Dated: December 18, 2014.

Leslie Kux,

Associate Commissioner for Policy.

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BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–N–2104]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of two Emergency Use Authorizations (EUAs) (the Authorizations) for two in vitro diagnostic devices for detection of the Ebola Zaire virus. FDA is issuing these Authorizations under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as requested by the Centers for Disease Control and Prevention (CDC). 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 are effective as of October 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 Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents; (2) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to U.S. military forces of attack with a biological, chemical, radiological, or nuclear agent or agents; (3) a determination by the Secretary of HHS that there is a public health emergency, or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of U.S. citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such agent or agents; or (4) the identification of a material threat by the Secretary of Homeland Security 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

[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.

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.

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 Zaire Virus

On September 22, 2006, then-Secretary of Homeland Security, 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 8, 2014, CDC submitted complete requests for, and on October 10, 2014, FDA issued, an EUA for the CDC Ebola Virus VP40 Real-time RT–PCR Assay and an EUA for the CDC Ebola Virus NP Real-time RT–PCR Assay, subject to the terms of these authorizations.

[2] Under 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 DHS Secretary of a material threat under 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).

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 two CDC in vitro diagnostic devices for detection of the Ebola Zaire virus subject to the terms of the Authorizations. The Authorizations in their entirety (not including the authorized versions of the fact sheets and other written materials) follow and provide explanations of the reasons for their issuance, as required by section 564(h)(1) of the FD&C Act.

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

October 10, 2014

Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
Atlanta, GA 30333

Dear Dr. Frieden:

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 Centers for Disease Control and Prevention (CDC) Ebola Virus NP Real-time RT-PCR Assay for the presumptive detection of Ebola Zaire virus on a specified instrument in individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors, by qualified laboratories designated by CDC, 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 CDC Ebola Virus NP Real-time RT-PCR Assay (as described in the Scope of Authorization section of this letter (Section II)) in individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors (as described in the Scope of Authorization section of this letter (Section II)) for the presumptive detection of Ebola Zaire virus by qualified laboratories designated by CDC, subject to the terms of this authorization.

[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).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the CDC Ebola Virus NP Real-time RT-PCR Assay for the presumptive detection of Ebola Zaire virus 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 can cause Ebola, 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 CDC Ebola Virus NP Real-time RT-PCR Assay, when used with the specified instrument, may be effective in diagnosing Ebola Zaire virus, and that the known and potential benefits of the CDC Ebola Virus NP Real-time RT-PCR Assay, when used with the specified instrument for diagnosing Ebola Zaire virus 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 CDC Ebola Virus NP Real-time RT-PCR Assay for diagnosing Ebola Zaire virus.[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 CDC Ebola Virus NP Real-time RT-PCR Assay by qualified laboratories designated by CDC for the presumptive detection of Ebola Zaire virus in individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors.

The Authorized CDC Ebola Virus NP Real-time RT-PCR Assay:

The CDC Ebola Virus NP Real-time RT-PCR Assay is a real-time reverse transcriptase PCR (rRT-PCR) for the *in vitro* qualitative detection of Ebola Zaire virus in whole blood, serum, and plasma specimens from individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors. The CDC Ebola Virus NP Real-time RT-PCR Assay can also be used with urine specimens when tested in conjunction with a patient-matched whole blood, serum, or plasma specimen. The test procedure consists of nucleic acid extraction using only the MagMax Pathogen RNA/DNA kit and the Dynal Bead Retriever followed by rRT-PCR on only the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument.

The CDC Ebola Virus NP Real-time RT-PCR Assay consists of two primer/probe sets: NP and RP (Rnase P). RNA is extracted from whole blood collected with EDTA as the anticoagulant, plasma, serum, or urine using only the MagMax Pathogen RNA/DNA kit on the Dynal Bead Retriever, not provided with the assay, prior to running on the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument. The resulting purified RNA is analyzed only on the

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

Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument using provided primer/probe sets and required reagents with appropriate controls in place.

The CDC Ebola Virus NP Real-time RT-PCR Assay includes the following assay controls:

- EBOV NP rRT-PCR Positive Control – Used as a control for PCR reagent function.
- NTC – A known negative template control (sterile, nuclease-free water) added during rRT-PCR reaction set-up. Used as a control for PCR reagent function and cross-contamination.
- HSC – A known negative extraction control (human A549 cells) that is **extracted concurrently** with the test samples and included as a sample during rRT-PCR set-up. Should be negative for NP, but positive for RP. Used as a control to demonstrate successful extraction and as a control for cross-contamination.
- RP – All clinical samples should be tested for human RNAse P gene (using the RP primer and probe set included in the EBOV NP rRT-PCR kit) to control for specimen quality and extraction.

The above described CDC Ebola Virus NP Real-time RT-PCR Assay, when labeled consistently with the labeling authorized by FDA entitled "Ebola Virus NP Real-Time RT-PCR Assay" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by CDC in consultation with FDA, is authorized to be distributed to and used by qualified laboratories designated by CDC under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described CDC Ebola Virus NP Real-time RT-PCR 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 CDC Ebola Virus NP Real-Time RT-PCR (EBOV NP rRT-PCR) Assay Results**

- **Fact Sheet for Patients: Understanding Results from the CDC Ebola Virus NP Real-Time RT-PCR (EBOV NP rRT-PCR) Assay**

As described in Section IV below, CDC is also authorized to make available additional information relating to the emergency use of the authorized CDC Ebola Virus NP Real-time RT-PCR 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 CDC Ebola Virus NP Real-time RT-PCR Assay in the specified population, when used for presumptive detection of Ebola Zaire virus, 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 CDC Ebola Virus NP Real-time RT-PCR Assay may be effective in the diagnosis of Ebola Zaire virus 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 CDC Ebola Virus NP Real-time RT-PCR Assay, when used to diagnose Ebola Zaire virus 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 CDC Ebola Virus NP Real-time RT-PCR 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 CDC Ebola Virus NP Real-time RT-PCR Assay described above is authorized to diagnose Ebola Zaire virus infection in individuals in affected areas with signs and symptoms of Ebola virus infection and/or 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 CDC Ebola Virus NP Real-time RT-PCR 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 CDC Ebola Virus NP Real-time RT-PCR 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:

Centers for Disease Control and Prevention (CDC)

A. CDC will distribute the authorized CDC Ebola Virus NP Real-time RT-PCR Assay with the authorized labeling, as may be revised by CDC in consultation with FDA, only to qualified laboratories designated by CDC.

B. CDC will provide to qualified laboratories designated by CDC the authorized CDC Ebola Virus NP Real-time RT-PCR Assay Fact Sheet for Health Care Providers and the authorized CDC Ebola Virus NP Real-time RT-PCR Assay Fact Sheet for Patients.

C. CDC will make available on its website the authorized CDC Ebola Virus NP Real-time RT-PCR Assay Fact Sheet for Health Care Providers and the authorized CDC Ebola Virus NP Real-time RT-PCR Assay Fact Sheet for Patients.

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

E. CDC will ensure that qualified laboratories designated by CDC using the authorized CDC Ebola Virus NP Real-time RT-PCR Assay have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

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

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

H. CDC 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 CDC becomes aware.

I. CDC is authorized to make available additional information relating to the emergency use of the authorized CDC Ebola Virus NP Real-time RT-PCR Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

J. CDC may request changes to the authorized CDC Ebola Virus NP Real-time RT-PCR Assay Fact Sheet for Health Care Providers or the authorized CDC Ebola Virus NP Real-time RT-PCR Assay Fact Sheet for Patients. Such requests will be made by CDC in consultation with FDA.

Qualified Laboratories Designated by CDC

K. Qualified laboratories designated by CDC will include with reports of the results of the CDC Ebola Virus NP Real-time RT-PCR 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. Qualified laboratories designated by CDC will perform the CDC Ebola Virus NP Real-time RT-PCR Assay only on the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument.

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

N. Qualified laboratories designated by CDC will collect information on the performance of the assay, and report to CDC 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 RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit.

CDC and Qualified Laboratories Designated by CDC

P. CDC and qualified laboratories designated by CDC 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 CDC Ebola Virus NP Real-time RT-PCR 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 CDC Ebola Virus NP Real-time RT-PCR 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 qualified laboratories designated by CDC;
- This test has been authorized only for the detection of Ebola Zaire virus 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 CDC Ebola Virus NP Real-time RT-PCR Assay may represent or suggest that this test is safe or effective for the diagnosis of Ebola Zaire virus.

The emergency use of the authorized CDC Ebola Virus NP Real-time RT-PCR 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,

Margaret A. Hamburg

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

Enclosures

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

October 10, 2014

Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
1600 Clifton Rd, MS D-14
Atlanta, GA 30333

Dear Dr. Frieden:

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 Centers for Disease Control and Prevention (CDC) Ebola Virus VP40 Real-time RT-PCR Assay for the presumptive detection of Ebola Zaire virus on a specified instrument in individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors, by qualified laboratories designated by CDC, 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay (as described in the Scope of Authorization section of this letter (Section II)) in individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors (as described in the Scope of Authorization section of this letter (Section II)) for the presumptive detection of Ebola Zaire virus by qualified laboratories designated by CDC, subject to the terms of this authorization.

[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).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the CDC Ebola Virus VP40 Real-time RT-PCR Assay for the presumptive detection of Ebola Zaire virus 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 can cause Ebola, 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay, when used with the specified instrument, may be effective in diagnosing Ebola Zaire virus, and that the known and potential benefits of the CDC Ebola Virus VP40 Real-time RT-PCR Assay, when used with the specified instrument for diagnosing Ebola Zaire virus 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay for diagnosing Ebola Zaire virus.[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 CDC Ebola Virus VP40 Real-time RT-PCR Assay by qualified laboratories designated by CDC for the presumptive detection of Ebola Zaire virus in individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors.

The Authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay:

The CDC Ebola Virus VP40 Real-time RT-PCR Assay is a real-time reverse transcriptase PCR (rRT-PCR) for the *in vitro* qualitative detection of Ebola Zaire virus in whole blood, serum, and plasma specimens from individuals in affected areas with signs and symptoms of Ebola virus infection and/or epidemiological risk factors. The CDC Ebola Virus VP40 Real-time RT-PCR Assay can also be used with urine specimens when tested in conjunction with a patient-matched whole blood, serum, or plasma specimen. The test procedure consists of nucleic acid extraction using only the MagMax Pathogen RNA/DNA kit and the Dynal Bead Retriever followed by rRT-PCR on only the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument.

The CDC Ebola Virus VP40 Real-time RT-PCR Assay consists of two primer/probe sets: VP40 and RP (Rnase P). RNA is extracted from whole blood collected with EDTA as the anticoagulant, plasma, serum, or urine using only the MagMax Pathogen RNA/DNA kit on the Dynal Bead Retriever, not provided with the assay, prior to running on the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument. The resulting purified RNA is analyzed only

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

on the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument using provided primer/probe sets and required reagents with appropriate controls in place.

The CDC Ebola Virus VP40 Real-time RT-PCR Assay includes the following assay controls:

- EBOV VP40 rRT-PCR Positive Control – Used as a control for PCR reagent function.
- NTC – A known negative template control (sterile, nuclease-free water) added during rRT-PCR reaction set-up. Used as a control for PCR reagent function and cross-contamination.
- HSC – A known negative extraction control (human A549 cells) that is **extracted concurrently** with the test samples and included as a sample during rRT-PCR set-up. Should be negative for VP40, but positive for RP. Used as a control to demonstrate successful extraction and as a control for cross-contamination.
- RP – All clinical samples should be tested for human RNAse P gene (using the RP primer and probe set included in the EBOV VP40 rRT-PCR kit) to control for specimen quality and extraction.

The above described CDC Ebola Virus VP40 Real-time RT-PCR Assay, when labeled consistently with the labeling authorized by FDA entitled "Ebola Virus VP40 Real-Time RT-PCR Assay" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by CDC in consultation with FDA, is authorized to be distributed to and used by qualified laboratories designated by CDC under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described CDC Ebola Virus VP40 Real-time RT-PCR 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 CDC Ebola Virus VP40 Real-Time RT-PCR (EBOV VP40 rRT-PCR) Assay Results**

- **Fact Sheet for Patients: Understanding Results from the CDC Ebola Virus VP40 Real-Time RT-PCR (EBOV VP40 rRT-PCR) Assay**

As described in Section IV below, CDC is also authorized to make available additional information relating to the emergency use of the authorized CDC Ebola Virus VP40 Real-time RT-PCR 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay in the specified population, when used for presumptive detection of Ebola Zaire virus, 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 CDC Ebola Virus

VP40 Real-time RT-PCR Assay may be effective in the diagnosis of Ebola Zaire virus 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay, when used to diagnose Ebola Zaire virus 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 CDC Ebola Virus VP40 Real-time RT-PCR 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay described above is authorized to diagnose Ebola Zaire virus infection in individuals in affected areas with signs and symptoms of Ebola virus infection and/or 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 CDC Ebola Virus VP40 Real-time RT-PCR 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 CDC Ebola Virus VP40 Real-time RT-PCR 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:

Centers for Disease Control and Prevention (CDC)

A. CDC will distribute the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay with the authorized labeling, as may be revised by CDC in consultation with FDA, only to qualified laboratories designated by CDC.

B. CDC will provide to qualified laboratories designated by CDC the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay Fact Sheet for Health Care Providers and the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay Fact Sheet for Patients.

C. CDC will make available on its website the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay Fact Sheet for Health Care Providers and the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay Fact Sheet for Patients.

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

E. CDC will ensure that qualified laboratories designated by CDC using the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.

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

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

H. CDC 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 CDC becomes aware.

I. CDC is authorized to make available additional information relating to the emergency use of the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

J. CDC may request changes to the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay Fact Sheet for Health Care Providers or the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay Fact Sheet for Patients. Such requests will be made by CDC in consultation with FDA.

Qualified Laboratories Designated by CDC

K. Qualified laboratories designated by CDC will include with reports of the results of the CDC Ebola Virus VP40 Real-time RT-PCR 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. Qualified laboratories designated by CDC will perform the CDC Ebola Virus VP40 Real-time RT-PCR Assay only on the Applied Biosystems (ABI) 7500 Fast Dx Real-Time PCR Instrument.

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

N. Qualified laboratories designated by CDC will collect information on the performance of the assay, and report to CDC 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 RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit.

CDC and Qualified Laboratories Designated by CDC

P. CDC and qualified laboratories designated by CDC 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 CDC Ebola Virus VP40 Real-time RT-PCR 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 CDC Ebola Virus VP40 Real-time RT-PCR 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 qualified laboratories designated by CDC;
- This test has been authorized only for the detection of Ebola Zaire virus 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 CDC Ebola Virus VP40 Real-time RT-PCR Assay may represent or suggest that this test is safe or effective for the diagnosis of Ebola Zaire virus.

The emergency use of the authorized CDC Ebola Virus VP40 Real-time RT-PCR Assay as described in this letter of authorization must comply with the conditions and all other terms of this authorization.

Page 7 – Dr. Frieden, Centers for Disease Control and Prevention

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

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

Enclosures

Dated: December 18, 2014.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2014–30108 Filed 12–23–14; 8:45 am]

BILLING CODE 4164–01–C

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2007–D–0369]

Bioequivalence Recommendations for Methylphenidate Hydrochloride Extended-Release Oral Suspension; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Bioequivalence Recommendations for Methylphenidate Hydrochloride Extended-Release Oral Suspension.'' The recommendations provide specific guidance on the design of bioequivalence (BE) studies to support abbreviated new drug applications (ANDAs) for methylphenidate hydrochloride (HCl) extended-release oral suspension.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comments on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by February 23, 2015.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to *http://www.regulations.gov*. Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Kris André, Center for Drug Evaluation and Research (HFD–600), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 4726, Silver Spring, MD 20993–0002, 240–402–7959.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of June 11, 2010 (75 FR 33311), FDA announced the availability of a guidance for industry, ''Bioequivalence Recommendations for Specific Products,'' which explained the process that would be used to make product-specific BE recommendations available to the public on FDA's Web site at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*. As described in that guidance, FDA adopted this process as a means to develop and disseminate product-specific BE recommendations and provide a meaningful opportunity for the public to consider and comment on those recommendations. This notice announces the availability of draft BE recommendations for methylphenidate HCl extended-release oral suspension.

New drug application 202100 for Quillivant XR (methylphenidate HCl) extended-release oral suspension was initially approved by FDA in September 2012. There are no approved ANDAs for this product. FDA is now issuing a draft guidance for industry on BE recommendations for generic methylphenidate HCl extended-release oral suspension (Draft Methylphenidate HCl Oral Suspension BE Recommendations).

In August 2014, Pfizer, Inc., manufacturer of the reference listed drug, Quillivant XR, submitted a citizen petition requesting that FDA establish certain BE requirements for any new drug product that references Quillivant XR and seeks approval by means of demonstrating BE to Quillivant XR (Docket No. FDA–2014–P–1269). FDA is reviewing the issues raised in the petition.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on the design of BE studies to support ANDAs for methylphenidate HCl extended-release oral suspension. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) either electronic or written