Chen, Ph.D.
Director, Regulatory Affairs
Roche Molecular Systems, Inc.
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Pleasanton, CA 94588

Dear Dr. Chen:

This letter is in response to your request¹ that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the LightMix® Ebola Zaire rRT-PCR Test for the presumptive detection of RNA from Ebola Zaire virus (detected in the West Africa outbreak of 2014) on specified instruments in EDTA whole blood or whole blood inactivated with TriPure 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 or similarly qualified non-U.S. laboratories, 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.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 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).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 LightMix® Ebola Zaire rRT-PCR Test (as described in the Scope of Authorization section of this letter (Section II)) in

¹ Roche Diagnostics is the exclusive distributor of the LightMix® Ebola Zaire rRT-PCR Test, manufactured by TIB MOLBIOL. The Conditions of Authorization (Section IV), unless otherwise specified, apply to Roche Diagnostics or Roche Molecular Systems, Inc. as the responsible parties for satisfying the Conditions of Authorization.

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

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).

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).

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 Ebola Zaire virus (detected in the West Africa outbreak of 2014) 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 LightMix® Ebola Zaire rRT-PCR Test for the presumptive detection of RNA from Ebola Zaire virus (detected in the West Africa outbreak of 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. Ebola Zaire virus (detected in the West Africa outbreak of 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 LightMix® Ebola Zaire rRT-PCR Test, when used with the specified instruments, may be effective in diagnosing Ebola virus (detected in the West Africa outbreak of 2014) infection, and that the known and potential benefits of the LightMix® Ebola Zaire rRT-PCR Test, when used with the specified instruments for diagnosing Ebola virus (detected in the West Africa outbreak of 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 LightMix® Ebola Zaire rRT-PCR Test for diagnosing Ebola virus (detected in the West Africa outbreak of 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 LightMix® Ebola Zaire rRT-PCR Test by CLIA High Complexity Laboratories, or similarly qualified non-U.S. laboratories, for the presumptive detection of RNA from Ebola Zaire virus (detected in the West Africa outbreak of 2014) in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

The Authorized LightMix® Ebola Zaire rRT-PCR Test:

The LightMix® Ebola Zaire rRT-PCR Test is a real-time reverse transcription polymerase chain reaction (rRT-PCR) intended for the qualitative detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) from whole blood (EDTA anticoagulant) or whole blood (EDTA anticoagulant) inactivated with TriPure. The assay is performed on nucleic acid extracted either with the MagNA Pure 96 DNA and Viral Nucleic Acid Kit using the automated MagNA Pure 96

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

System or with the manual High Pure Viral Nucleic Acid Kit using the LightCycler® 480 Instrument or cobas z 480 Analyzer with LightCycler® Multiplex RNA Virus Master reagents for amplification and detection.

The LightMix® Ebola Zaire rRT-PCR Test kit includes the following components:

- 1 Vial Ebola Zaire Mix (96 reactions), containing: 1) lyophilized primer and FAM-labeled probe sequences that specifically detect Ebola Zaire virus in whole blood; and 2) lyophilized primer and R6G-labeled probe sequences that specifically detect an endogenous human house-keeping gene, RNase P, used as an internal process control with each clinical specimen to indicate that adequate isolation of nucleic acid resulted from the clinical specimen and PCR has worked properly from the extracted nucleic acid.
- 1 Vial Ebola Positive Control (RNA) (32 reactions), containing lyophilized synthetic RNA, designed to react with the Ebola Zaire Mix to indicate whether the Ebola Zaire RT-PCR has worked properly.

The above described LightMix® Ebola Zaire rRT-PCR Test, when labeled consistently with the labeling authorized by FDA entitled “LightMix® Ebola Zaire rRT-PCR Test Instructions for Use” (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#ebola>), which may be revised only by Roche Molecular Systems, Inc. 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 LightMix® Ebola Zaire rRT-PCR Test is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to health care professionals and patients:

- **Fact Sheet for Health Care Providers: Interpreting LightMix® Ebola Zaire rRT-PCR Test Results**
- **Fact Sheet for Patients: Understanding Results from the LightMix® Ebola Zaire rRT-PCR Test**

As described in Section IV below, Roche Diagnostics and Roche Molecular Systems, Inc. are also authorized to make available additional information relating to the emergency use of the authorized LightMix® Ebola Zaire rRT-PCR Test that is consistent with, and does not exceed, the terms of this letter of authorization.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the authorized LightMix® Ebola Zaire rRT-PCR Test in the specified population, when used for presumptive detection of RNA from Ebola Zaire virus (detected in the West Africa outbreak of 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 LightMix® Ebola Zaire rRT-PCR Test may be effective in the diagnosis of infection with Ebola Zaire virus (detected in the West Africa outbreak of 2014) 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 LightMix® Ebola Zaire rRT-PCR Test, when used to diagnose infection with Ebola Zaire virus (detected in the West Africa outbreak of 2014) 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 LightMix® Ebola Zaire rRT-PCR 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 LightMix® Ebola Zaire rRT-PCR Test described above is authorized to diagnose infection with 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 LightMix® Ebola Zaire rRT-PCR 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 LightMix® Ebola Zaire rRT-PCR 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:

Roche Diagnostics or Roche Molecular Systems, Inc.

- A. Roche Diagnostics will distribute the authorized LightMix® Ebola Zaire rRT-PCR Test with the authorized labeling, as may be revised only by Roche Molecular Systems, Inc. in consultation with FDA, only to CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories.
- B. Roche Diagnostics will provide to CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories the authorized LightMix® Ebola Zaire rRT-PCR Test Fact Sheet for Health Care Providers and the authorized LightMix® Ebola Zaire rRT-PCR Test Fact Sheet for Patients.
- C. Roche Diagnostics will make available on its website the LightMix® Ebola Zaire rRT-PCR Test Fact Sheet for Health Care Providers and the authorized LightMix® Ebola Zaire rRT-PCR Test Fact Sheet for Patients.
- D. Roche Diagnostics 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. Roche Diagnostics will ensure that CLIA High Complexity Laboratories or similarly qualified non-U.S. laboratories using the authorized LightMix® Ebola Zaire rRT-PCR Test 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, Roche Diagnostics will maintain records of device usage.
- G. Roche Diagnostics will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which Roche Molecular Systems, Inc. becomes aware.
- H. Roche Diagnostics is authorized to make available additional information relating to the emergency use of the authorized LightMix® Ebola Zaire rRT-PCR Test that is consistent with, and does not exceed, the terms of this letter of authorization.
- I. Roche Molecular Systems, Inc. will provide TIB MOLBIOL with a copy of this EUA, and communicate to TIB MOLBIOL any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets, Instructions For Use).
- J. Roche Molecular Systems, Inc. only may request changes to the authorized LightMix® Ebola Zaire rRT-PCR Test Fact Sheet for Health Care Providers or the authorized LightMix® Ebola Zaire rRT-PCR Test Fact Sheet for Patients. Such requests will be made only by Roche Molecular Systems, Inc. in consultation with FDA.
- K. Roche Diagnostics, assuming the medical device reporting responsibilities of the manufacturer of the LightMix® Ebola Zaire rRT-PCR Test, will track adverse events and report to FDA as described in 21 CFR Part 803.

- L. Roche Molecular Systems, Inc. will comply with the applicable labeling requirements specified in the Waiver of Certain Requirements (Section III).
- M. Roche Molecular Systems, Inc. will notify FDA of any proposed change in its status as exclusive distributor of the LightMix® Ebola Zaire rRT-PCR Test, including any proposed authorization of additional distributors.

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

- N. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will include with reports of the results of the LightMix® Ebola Zaire rRT-PCR 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.
- O. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will perform the LightMix® Ebola Zaire rRT-PCR Test on only the LightCycler® 480 Instrument and cobas z 480 Analyzer.
- P. 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.
- Q. CLIA High Complexity Laboratories and similarly qualified non-U.S. laboratories will collect information on the performance of the assay, and report to Roche Diagnostics any suspected occurrence of false positive or false negative results of which they become aware.
- R. All laboratory personnel using the assay should be appropriately trained in LightMix® Ebola Zaire rRT-PCR Test on the specified instruments and use appropriate laboratory and personal protective equipment when handling this kit.

Roche Diagnostics, Roche Molecular Systems, Inc., CLIA High Complexity Laboratories, and Similarly Qualified Non-U.S. Laboratories

- S. Roche Diagnostics, Roche Molecular Systems, Inc., 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

- T. All advertising and promotional descriptive printed matter relating to the use of the authorized LightMix® Ebola Zaire rRT-PCR 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.

U. All advertising and promotional descriptive printed matter relating to the use of the authorized LightMix® Ebola Zaire rRT-PCR Test shall clearly and conspicuously state that:

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an Emergency Use Authorization 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 Ebola Zaire virus (detected in the West Africa outbreak of 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 LightMix® Ebola Zaire rRT-PCR Test may represent or suggest that this test is safe or effective for the diagnosis of infection with Ebola virus.

The emergency use of the authorized LightMix® Ebola Zaire rRT-PCR 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