



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-3330]

Authorizations of Emergency Use of In Vitro Diagnostic Devices for Detection and/or Diagnosis of Zika Virus; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of four Emergency Use Authorizations (EUAs) (the Authorizations) for four in vitro diagnostic devices for detection and/or diagnosis of Zika virus in response to the Zika virus outbreak in the Americas. FDA issued these Authorizations under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as requested by Siemens Healthcare Diagnostics, Inc., Luminex Corporation, InBios International, Inc., and Roche Molecular Systems, Inc. The Authorizations contain, among other things, conditions on the emergency use of the authorized in vitro diagnostic devices. The Authorizations follow the February 26, 2016, determination by the Secretary of Health and Human Services (HHS) 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. On the basis of such determination, the Secretary of HHS declared on February 26, 2016, that circumstances exist justifying the authorization of 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 the

FD&C Act. The Authorizations, which include an explanation of the reasons for issuance, are reprinted in this document.

DATES: The Authorization for Siemens Healthcare Diagnostics, Inc., is effective as of July 29, 2016; the Authorization for Luminex Corporation is effective as of August 4, 2016; the Authorization for InBios International, Inc., is effective as of August 17, 2016; and the Authorization for Roche Molecular Systems, Inc., is effective as of August 26, 2016.

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: Michael Mair, Office of Counterterrorism and Emerging Threats, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 1, rm. 4336, 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 Centers for Disease Control and Prevention (to the extent feasible and appropriate given the applicable circumstances), FDA<sup>1</sup> 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 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

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<sup>1</sup> 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.

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 and/or Diagnosis of Zika Virus

On February 26, 2016, the Secretary of 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. On February 26, 2016, 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 diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection, subject to the terms of any authorization issued under section 564 of the FD&C Act. Notice of the determination and declaration of the Secretary was published in the Federal Register on March 2, 2016 (81 FR 10878). On July 21, 2016, Siemens Healthcare Diagnostics, Inc., requested, and on July 29, 2016, FDA issued, an EUA for the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit, subject to the terms of the Authorization. On August 1, 2016, Luminex Corporation requested, and on August 4, 2016, FDA issued, an EUA for the xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA Assay, subject to the terms of the Authorization. On July 21, 2016, InBios International, Inc., requested, and on August 17, 2016, FDA issued, an EUA for the ZIKV *Detect*<sup>™</sup> IgM Capture ELISA, subject to the terms of the Authorization. On August 18, 2016, Roche Molecular Systems, Inc., requested, and on August 26, 2016, FDA issued, an EUA for the *LightMix*<sup>®</sup> Zika *rRT-PCR Test*, subject to the terms of the Authorization.

### 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 four in vitro diagnostic devices for detection and/or diagnosis of Zika 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 an explanation of the reasons for their issuance, as required by section 564(h)(1) of the FD&C Act:

[PHOTO]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

July 29, 2016

Ingrid Mehlhorn  
Regulatory Affairs  
Siemens Healthcare Diagnostics Inc.  
725 Potter St.  
Berkeley, CA 94710

Dear Dr. Mehlhorn:

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 Siemens Healthcare Diagnostics Inc.'s ("Siemens") VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 epidemiologic 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).<sup>1</sup> Assay results are for the identification of Zika virus RNA. Zika virus RNA is generally detectable in these specimens during the acute phase of infection (approximately 7 days in serum, possibly longer in urine, following onset of symptoms, if present). Positive results are indicative of current infection.

On February 26, 2016, 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 United States citizens living abroad and that involves Zika virus.<sup>2</sup> 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

<sup>1</sup> 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."

<sup>2</sup> 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 a significant potential for a public health emergency.

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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).<sup>3</sup>

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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit (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 epidemiologic 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit, when used with the specified instrument 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit for detecting Zika virus and diagnosing Zika virus infection.<sup>4</sup>

### **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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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.,

<sup>3</sup> HHS. *Determination and Declaration Regarding Emergency Use of in Vitro Diagnostic Tests for Detection of Zika Virus and/or Diagnosis of Zika Virus Infection*. 81 Fed. Reg. 10878 (March 2, 2016).

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

history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiologic criteria for which Zika virus testing may be indicated).

#### **The Authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit**

The VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit is a real-time PCR (RT-PCR) assay for the qualitative detection of RNA from Zika virus in serum, EDTA plasma, and urine (collected alongside a patient-matched serum or plasma specimen) and other authorized specimen types.

To perform the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR), samples are first extracted to isolate the Zika virus RNA. Nucleic acids are isolated and purified from the sample using either the Siemens' automated VERSANT<sup>®</sup> kPCR Sample Preparation (SP) system (also referred to as VERSANT<sup>®</sup> kPCR Molecular System SP) with the VERSANT<sup>®</sup> MiPLX Software Solution and the VERSANT<sup>®</sup> Sample Preparation 1.0 Reagents or with the QIAamp viral RNA Mini Kit with manual extraction, or with other authorized extraction methods. An Internal Control sequence is added to the sample prior to extraction and is used as a control for the sample extraction and the amplification reaction.

Purified RNA is then added to a PCR plate containing Zika Enzyme Mix and Zika Primer/Probe Mix, and the wells are sealed. The purified nucleic acids are first reverse transcribed into cDNAs. In the process, the probes anneal to the specific target sequences located between the respective forward and reverse primers. The assay targets two regions of the Zika virus genome. The dual-labeled probes include fluorescent dyes and quenchers and specifically detect the presence of Zika virus and Internal Control amplicons during amplification. During the extension phase of the PCR cycle, the 5' nuclease activity of Taq polymerase degrades the probes, causing the reporter dyes to separate from the quencher dyes, generating fluorescent signals. With each cycle, additional reporter dye molecules are cleaved from their respective probes, increasing the fluorescence intensity.

The RT-PCR is performed on the QuantStudio™ 5 Real-Time PCR System (Thermo Fisher Scientific), the CFX96 Touch™ Real-Time PCR Detection System (Bio-Rad), the Applied Biosystems<sup>®</sup> 7500 Fast Dx Real-Time PCR Instrument (Thermo Fisher Scientific) or other authorized instruments.

The VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit includes the following materials, or other authorized materials or ancillary products:

- Zika Enzyme Mix
- Zika Primer/Probe Mix
- Zika Internal Control
- Zika Negative Control
- Zika Positive Control
- Water (nuclease free)

The VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit requires the following control materials, or other authorized control materials, to be included in each run; all assay controls listed below must generate expected results in order for a test to be considered valid:

- VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Internal Control

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- o The internal control consists of a non-Zika virus RNA that is added and co-purified with each specimen, Positive Control, and Negative Control, and that is amplified by a specific primers and probe set.
  - o The internal control RNA controls for sample extraction, reverse transcription, amplification and detection, and also ensures the absence of non-specific PCR inhibition of a sample.
- VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Negative Control
  - o PCR grade water.
  - o A negative control should be included in each run of specimen extractions to monitor Zika virus contamination.
- VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Positive Control
  - o Inactivated Cultured Zika Virus Strain MR766.
  - o A positive control is included in each run of specimen extractions to monitor nucleic acid isolation and detection of Zika virus RNA.

To produce a valid run, the test controls must meet the performance specifications outlined in the Instructions for Use.

The above described VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit, when labeled consistently with the labeling authorized by FDA entitled “VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Instructions for Use” (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), which may be revised by Siemens 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to health care providers, pregnant women, and other patients:

- Fact Sheet for Health Care Providers: Interpreting VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Test Results
- Fact Sheet for Pregnant Women: Understanding Results from the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit
- Fact Sheet for Patients: Understanding Results from the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit

As described in Section IV below, Siemens is also authorized to make available additional information relating to the emergency use of the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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),

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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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit, 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 geographic regions during a period of active Zika virus transmissions at the time of travel, or other epidemiologic 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit.
- 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:

**Siemens Healthcare Diagnostics Inc. and Its Authorized Distributor(s)**

- A. Siemens and its authorized distributor(s) will distribute the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit with the authorized labeling, as may be revised by Siemens in consultation with DMD/OIR/CDRH, only to authorized laboratories.
- B. Siemens and its authorized distributor(s) will provide to authorized laboratories the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Health Care Providers, the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Pregnant Women, and the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Patients.
- C. Siemens and its authorized distributor(s) will make available on their websites the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Health Care Providers, the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Pregnant Women, and the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Patients.
- D. Siemens 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. Siemens and its authorized distributor(s) will ensure that authorized laboratories using the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>5</sup>
- F. Through a process of inventory control, Siemens and its authorized distributor(s) will maintain records of device usage.
- G. Siemens and its authorized distributor(s) will collect information on the performance of the test. Siemens 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 Siemens becomes aware.
- H. Siemens and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit that is consistent with, and does not exceed, the terms of this letter of authorization.

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<sup>5</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Siemens and authorized laboratories consult with the applicable country, state or territory health department(s). According to CDC, Zika is a nationally notifiable condition (see <http://www.cdc.gov/zika/>).

**Siemens Healthcare Diagnostics Inc.**

- I. Siemens will notify FDA of any authorized distributor(s) of the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit, including the name, address, and phone number of any authorized distributor(s).
- J. Siemens 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. Siemens may request changes to the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Health Care Providers, the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Pregnant Women, and the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit Fact Sheet for Patients. Such requests will be made by Siemens in consultation with, and require concurrence of, DMD/OIR/CDRH.
- L. Siemens may request the addition of other instruments for use with the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit. Such requests will be made by Siemens in consultation with, and require concurrence of, DMD/OIR/CDRH.
- M. Siemens may request the addition of other extraction methods for use with the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit. Such requests will be made by Siemens in consultation with, and require concurrence of, DMD/OIR/CDRH.
- N. Siemens may request the addition of other specimen types for use with the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit. Such requests will be made by Siemens in consultation with, and require concurrence of, DMD/OIR/CDRH.
- O. Siemens may request the addition of other control materials for use with the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit. Such requests will be made by Siemens in consultation with, and require concurrence of, DMD/OIR/CDRH.
- P. Siemens may request the addition of other materials and ancillary reagents for use with the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit. Such requests will be made by Siemens in consultation with, and require concurrence of, DMD/OIR/CDRH.
- Q. Siemens will assess traceability<sup>6</sup> of the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit with FDA-recommended reference material(s). After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, Siemens will update its labeling to reflect the additional testing.
- R. Siemens will track adverse events and report to FDA under 21 CFR Part 803.

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<sup>6</sup> Traceability refers to tracing analytical sensitivity/reactivity back to a FDA recommended reference material.

**Authorized Laboratories**

- S. Authorized laboratories will include with reports of the results of the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit the authorized Fact Sheet for Health Care Providers, the authorized Fact Sheet for Pregnant Women, 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 VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit on the QuantStudio<sup>™</sup> 5 Real-Time PCR System, the CFX96 Touch<sup>™</sup> Real-Time PCR Detection System, the Applied Biosystems<sup>®</sup> 7500 Fast Dx Real-Time PCR Instrument or other authorized instruments.
- U. Authorized laboratories will perform the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit using either the VERSANT<sup>®</sup> kPCR Sample Preparation (SP) system (also referred to as VERSANT<sup>®</sup> kPCR Molecular System SP) with the VERSANT<sup>®</sup> MiPLX Software Solution and the VERSANT<sup>®</sup> Sample Preparation 1.0 Reagents or with the QIAamp viral RNA Mini Kit with manual extraction, or with other authorized extraction methods.
- V. Authorized laboratories will perform the VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit on serum, EDTA plasma, or urine (collected alongside a patient-matched serum or plasma specimen) or with other authorized specimen types.
- W. Authorized laboratories will have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>7</sup>
- X. Authorized laboratories will collect information on the performance of the test and report to Siemens, any suspected occurrence of false positive or false negative results of which they become aware.
- Y. 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.

**Siemens Healthcare Diagnostics Inc., its Authorized Distributor(s) and Authorized Laboratories**

- Z. Siemens, 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**

- AA. All advertising and promotional descriptive printed matter relating to the use of the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit shall be consistent with the

<sup>7</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Siemens and authorized laboratories consult with the applicable country, state or territory health department(s). According to CDC, Zika is a nationally notifiable condition. <http://www.cdc.gov/zika/>.

Page 9 – Mrs. Mehlhorn, Siemens Healthcare Diagnostics Inc.

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.

BB. All advertising and promotional descriptive printed matter relating to the use of the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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.

No advertising or promotional descriptive printed matter relating to the use of the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit may represent or suggest that this test is safe or effective for the diagnosis of Zika virus infection.

The emergency use of the authorized VERSANT<sup>®</sup> Zika RNA 1.0 Assay (kPCR) Kit 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,



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Luciana Borio, M.D.  
Acting Chief Scientist  
Food and Drug Administration

Enclosures



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

August 4, 2016

Mr. Roy Johnson  
 Manager, Regulatory Affairs  
 Luminex Corporation  
 12212 Technology Blvd.  
 Austin, TX 78727

Dear Mr. Johnson:

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 Luminex Corporation's ("Luminex") xMAP® MultiFLEX™ Zika RNA Assay for the qualitative detection of RNA from Zika virus in human serum, 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 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).<sup>1</sup> Assay 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<sup>2</sup>, 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, 2016, 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.<sup>3</sup> 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

<sup>1</sup> 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."

<sup>2</sup> Available at <http://www.cdc.gov/zika/laboratories/lab-guidance.html> (last updated on July 26, 2016).

<sup>3</sup> 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 a significant potential for a public health emergency.

Page 2 – Mr. Johnson, Luminex Corporation

and/or diagnosis of Zika virus infection, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).<sup>4</sup>

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 xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA 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 xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA 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 xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA Assay, when used with the specified instrument 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 xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA 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 xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA Assay for detecting Zika virus and diagnosing Zika virus infection.<sup>5</sup>

### **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 xMAP<sup>®</sup> MultiFLEX<sup>™</sup> Zika RNA 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).

<sup>4</sup> HHS. *Determination and Declaration Regarding Emergency Use of in Vitro Diagnostic Tests for Detection of Zika Virus and/or Diagnosis of Zika Virus Infection*. 81 Fed. Reg. 10878 (March 2, 2016).

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

**The Authorized xMAP® MultiFLEX™ Zika RNA Assay**

The xMAP® MultiFLEX™ Zika RNA Assay is a real-time PCR (RT-PCR) assay for the qualitative detection of RNA from Zika virus in serum, plasma, and urine (collected alongside a patient-matched serum or plasma specimen) and other authorized specimen types.

To perform the xMAP® MultiFLEX™ Zika RNA Assay, samples are first extracted to isolate the Zika virus RNA. Nucleic acids are isolated and purified from the sample using the BioMerieux's NucliSENS easyMag nucleic acid extraction system, or other authorized extraction methods. An Internal Control sequence is added to the sample prior to extraction and is used as a control for the sample extraction and the amplification reaction.

Extracted total nucleic acid is then simultaneously amplified using target specific primers and probes for RT-PCR followed by amplicon hybridization to probe-coupled microspheres. Streptavidin-conjugated R-Phycoerythrin (SAPE) is added, and detection of the targets of interest is performed on a Luminex IVD xMAP instrument (MAGPIX or Luminex 100/200) or other authorized instruments.

The xMAP® MultiFLEX™ Zika RNA Assay includes the following materials, or other authorized materials or ancillary products:

- Primer Mix
- Streptavidin-Phycoerythrin (SAPE)
- Microsphere mix
- Buffer A
- Buffer B
- MS2 bacteriophage RNA extraction control

The xMAP® MultiFLEX™ Zika RNA Assay requires the following control materials, or other authorized control materials; all assay controls listed below must generate expected results in order for a test to be considered valid:

- Internal Control (Bacteriophage MS2)

This internal positive control is added to each test sample as well as to each external control prior to extraction. The internal control allows the user to ascertain whether the extraction and reverse-transcription/ amplification steps of the assay are functioning correctly.

- No Template Control (NTC)

No Template Controls (NTCs) for the amplification/ detection steps are DNase- and RNase-free distilled water in place of specimen nucleic acids and must be included in each assay run. The NTC is a control for contamination or improper function of the assay reagents which could result in false positive results.

- External Positive Control

An External Positive Control may be used with the xMAP® MultiFLEX™ Zika RNA Assay based on local guidelines or laboratory standard operating procedures (SOPs). The External

Page 4 – Mr. Johnson, Luminex Corporation

Positive Control should be processed with the same workflow as clinical specimens. A positive result for the Zika virus specific RNA confirms the assay is performing as expected.

To produce a valid run, the test controls must meet the performance specifications outlined in the Instructions for Use.

The above described xMAP® MultiFLEX™ Zika RNA Assay, when labeled consistently with the labeling authorized by FDA entitled “xMAP® MultiFLEX™ Zika RNA Assay Instructions for Use” (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), which may be revised by Luminex 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 xMAP® MultiFLEX™ Zika RNA 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 providers, pregnant women, and other patients:

- Fact Sheet for Health Care Providers: Interpreting xMAP® MultiFLEX™ Zika RNA Assay Results
- Fact Sheet for Pregnant Women: Understanding Results from the xMAP® MultiFLEX™ Zika RNA Assay
- Fact Sheet for Patients: Understanding Results from the xMAP® MultiFLEX™ Zika RNA Assay

As described in Section IV below, Luminex is also authorized to make available additional information relating to the emergency use of the authorized xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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 geographic regions during a period of 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 xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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:

#### **Luminex Corporation and Its Authorized Distributor(s)**

- A. Luminex and its authorized distributor(s) will distribute the authorized xMAP® MultiFLEX™ Zika RNA Assay with the authorized labeling, as may be revised by Luminex in consultation with DMD/OIR/CDRH, only to authorized laboratories.
- B. Luminex and its authorized distributor(s) will provide to authorized laboratories the authorized xMAP® MultiFLEX™ Zika RNA Assay Fact Sheet for Health Care Providers, the authorized xMAP® MultiFLEX™ Zika RNA Assay for Pregnant

Page 6 – Mr. Johnson, Luminex Corporation

Women, and the authorized xMAP® MultiFLEX™ Zika RNA Assay Fact Sheet for Patients.

- C. Luminex and its authorized distributor(s) will make available on their websites the authorized xMAP® MultiFLEX™ Zika RNA Assay Fact Sheet for Health Care Providers, the authorized xMAP® MultiFLEX™ Zika RNA Assay Fact Sheet for Pregnant Women, and the authorized xMAP® MultiFLEX™ Zika RNA Assay Fact Sheet for Patients.
- D. Luminex 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. Luminex and its authorized distributor(s) will ensure that authorized laboratories using the authorized xMAP® MultiFLEX™ Zika RNA Assay have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>6</sup>
- F. Through a process of inventory control, Luminex and its authorized distributor(s) will maintain records of device usage.
- G. Luminex and its authorized distributor(s) will collect information on the performance of the test. Luminex 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 Luminex becomes aware.
- H. Luminex and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized xMAP® MultiFLEX™ Zika RNA Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

#### **Luminex Corporation**

- I. Luminex will notify FDA of any authorized distributor(s) of the xMAP® MultiFLEX™ Zika RNA Assay, including the name, address, and phone number of any authorized distributor(s).
- J. Luminex 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. Luminex may request changes to the authorized xMAP® MultiFLEX™ Zika RNA Assay for Health Care Providers, the authorized xMAP® MultiFLEX™ Zika RNA Assay Fact Sheet for Pregnant Women, and the authorized xMAP® MultiFLEX™

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<sup>6</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Luminex 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/>).

Page 7 – Mr. Johnson, Luminex Corporation

Zika RNA Assay Fact Sheet for Patients. Such requests will be made by Luminex in consultation with, and require concurrence of, DMD/OIR/CDRH.

- L. Luminex may request the addition of other instruments for use with the authorized xMAP® MultiFLEX™ Zika RNA Assay. Such requests will be made by Luminex in consultation with, and require concurrence of, DMD/OIR/CDRH.
- M. Luminex may request the addition of other extraction methods for use with the authorized xMAP® MultiFLEX™ Zika RNA Assay. Such requests will be made by Luminex in consultation with, and require concurrence of, DMD/OIR/CDRH.
- N. Luminex may request the addition of other specimen types for use with the authorized xMAP® MultiFLEX™ Zika RNA Assay. Such requests will be made by Luminex in consultation with, and require concurrence of, DMD/OIR/CDRH.
- O. Luminex may request the addition of other control materials for use with the authorized xMAP® MultiFLEX™ Zika RNA Assay. Such requests will be made by Luminex in consultation with, and require concurrence of, DMD/OIR/CDRH.
- P. Luminex may request the addition of other materials and ancillary reagents for use with the authorized xMAP® MultiFLEX™ Zika RNA Assay. Such requests will be made by Luminex in consultation with, and require concurrence of, DMD/OIR/CDRH.
- Q. Luminex will assess traceability<sup>7</sup> of the xMAP® MultiFLEX™ Zika RNA Assay with FDA-recommended reference material(s). After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, Luminex will update its labeling to reflect the additional testing.
- R. Luminex 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 xMAP® MultiFLEX™ Zika RNA Assay the authorized Fact Sheet for Health Care Providers, the authorized Fact Sheet for Pregnant Women, 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 xMAP® MultiFLEX™ Zika RNA Assay on a Luminex IVD xMAP instrument (MAGPIX or Luminex 100/200) or other authorized instruments.
- U. Authorized laboratories will perform the xMAP® MultiFLEX™ Zika RNA Assay using the BioMerieux's NucliSENS easyMag nucleic acid extraction system or other authorized extraction methods.

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<sup>7</sup> Traceability refers to tracing analytical sensitivity/reactivity back to a FDA recommended reference material.

Page 8 – Mr. Johnson, Luminex Corporation

- V. Authorized laboratories will perform the xMAP® MultiFLEX™ Zika RNA Assay on serum, plasma, or urine (collected alongside a patient-matched serum or plasma specimen) or with other authorized specimen types.
- W. Authorized laboratories will have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>8</sup>
- X. Authorized laboratories will collect information on the performance of the test and report to Luminex, any suspected occurrence of false positive or false negative results of which they become aware.
- Y. 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.

**Luminex Corporation, its Authorized Distributor(s) and Authorized Laboratories**

- Z. Luminex, 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**

- AA. All advertising and promotional descriptive printed matter relating to the use of the authorized xMAP® MultiFLEX™ Zika RNA 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.
- BB. All advertising and promotional descriptive printed matter relating to the use of the authorized xMAP® MultiFLEX™ Zika RNA 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.

<sup>8</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Luminex 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/>).

Page 9 – Mr. Johnson, Luminex Corporation

No advertising or promotional descriptive printed matter relating to the use of the authorized xMAP® MultiFLEX™ Zika RNA 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 xMAP® MultiFLEX™ Zika RNA 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



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

August 17, 2016

Estela Raychaudhuri  
President  
InBios International, Inc.  
562 1<sup>st</sup> Avenue S., Suite 600  
Seattle, WA 98104

Dear Ms. Raychaudhuri:

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 InBios International, Inc.'s ("InBios"), ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA for the presumptive detection of Zika virus IgM antibodies in human sera collected from individuals meeting the Centers for Disease Control and Prevention (CDC) Zika virus clinical criteria (e.g., a history of 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 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,<sup>1</sup> pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3). Where there are presumptive Zika positive, possible Zika positive, or presumptive other flavivirus positive results from the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA, confirmation of the presence of anti-Zika IgM antibodies or other flavivirus IgM antibodies requires additional testing, as described in the Scope of Authorization of this letter (Section II) and in the authorized Instructions for Use document, and/or consideration alongside test results for other patient-matched specimens using the latest CDC guideline for the diagnosis of Zika virus infection.

On February 26, 2016, 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 United States citizens living abroad and that involves Zika virus.<sup>2</sup> 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

<sup>1</sup> For ease of reference, this letter will refer to "laboratories in the United States 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."

<sup>2</sup> 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 a significant potential for a public health emergency.

Page 2 – Ms. Raychaudhuri, InBios International, Inc.

diagnosis of Zika virus infection, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).<sup>3</sup>

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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA (as described in the Scope of Authorization section of this letter (Section II)) in individuals meeting CDC Zika virus clinical criteria (e.g., a history of 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 presumptive 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA for the presumptive detection of Zika virus-specific IgM antibodies 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA may be effective in diagnosing Zika virus infection, and that the known and potential benefits of the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA for diagnosing Zika virus infection outweigh the known and potential risks of such product, when, for presumptive Zika positive, possible Zika positive, and presumptive other flavivirus positive results, additional testing (as described in the Instructions for Use document) is performed and/or test results for other patient-matched specimens (using the latest CDC guideline for the diagnosis of Zika virus infection) are considered; and
3. There is no adequate, approved, and available alternative to the emergency use of the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA for diagnosing Zika virus infection.<sup>4</sup>

### **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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA by authorized laboratories for the presumptive detection of Zika virus-specific IgM antibodies in individuals meeting CDC Zika virus clinical criteria (e.g., a history of 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

<sup>3</sup> HHS. *Determination and Declaration Regarding Emergency Use of In Vitro Diagnostic Tests for Detection of Zika Virus and/or Diagnosis of Zika Virus Infection*. 81 Fed. Reg. 10878 (March 2, 2016).

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

Page 3 – Ms. Raychaudhuri, InBios International, Inc.

criteria for which Zika virus testing may be indicated) when, for presumptive Zika positive, possible Zika positive, and presumptive other flavivirus positive results, additional testing (as described in the Instructions for Use document) is performed<sup>5</sup> and/or test results for other patient-matched specimens (using the latest CDC guideline for the diagnosis of Zika virus infection) are considered.

#### **The Authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA**

The ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA is an IgM antibody capture enzyme-linked immunosorbent assay for the *in vitro* presumptive detection of Zika virus-specific IgM antibodies in human sera and other authorized specimen types from individuals meeting CDC Zika virus clinical criteria (e.g., a history of 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 test procedure is based on capturing human IgM antibodies from the patient specimen on a microtiter plate using anti-human-IgM antibody followed by the addition of Zika virus specific antigen and detector conjugate.

One of the limitations of this test is the possibility of false positive results in patients with a history of infection with other flaviviruses. For presumptive Zika positive, possible Zika positive, and presumptive other flavivirus positive specimens, additional testing (as described in the Instructions for Use document) and/or consideration of test results for other patient-matched specimens, using the latest CDC guideline for the diagnosis of Zika virus infection, is therefore required to confirm Zika virus infection.

The assay uses a purified antibody specific for human IgM that is immobilized on a test plate to capture IgM antibodies from a human specimen. A serum specimen from a patient and positive and negative controls are added to the test plate, and incubated to allow the IgM antibodies from the specimen to bind to the immobilized antibody. After washing, Ready-To-Use Zika virus antigen (Zika Ag), a Cross-reactive Control Antigen (CCA), and a Normal Cell Antigen (NCA) are added separately to appropriate locations on the ELISA plate and allowed to incubate. During incubation the Zika Ag binds to any Zika virus-specific IgM antibodies captured on the plate. Following a washing step, a flavivirus specific monoclonal antibody conjugated to horseradish peroxidase is then added which binds to any immobilized Zika Ag and generates a colorimetric optical signal upon addition of a chromogenic substrate that can be measured by a spectrophotometer or other instruments that may be authorized. Any signals generated in the wells exposed to CCA and NCA are analyzed as part of the test procedure and used to aid in the interpretation of the ELISA results.

The ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA includes the following materials, or other authorized materials:

- **Coated Microtiter Test Strips for IgM:** ELISA plate strip holder with 96 (12x8 strips) polystyrene microtiter wells pre-coated with capture antibodies specific for human IgM.

<sup>5</sup> As discussed in the Instructions for Use document, the additional testing for presumptive Zika positive and possible Zika positive results is to be performed using the latest CDC guideline for the diagnosis of Zika virus infection, and the additional testing for presumptive other flavivirus positive results is to be performed with FDA-cleared Dengue and West Nile virus IgM devices.

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- **ZIKV Sample Dilution Buffer:** The buffer solution is used to dilute all serum specimens and controls prior to testing in the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA.
- **Ready-To-Use ZIKV Recombinant Antigen for IgM (Zika Ag):** The Zika Ag comprises the Zika envelope glycoproteins and is used in the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA.
- **Cross-reactive Control Antigen for ZIKV IgM (CCA):** The CCA cocktail is used to aid in the interpretation of the ELISA results.
- **Normal Cell Antigen for ZIKV IgM (NCA):** The NCA is used to aid in the interpretation of the ELISA results.
- **100X Conjugate for ZIKV IgM:** This is horseradish peroxidase-labeled monoclonal anti-Flavivirus antibody used to generate the optical signal measured by the ELISA spectrophotometer.
- **Conjugate Diluent for ZIKV:** This solution is used to dilute the 100X Conjugate for ZIKV IgM solution during the ELISA procedure.
- **10X Wash Buffer:** Concentrated wash buffer used during the ELISA procedure.
- **Liquid Tetramethylbenzidine Substrate:** Chromogenic substrate that reacts with the horseradish peroxidase conjugate to generate the optical signal measured by the ELISA spectrophotometer.
- **Stop Solution:** Used to terminate the reaction between the chromogenic substrate and the horseradish peroxidase conjugate.

The ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA requires the following control materials or other authorized control materials provided with the kit:

- **ZIKV IgM Positive Control:** The positive control aids in verifying the validity of the kit.
- **ZIKV IgM Negative Control:** The negative control aids in verifying the validity of the kit.

Controls listed above must be included on each 96-well plate. Controls must generate expected results in order for a plate to be considered valid.

The ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA also requires the use of additional materials and ancillary reagents commonly used in clinical laboratories and that are described in the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Instructions for Use.

The above described ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA, when labeled consistently with the labeling authorized by FDA entitled “ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Instructions for Use”

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(available at <http://www.fda.gov/MedicalDevices/%20Safety/EmergencySituations/ucm161496.htm>), 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. This labeling may be revised by InBios in consultation with, and with concurrence of, the Division of Microbiology Devices (DMD)/Office of In Vitro Diagnostics and Radiological Health (OIR)/Center for Devices and Radiological Health (CDRH).

The above described ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to health care providers, pregnant women, and other patients:

- Fact Sheet for Health Care Providers: Interpreting ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Results
- Fact Sheet for Pregnant Women: Understanding Results from the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA
- Fact Sheet for Patients: Understanding Results from the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA

Other Fact Sheets developed by InBios in consultation with, and with concurrence of, the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and DMD/OIR/CDRH may be authorized to accompany the above described ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA and to be made available to health care providers, pregnant women, and other patients.

As described in Section IV below, InBios is also authorized to make available additional information relating to the emergency use of the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA in the specified population, when used for presumptive detection of Zika virus-specific IgM antibodies 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA may be effective in the 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA, when used 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.

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The emergency use of the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA described above is authorized to diagnose Zika virus infection in individuals meeting CDC Zika virus clinical criteria (e.g., a history of 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).

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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA 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 ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA.
- 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:

#### InBios and Its Authorized Distributor(s)

- A. InBios and its authorized distributor(s) will distribute the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA with the authorized labeling only to authorized laboratories. InBios may request changes to the authorized labeling. Such requests will be made by InBios in consultation with, and require concurrence of, DMD/OIR/CDRH.
- B. InBios and its authorized distributor(s) will provide to authorized laboratories the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Health Care Providers, the

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authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Pregnant Women, and the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Patients, and any additional ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheets for Health Care Providers, Pregnant Women, and Patients that OCET/OCS/OC and DMD/OIR/CDRH may authorize.

- C. InBios and its authorized distributor(s) will make available on their websites the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Health Care Providers, the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Pregnant Women, and the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Patients, and any additional ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheets for Health Care Providers, Pregnant Women, and Patients that OCET/OCS/OC and DMD/OIR/CDRH may authorize.
- D. InBios 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. InBios and its authorized distributor(s) will ensure that authorized laboratories using the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>6</sup>
- F. Through a process of inventory control, InBios and its authorized distributor(s) will maintain records of device usage.
- G. InBios and its authorized distributor(s) will collect information on the performance of the assay. InBios will report to FDA any suspected occurrence of false negative results and significant deviations from the established performance characteristics of the assay of which InBios becomes aware.
- H. InBios and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA that is consistent with, and does not exceed, the terms of this letter of authorization.

**InBios**

- I. InBios will notify FDA of any authorized distributor(s) of the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA, including the name, address, and phone number of any authorized distributor(s).
- J. InBios 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).

<sup>6</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that InBios and authorized laboratories consult with the applicable country, state, or territory health department(s). According to CDC, Zika is a nationally notifiable condition (see <http://www.cdc.gov/zika/>).

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- K. InBios may request changes to the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Health Care Providers, the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Pregnant Women, and the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheet for Patients. InBios may also request that InBios develop new ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheets for Health Care Providers, Pregnant Women, and Patients, if appropriate, and may request changes to such Fact Sheets. All such requests listed in this condition of authorization will be made by InBios in consultation with, and require concurrence of, OCET/OCS/OC and DMD/OIR/CDRH.
- L. InBios may request the addition of other instruments for use with the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA. Such requests will be made by InBios in consultation with, and require concurrence of, DMD/OIR/CDRH.
- M. InBios may request the addition of other ancillary reagents for use with the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA. Such requests will be made by InBios in consultation with, and require concurrence of, DMD/OIR/CDRH.
- N. InBios may request the addition of other specimen types for use with the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA. Such requests will be made by InBios in consultation with, and require concurrence of, DMD/OIR/CDRH.
- O. InBios may request the addition of other control materials for use with the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA. Such requests will be made by InBios in consultation with, and require concurrence of, DMD/OIR/CDRH.
- P. InBios may request substitution for or changes to the authorized materials used in the detection process of the human anti-Zika IgM in the specimen. Such requests will be made by InBios in consultation with, and require concurrence of, DMD/OIR/CDRH.
- Q. InBios will track adverse events and report to FDA under 21 CFR Part 803.
- R. InBios will evaluate the performance of the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA with a FDA-recommended or established panel(s) of characterized clinical specimens, and will submit that performance data to FDA. After DMD/OIR/CDRH's review of and concurrence with the data, InBios will update its labeling, in consultation with, and with concurrence of, DMD/OIR/CDRH, to reflect the additional testing.

**Authorized Laboratories**

- S. Authorized laboratories will include with reports of the results of the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA the authorized Fact Sheet for Health Care Providers, the authorized Fact Sheet for Pregnant Women, and the authorized Fact Sheet for Patients, and any additional ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA Fact Sheets for Health Care Providers, Pregnant Women, and Patients that OCET/OCS/OC and DMD/OIR/CDRH may authorize. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

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- T. Authorized laboratories will perform the ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA on serum or with other authorized specimen types.
- U. Within the United States and its territories, authorized laboratories will report all presumptive Zika positive, possible Zika positive, and presumptive other flavivirus positive results to InBios.
- V. Authorized laboratories will have a process in place to assure that, for presumptive Zika positive, possible Zika positive, and presumptive other flavivirus positive results, additional testing (as described in the Instructions for Use document) is performed and/or test results for other patient-matched specimens, using the latest CDC guideline for the diagnosis of Zika virus infection, are considered.
- W. Authorized laboratories will have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>7</sup>
- X. Authorized laboratories will collect information on the performance of the assay and report to InBios any suspected occurrence of false negative results and significant deviations from the established performance characteristics of which they become aware.
- Y. All laboratory personnel using the assay should be appropriately trained in performing and interpreting immunoassays techniques, use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.

**InBios, Its Authorized Distributor(s), and Authorized Laboratories**

- Z. InBios, 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**

- AA. All advertising and promotional descriptive printed matter relating to the use of the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA shall be consistent with the authorized 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.
- BB. All advertising and promotional descriptive printed matter relating to the use of the authorized ZIKV *Detect*<sup>TM</sup> IgM Capture ELISA 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;

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

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- This test has been authorized only for the diagnosis of Zika virus infection 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* 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.

No advertising or promotional descriptive printed matter relating to the use of the authorized ZIKV *Detect*<sup>™</sup> IgM Capture ELISA may represent or suggest that this test is safe or effective for the diagnosis of Zika virus infection.

The emergency use of the authorized ZIKV *Detect*<sup>™</sup> IgM Capture ELISA 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



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

August 26, 2016

Jintao Chen, Ph.D.  
Director, Regulatory Affairs  
Roche Molecular Systems, Inc.  
4300 Hacienda Drive  
Pleasanton, CA 94588

Dear Dr. Chen:

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 Roche Molecular Systems, Inc.'s *LightMix*<sup>®</sup> *Zika rRT-PCR Test* for the qualitative detection of RNA from Zika virus in human serum and EDTA plasma 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).<sup>1</sup> 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,<sup>2</sup> approximately 7 days following onset of symptoms, if present. Positive results are indicative of current infection.

On February 26, 2016, 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.<sup>3</sup> 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

<sup>1</sup> 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."

<sup>2</sup> Available at <http://www.cdc.gov/zika/laboratories/lab-guidance.html> (last updated on August 24, 2016).

<sup>3</sup> 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 a significant potential for a public health emergency.

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and/or diagnosis of Zika virus infection, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).<sup>4</sup>

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*<sup>®</sup> *Zika rRT-PCR Test* (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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test* 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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test*, 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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test* 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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test* for detecting Zika virus and diagnosing Zika virus infection.<sup>5</sup>

### **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*<sup>®</sup> *Zika rRT-PCR Test* 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).

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<sup>4</sup> HHS. *Determination and Declaration Regarding Emergency Use of in Vitro Diagnostic Tests for Detection of Zika Virus and/or Diagnosis of Zika Virus Infection*. 81 Fed. Reg. 10878 (March 2, 2016).

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

**The Authorized *LightMix*<sup>®</sup> *Zika* rRT-PCR Test**

The *LightMix*<sup>®</sup> *Zika* rRT-PCR Test is a real-time reverse transcription polymerase chain reaction (rRT-PCR) assay for the qualitative detection of RNA from Zika virus in human serum, EDTA plasma, and other authorized specimen types.

To perform the *LightMix*<sup>®</sup> *Zika* rRT-PCR Test, specimens are first extracted to isolate the Zika virus RNA. Nucleic acids are isolated and purified from the sample using either the automated Roche MagNA Pure 96 System together with the Roche MagNA Pure 96 DNA and Viral NA Large Volume reagent kit or the MagNA Pure Compact Instrument and MagNA Pure Compact Nucleic Acid Isolation Kit I - Large Volume, or other authorized extraction methods.

The purified RNA is reverse transcribed into cDNA, which is then amplified. The Roche LightCycler<sup>®</sup> Multiplex RNA Virus Master reagent, which contains reagents and enzymes for reverse transcription and specific amplification of the Zika virus targeted region, is added. The rRT-PCR is performed on the Roche LightCycler<sup>®</sup> 480 Instrument II, Roche cobas z 480 Analyzer (open channel) or other authorized instruments.

The *LightMix*<sup>®</sup> *Zika* rRT-PCR Test includes the following materials, or other authorized materials:

- **LightMix<sup>®</sup> Zika rRT-PCR Test PSR (1 Vial):** Contains pathogen-specific reagent (PSR), i.e., lyophilized primers and FAM-labeled probe that specifically detect Zika viral RNA.
- **LightMix<sup>®</sup> Zika rRT-PCR Test ivRNA Positive Control (1 Vial):** Contains lyophilized synthetic RNA, designed to react with the LightMix<sup>®</sup> Zika rRT-PCR Test PSR to indicate whether the *LightMix*<sup>®</sup> *Zika* rRT-PCR Test has worked properly.

The *LightMix*<sup>®</sup> *Zika* rRT-PCR Test 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 *LightMix*<sup>®</sup> *Zika* rRT-PCR Test Instructions for Use:

- **Negative Process Control:** PCR-grade water is used in place of clinical samples from the beginning of the sample extraction process. The Negative Process Control is run in parallel with clinical specimens in each specimen extraction run.
- **Negative rRT-PCR Control:** PCR-grade water is used at the rRT-PCR step to test for absence of cross-contamination.
- **Positive Control:** Contains a synthetic RNA transcript containing the virus region targeted by the *LightMix*<sup>®</sup> *Zika* rRT-PCR Test. The Positive Control is used starting at the rRT-PCR step, then run in parallel with clinical specimens and the negative controls in each assay run.
- **Extraction Control:** The Extraction Control is the Roche RNA Process Control LSR (RPC). The Extraction Control is run together with every clinical specimen from the

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beginning of the extraction process and is detected by rRT-PCR using a primer pair and a Cy5-labeled probe that are different from the Zika virus specific primer pair and probe.

The *LightMix*<sup>®</sup> *Zika rRT-PCR Test* also requires the use of additional materials and ancillary reagents commonly used in clinical laboratories and that are described in the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Instructions for Use.

The above described *LightMix*<sup>®</sup> *Zika rRT-PCR Test*, when labeled consistently with the labeling authorized by FDA entitled “Instructions for Use: *LightMix*<sup>®</sup> *Zika rRT-PCR Test*” (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), which may be revised by Roche Molecular Systems, Inc. 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 *LightMix*<sup>®</sup> *Zika 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 providers, pregnant women, and other patients:

- Fact Sheet for Health Care Providers: Interpreting *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Results
- Fact Sheet for Pregnant Women: Understanding Results from the *LightMix*<sup>®</sup> *Zika rRT-PCR Test*
- Fact Sheet for Patients: Understanding Results from the *LightMix*<sup>®</sup> *Zika rRT-PCR Test*

As described in Section IV below, Roche Molecular Systems, Inc., Roche Diagnostics, and other authorized distributor(s) are also authorized to make available additional information relating to the emergency use of the authorized *LightMix*<sup>®</sup> *Zika 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*<sup>®</sup> *Zika rRT-PCR Test* 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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test* 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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test*, 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

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(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 *LightMix*<sup>®</sup> *Zika 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 HHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the *LightMix*<sup>®</sup> *Zika rRT-PCR Test* 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 geographic regions 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 *LightMix*<sup>®</sup> *Zika 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*<sup>®</sup> *Zika 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<sup>6</sup>

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

#### **Roche Molecular Systems, Inc., Roche Diagnostics, and/or Other Authorized Distributor(s)<sup>7</sup>**

<sup>6</sup> Unless otherwise specified, Roche Molecular Systems, Inc. and Roche Diagnostics are the responsible parties for satisfying the Conditions of Authorization.

<sup>7</sup> At the time of authorization, Roche Diagnostics is the sole authorized distributor of the *LightMix*<sup>®</sup> *Zika rRT-PCR Test*, manufactured by TIB MOLBIOL GmbH.

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- A. Roche Diagnostics and other authorized distributor(s) will distribute the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* with the authorized labeling only to authorized laboratories. Changes to the authorized labeling may be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- B. Roche Diagnostics and other authorized distributor(s) will provide to authorized laboratories the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Health Care Providers, the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Pregnant Women, and the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Patients.
- C. Roche Diagnostics and other authorized distributor(s) will make available on their websites the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Health Care Providers, the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Pregnant Women, and the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Patients.
- D. Roche Diagnostics and other authorized distributor(s) will inform authorized laboratories and relevant public health authority(ies) of this EUA, including the terms and conditions herein.
- E. Roche Diagnostics and other authorized distributor(s) will ensure that the authorized laboratories using the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>8</sup>
- F. Through a process of inventory control, Roche Diagnostics and other authorized distributor(s) will maintain records of device usage.
- G. Roche Diagnostics and other authorized distributor(s) will collect information on the performance of the test and provide this information to Roche Molecular Systems, Inc. Roche Molecular Systems, Inc. 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 Roche Molecular Systems, Inc. becomes aware.
- H. Roche Molecular Systems, Inc., Roche Diagnostics, and other authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* that is consistent with, and does not exceed, the terms of this letter of authorization.

**Roche Molecular Systems, Inc.**

- I. Roche Molecular Systems, Inc. will notify FDA of any additional authorized distributor(s) of the *LightMix*<sup>®</sup> *Zika rRT-PCR Test*, including the name, address, and phone number of any additional, authorized distributor(s).

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<sup>8</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Roche Molecular Systems, Inc., Roche Diagnostics, 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/>).

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- J. Roche Molecular Systems, Inc. will provide Roche Diagnostics, other authorized distributor(s), and TIB MOLBIOL GmbH with a copy of this EUA, and communicate to Roche Diagnostics, other authorized distributor(s), and TIB MOLBIOL GmbH any subsequent amendments that might be made to this EUA and its authorized accompanying materials (e.g., Fact Sheets, Instructions for Use).
- K. Roche Molecular Systems, Inc. may request changes to the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Health Care Providers, the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Pregnant Women, and the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* Fact Sheet for Patients. Such requests will be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- L. Roche Molecular Systems, Inc. may request the addition of other instruments for use with the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test*. Such requests will be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- M. Roche Molecular Systems, Inc. may request the addition of other extraction methods for use with the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test*. Such requests will be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- N. Roche Molecular Systems, Inc. may request the addition of other specimen types for use with the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test*. Such requests will be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- O. Roche Molecular Systems, Inc. may request the addition of other control materials for use with the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test*. Such requests will be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- P. Roche Molecular Systems, Inc. may request the addition and/or substitution of other ancillary reagents and materials for use with the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test*. Such requests will be made by Roche Molecular Systems, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.
- Q. Roche Molecular Systems, Inc. will assess traceability<sup>9</sup> of the *LightMix*<sup>®</sup> *Zika rRT-PCR Test* with FDA-recommended reference material(s). After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, Roche Molecular Systems, Inc. will update its labeling to reflect the additional testing.
- R. Roche Molecular Systems, Inc., assuming the medical device reporting responsibilities of the manufacturer of the *LightMix*<sup>®</sup> *Zika rRT-PCR Test*, will track adverse events and report to FDA under 21 CFR Part 803.

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<sup>9</sup> Traceability refers to tracing analytical sensitivity/reactivity back to a FDA recommended reference material.

**Authorized Laboratories**

- S. Authorized laboratories will include with reports of the results of the *LightMix*<sup>®</sup> *Zika rRT-PCR Test* the authorized Fact Sheet for Health Care Providers, the authorized Fact Sheet for Pregnant Women, 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 *LightMix*<sup>®</sup> *Zika rRT-PCR Test* on the Roche LightCycler<sup>®</sup> 480 Instrument II, Roche cobas z 480 Analyzer (open channel), or other authorized instruments.
- U. Authorized laboratories will perform the *LightMix*<sup>®</sup> *Zika rRT-PCR Test* using the automated Roche MagNA Pure 96 System together with the Roche MagNA Pure 96 DNA and Viral NA Large Volume reagent kit, the MagNA Pure Compact Instrument and MagNA Pure Compact Nucleic Acid Isolation Kit I - Large Volume, or other authorized extraction methods.
- V. Authorized laboratories will perform the *LightMix*<sup>®</sup> *Zika rRT-PCR Test* on human serum, EDTA plasma, or with other authorized specimen types.
- W. Authorized laboratories will have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.<sup>10</sup>
- X. Authorized laboratories will collect information on the performance of the test and report to Roche Diagnostics any suspected occurrence of false positive or false negative results of which they become aware.
- Y. All laboratory personnel using the test should be appropriately trained in rRT-PCR techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling.

**Roche Molecular Systems, Inc., Roche Diagnostics, Other Authorized Distributor(s), and Authorized Laboratories**

- Z. Roche Molecular Systems, Inc., Roche Diagnostics, other 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**

- AA. All advertising and promotional descriptive printed matter relating to the use of the authorized *LightMix*<sup>®</sup> *Zika 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

<sup>10</sup> For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Roche Molecular Systems, Inc., Roche Diagnostics, 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/>).

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requirements set forth in the Act and FDA regulations.

BB. All advertising and promotional descriptive printed matter relating to the use of the authorized *LightMix*<sup>®</sup> *Zika 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 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.

No advertising or promotional descriptive printed matter relating to the use of the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* may represent or suggest that this test is safe or effective for the diagnosis of Zika virus infection.

The emergency use of the authorized *LightMix*<sup>®</sup> *Zika rRT-PCR Test* 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,



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

Enclosures

[END PHOTO]

Dated: October 24, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-26066 Filed: 10/27/2016 8:45 am; Publication Date: 10/28/2016]