November 21, 2016

Stacy Ferguson
Regulatory Affairs Project Manager
Abbott Molecular Inc.
1300 East Touhy Avenue
Des Plaines, IL 60018

Dear Ms. Ferguson:

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 Abbott Molecular Inc.'s ("Abbott") RealTi*m*e ZIKA assay for the qualitative detection of RNA from Zika virus in human serum, EDTA plasma, and urine (collected alongside a patient-matched serum or plasma specimen) from individuals meeting Centers for Disease Control and Prevention (CDC) Zika virus clinical criteria (e.g., clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated), by laboratories in the United States (U.S.) that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests, or by 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).[1] Test results are for the identification of Zika virus RNA. Zika virus RNA is generally detectable in these specimens during the acute phase of infection and, according to the updated CDC Guidance for U.S. Laboratories Testing for Zika Virus Infection,[2] up to 14 days in serum and urine (possibly longer in urine), following onset of symptoms, if present. Positive results are indicative of current infection.

On February 26, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of Health and Human Services (HHS) determined that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves Zika virus.[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 then declared that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).[4]

---

[1] For ease of reference, this letter will refer to "laboratories in the United States (U.S.) that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high complexity tests, or by similarly qualified non-U.S. laboratories" as "authorized laboratories."
[2] Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html (last updated on November 16, 2016).
[3] As amended by the Pandemic and All Hazards Preparedness Reauthorization Act, Pub. L. No. 113-5, under section 564(b)(1)(C) of the Act, the Secretary may make a determination of a public health emergency, or of significant potential for a public health emergency.
[5] HHS. *Determination and Declaration Regarding Emergency Use of in Vitro Diagnostic Tests for Detection of Zika*

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 Abbott RealTi*m*e ZIKA assay (as described in the Scope of Authorization section of this letter (Section II)) in individuals meeting CDC Zika virus clinical criteria (e.g., clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated) (as described in the Scope of Authorization section of this letter (Section II)) for the detection of Zika virus infection by authorized laboratories, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Abbott RealTi*m*e ZIKA assay for the detection of Zika virus and diagnosis of Zika virus infection 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 Zika virus can cause Zika virus infection, a serious or life-threatening disease or condition to humans infected with the virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the Abbott RealTi*m*e ZIKA assay, when used with the specified instrument(s) and in accordance with the Scope of Authorization, may be effective in detecting Zika virus and diagnosing Zika virus infection, and that the known and potential benefits of the Abbott RealTi*m*e Zika assay for detecting Zika virus and diagnosing Zika 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 Abbott RealTi*m*e ZIKA assay for detecting Zika virus and diagnosing Zika virus 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 Abbott RealTi*m*e ZIKA assay by authorized laboratories for the detection of RNA from Zika virus and diagnosis of Zika virus infection in individuals meeting CDC Zika virus clinical criteria (e.g., clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated).

The Authorized Abbott RealTi*m*e ZIKA assay

The Abbott RealTi*m*e ZIKA assay is a real-time reverse transcription polymerase chain reaction (RT-PCR) assay for the qualitative detection of RNA from Zika virus in human serum, EDTA

Virus and/or Diagnosis of Zika Virus Infection. 81 Fed. Reg. 10878 (March 2, 2016).

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

plasma, urine (collected alongside a patient-matched serum or plasma specimen) and other authorized specimen types.

To perform the Abbott RealTi*m*e ZIKA assay, nucleic acids are isolated from the sample and purified using the Abbott *m*Sample Preparation System on the Abbott *m*2000*sp* instrument, an automated instrument for performing sample preparation, or other authorized instruments. Magnetic microparticle technology captures nucleic acids, and the particles are washed to remove unbound sample components. The bound nucleic acids are eluted and transferred to a 96 deep-well plate. The purified nucleic acid is reverse transcribed into cDNA which is then amplified in the Abbott *m*2000*rt* instrument, or other authorized instruments. This is followed by the detection of the target of interest.

The Abbott RealTi*m*e ZIKA assay uses the following materials, or other authorized materials or ancillary products:

- Abbott *m*Sample Preparation System, containing
  - Abbott *m*Lysis
  - *m*Wash 1
  - *m*Wash 2
  - *m*Elution Buffer
  - *m*Microparticles reagent bottles

- Abbott RealTi*m*e ZIKA Amplification Reagent Kit, containing
  - Abbott RealTi*m*e ZIKA Internal Control in negative human serum
  - Abbott RealTi*m*e ZIKA Amplification Reagent (Thermostable rTth Polymerase Enzyme; ZIKA Amplification Reagent with primers, probes and nucleotides; Activation Reagent)

The Abbott RealTi*m*e ZIKA assay requires the following control materials, or other authorized control materials, to be included in each run; all controls listed below must generate expected results in order for a test to be considered valid, as outlined in the Abbott RealTi*m*e ZIKA Instructions for Use:

- Abbott RealTi*m*e ZIKA Control Kit
  - Abbott RealTi*m*e ZIKA Negative Control: Negative human plasma is used for monitoring of contaminations.
  - Abbott RealTi*m*e ZIKA Positive Control: Inactivated Zika virus (strain PRVABC59) in human serum monitors for substantial reagent failure and is used throughout the extraction and PCR set-up for each run.

- Internal Control: noninfectious Armored RNA with internal control sequences in negative human plasma. It confirms the validity of the extraction process and identifies potential PCR inhibition; it is used throughout the extraction and PCR set-up for each sample.

To produce a valid run the test controls must meet the performance specifications outlined in the Abbott RealTi*m*e ZIKA Instructions for Use.

The Abbott RealTi*m*e ZIKA assay also requires the use of additional materials and ancillary reagents commonly used in clinical laboratories and that are described in the authorized Abbott RealTi*m*e ZIKA Instructions for Use.

The above described Abbott RealTi*m*e ZIKA assay, when labeled consistently with the labeling authorized by FDA entitled "Abbott RealTi*m*e ZIKA Instructions for Use" and "Abbott RealTi*m*e ZIKA Control Kit" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by Abbott in consultation with the Division of Microbiology Devices (DMD)/Office of In Vitro Diagnostics and Radiological Health (OIR)/Center for Devices and Radiological Health (CDRH), is authorized to be distributed to and used by authorized laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described Abbott RealTi*m*e ZIKA assay is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to healthcare providers and patients, including pregnant women:

- Fact Sheet for Healthcare Providers: Interpreting Abbott RealTi*m*e ZIKA Assay Results
- Fact Sheet for Patients: Understanding Results from the Abbott RealTi*m*e ZIKA Assay

As described in Section IV below, Abbott and its authorized distributors are also authorized to make available additional information relating to the emergency use of the authorized Abbott RealTi*m*e ZIKA 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 Abbott RealTi*m*e ZIKA assay in the specified population, when used for detection of Zika virus and to diagnose Zika virus infection and used consistently with the Scope of Authorization of this letter (Section II), 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 Abbott RealTi*m*e ZIKA assay may be effective in the detection of Zika virus and diagnosis of Zika virus infection, when used consistently with the Scope of Authorization of this letter (Section II), 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 Abbott RealTi*m*e ZIKA assay, when used for detection of Zika virus and to diagnose Zika virus infection in the specified population (as described in the Scope of Authorization of this letter (Section II)), meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Abbott RealTi*m*e ZIKA 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 HHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the Abbott RealTi*m*e ZIKA assay described above is authorized to detect Zika virus and diagnose Zika virus infection in individuals meeting CDC Zika virus clinical criteria (e.g., clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika virus transmissions at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated).

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 Abbott RealTi*m*e ZIKA 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 Abbott RealTi*m*e ZIKA 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:

Abbott Molecular Inc. and Its Authorized Distributor(s)

A. Abbott and its authorized distributor(s) will distribute the authorized Abbott RealTi*m*e ZIKA assay with the authorized labeling only to authorized laboratories. Changes to the authorized labeling may be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

B. Abbott and its authorized distributor(s) will provide to authorized laboratories the authorized Abbott RealTi*m*e ZIKA assay Fact Sheet for Healthcare Providers and the authorized Abbott RealTi*m*e ZIKA assay Fact Sheet for Patients.

C. Abbott and its authorized distributor(s) will make available on their websites the

authorized Abbott RealTi*m*e ZIKA assay Fact Sheet for Healthcare Providers and the authorized Abbott RealTi*m*e ZIKA assay Fact Sheet for Patients.

D. Abbott and its authorized distributor(s) will inform authorized laboratories and relevant public health authority(ies) of this EUA, including the terms and conditions herein.

E. Abbott and its authorized distributor(s) will ensure that the authorized laboratories using the authorized Abbott RealTi*m*e ZIKA assay have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.[6]

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

G. Abbott and its authorized distributor(s) will collect information on the performance of the test. Abbott will report to FDA any suspected occurrence of false positive and false negative results and significant deviations from the established performance characteristics of the test of which Abbott becomes aware.

H. Abbott and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized Abbott RealTi*m*e ZIKA assay that is consistent with, and does not exceed, the terms of this letter of authorization.

Abbott Molecular Inc.

I. Abbott will notify FDA of any authorized distributor(s) of the Abbott RealTi*m*e ZIKA assay, including the name, address, and phone number of any authorized distributor(s).

J. Abbott will provide its authorized distributor(s) with a copy of this EUA, and communicate to its authorized distributor(s) any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets, Instructions for Use).

K. Abbott may request changes to the authorized Abbott RealTi*m*e ZIKA assay Fact Sheet for Healthcare Providers and the authorized Abbott RealTi*m*e ZIKA assay Fact Sheet for Patients. Such requests will be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

L. Abbott may request the addition of other instruments for use with the authorized Abbott RealTi*m*e ZIKA assay. Such requests will be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

[7] For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Abbott, other authorized distributor(s), and authorized laboratories consult with the applicable country, state or territory health department(s). According to CDC, Zika virus disease is a nationally notifiable condition (see http://www.cdc.gov/zika/).

M. Abbott may request the addition of other extraction methods for use with the authorized Abbott RealTi*m*e ZIKA assay. Such requests will be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

N. Abbott may request the addition of other specimen types for use with the authorized Abbott RealTi*m*e ZIKA assay. Such requests will be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

O. Abbott may request the addition of other control materials for use with the authorized Abbott RealTi*m*e ZIKA assay. Such requests will be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

P. Abbott may request the addition and/or substitution of other ancillary reagents and materials for use with the authorized Abbott RealTi*m*e ZIKA assay. Such requests will be made by Abbott in consultation with, and require concurrence of, DMD/OIR/CDRH.

Q. Abbott will assess traceability[7] of the Abbott RealTi*m*e ZIKA assay with FDA-recommended reference material(s). After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, Abbott will update its labeling to reflect the additional testing.

R. Abbott, assuming the medical device reporting responsibilities of the manufacturer of the Abbott RealTi*m*e ZIKA assay, will track adverse events and report to FDA under 21 CFR Part 803.

Authorized Laboratories

S. Authorized laboratories will include with reports of the results of the Abbott RealTi*m*e ZIKA assay the authorized Fact Sheet for Healthcare 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.

T. Authorized laboratories will perform the Abbott RealTi*m*e ZIKA assay using nucleic acid extraction and PCR set-up procedures automated by the Abbott *m*2000*sp* instruments, or other authorized instruments.

U. Authorized laboratories will perform the Abbott RealTi*m*e ZIKA assay on the Abbott *m*2000*rt* instrument, or other authorized instruments.

V. Authorized laboratories will perform the Abbott RealTi*m*e ZIKA assay using the Abbott *m*Sample Preparation System for nucleic acid extraction, or other authorized extraction methods.

W. Authorized laboratories will perform the Abbott RealTi*m*e ZIKA assay on human serum, EDTA plasma, or urine (collected alongside a patient-matched serum or plasma specimen) or other authorized specimen types.

[7] Traceability refers to tracing analytical sensitivity/reactivity back to a FDA recommended reference material.

X. Authorized laboratories will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.[8]

Y. Authorized laboratories will collect information on the performance of the test and report to Abbott any suspected occurrence of false positive or false negative results of which they become aware.

Z. All laboratory personnel using the test should be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.

Abbott Molecular Inc., Its Authorized Distributor(s) and Authorized Laboratories

AA. Abbott, its authorized distributor(s), and authorized 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

BB. All advertising and promotional descriptive printed matter relating to the use of the authorized Abbott RealTi*m*e ZIKA 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.

CC. All advertising and promotional descriptive printed matter relating to the use of the authorized Abbott RealTi*m*e ZIKA 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 authorized laboratories;
- This test has been authorized only for the detection of RNA from Zika virus and diagnosis of Zika virus infection, 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* diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

[8] For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Abbott, other authorized distributor(s), and authorized laboratories consult with the applicable country, state or territory health department(s). According to CDC, Zika virus disease is a nationally notifiable condition. http://www.cdc.gov/zika/.

No advertising or promotional descriptive printed matter relating to the use of the authorized Abbott RealTi*m*e ZIKA assay may represent or suggest that this test is safe or effective for the diagnosis of Zika virus infection.

The emergency use of the authorized Abbott RealTi*m*e ZIKA 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* diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

_____

Robert M. Califf, M.D.
Commissioner of Food and Drugs

Enclosures