DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

June 17, 2016

Ken Hood, MBA
Senior Director, Regulatory Affairs
Hologic, Inc.
10210 Genetic Center Drive
San Diego, CA 92121

Dear Mr. Hood:

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 Hologic, Inc.'s Aptima® Zika Virus assay for the qualitative detection of RNA from Zika virus in human serum and plasma specimens 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).[1] Assay results are for the identification of Zika viral RNA. Zika viral RNA is generally detectable in serum during the acute phase of infection (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 United States citizens living abroad and that involves Zika virus.[2] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).[3]

---

[1] For ease of reference, this letter will refer to "laboratories in the United States (U.S.) that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, to perform high complexity tests, or by similarly qualified non-U.S. laboratories" as "authorized laboratories."

[2] 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.

[3] 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).

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 Aptima® Zika Virus 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 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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 Aptima® Zika Virus assay for detecting Zika virus and diagnosing Zika virus infection.[4]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized Aptima® Zika Virus 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 epidemiologic criteria for which Zika virus testing may be indicated).

The Authorized Aptima® Zika Virus Assay

Hologic, Inc.'s Aptima® Zika Virus assay is a transcription-based nucleic acid amplification test for the *in vitro* qualitative detection of Zika virus RNA in serum and plasma specimens collected from 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.,

[4] 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 Aptima® Zika Virus assay can also be used with other authorized specimen types. The Aptima® Zika Virus assay involves three main steps, which take place in a single tube: sample preparation, Zika virus RNA target amplification by transcription-mediated amplification, and detection of the amplification products (amplicon) by the Hybridization Protection Assay. The Aptima® Zika Virus assay is performed using the Panther System or other authorized instruments. The Panther System automates the processing, interpretation, and management of nucleic acid testing. The assay incorporates an internal control, or other authorized control materials, to monitor nucleic acid capture, amplification, and detection, as well as operator or instrument error.

The Aptima® Zika Virus assay kit includes the following materials or other authorized materials: Internal Control Reagent, Target Capture Reagent, Amplification Reagent, Enzyme Reagent, Probe Reagent, Selection Reagent, and Aptima® Zika Virus assay positive and negative calibrators. The following ancillary kits or other authorized ancillary reagents are required for Aptima® Zika Virus assay, but not included with the test: Aptima® Auto Detect Reagents kit and Aptima® Assay Fluids kit.

The above described Aptima® Zika Virus assay, when labeled consistently with the labeling authorized by FDA entitled "Aptima® Zika Virus assay Instructions for Use" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by Hologic, 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 Aptima® Zika Virus 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 Aptima® Zika Virus Assay Test Results
- Fact Sheet for Pregnant Women: Understanding Results from the Aptima® Zika Virus Assay Test
- Fact Sheet for Patients: Understanding Results from the Aptima® Zika Virus Assay

As described in Section IV below, Hologic, Inc. is also authorized to make available additional information relating to the emergency use of the authorized Aptima® Zika Virus 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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 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 Aptima® Zika Virus 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 Aptima® Zika Virus 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:

Hologic, Inc. and Its Authorized Distributor(s)

A. Hologic, Inc. and its authorized distributor(s) will distribute the authorized Aptima® Zika Virus assay with the authorized labeling, as may be revised by Hologic, Inc. in consultation with DMD/OIR/CDRH, only to authorized laboratories.

B. Hologic, Inc. and its authorized distributor(s) will provide to authorized laboratories the authorized Aptima® Zika Virus Assay Fact Sheet for Health Care Providers, the authorized Aptima® Zika Virus Assay Fact Sheet for Pregnant Women, and the authorized Aptima® Zika Virus Assay Fact Sheet for Patients.

C. Hologic, Inc. and its authorized distributor(s) will make available on their website(s) the authorized Aptima® Zika Virus Assay Fact Sheet for Health Care Providers, the authorized Aptima® Zika Virus Assay Fact Sheet for Pregnant Women, and the authorized Aptima® Zika Virus Assay Fact Sheet for Patients.

D. Hologic, Inc. 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. Hologic, Inc. and its authorized distributor(s) will ensure that authorized laboratories using the authorized Aptima® Zika Virus assay have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.[5]

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

G. Hologic, Inc. and its authorized distributor(s) will collect information on the performance of the test. Hologic, 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 Hologic, Inc. becomes aware.

H. Hologic, Inc. and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized Aptima® Zika Virus assay that is consistent with, and does not exceed, the terms of this letter of authorization.

Hologic, Inc.

I. Hologic, Inc. will notify FDA of any authorized distributor(s) of the Aptima® Zika Virus assay, including the name, address, and phone number of any authorized distributor(s).

J. Hologic, Inc. 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

[5] For questions related to reporting Zika test results to relevant public health authorities, it is recommended that Hologic, Inc. 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/.

made to this EUA and its authorized accompanying materials (e.g., fact sheets, instructions for use).

K. Hologic, Inc. may request changes to the authorized Aptima® Zika Virus Assay Fact Sheet for Health Care Providers, the authorized Aptima® Zika Virus Assay Fact Sheet for Pregnant Women, and the authorized Aptima® Zika Virus Assay Fact Sheet for Patients. Such requests will be made by Hologic, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.

K. Hologic, Inc. may request the addition of other instruments for use with the authorized Aptima® Zika Virus assay. Such requests will be made by Hologic, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.

L. Hologic, Inc. may request the addition of other ancillary reagents for use with the authorized Aptima® Zika Virus assay. Such requests will be made by Hologic, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.

M. Hologic, Inc. may request the addition of other specimen types for use with the authorized Aptima® Zika Virus assay. Such requests will be made by Hologic, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.

N. Hologic, Inc. may request the addition of other control materials for use with the authorized Aptima® Zika Virus assay. Such requests will be made by Hologic, Inc. in consultation with, and require concurrence of, DMD/OIR/CDRH.

O. Hologic, Inc. will assess traceability[6] of the Aptima® Zika Virus assay with an FDA-recommended reference material. After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, Hologic, Inc. will update its labeling to reflect the additional testing.

P. Hologic, Inc. will track adverse events and report to FDA under 21 CFR Part 803.

Authorized Laboratories

Q. Authorized laboratories will include with reports of the results of the Aptima® Zika Virus 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.

R. Authorized laboratories will perform the Aptima® Zika Virus assay on the Panther System or other authorized instruments.

S. Authorized laboratories will perform the Aptima® Zika Virus assay using the Aptima® Auto Detect Reagents kit and Aptima® Assay Fluids kit or other authorized ancillary reagents.

---

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

T. Authorized laboratories will perform the Aptima® Zika Virus assay on serum, plasma, or other authorized specimen types.

U. Authorized laboratories will have a process in place for reporting test results to health care providers and relevant public health authorities, as appropriate.[7]

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

W. All laboratory personnel using the test should be appropriately trained in nucleic acid amplification techniques and use appropriate laboratory and personal protective equipment when handling this kit.

Hologic, Inc., Its Authorized Distributor(s) and Authorized Laboratories

X. Hologic, Inc., 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

Y. All advertising and promotional descriptive printed matter relating to the use of the authorized Aptima® Zika Virus 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.

Z. All advertising and promotional descriptive printed matter relating to the use of the authorized Aptima® Zika Virus 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.

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

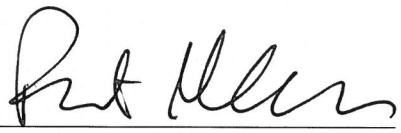
No advertising or promotional descriptive printed matter relating to the use of the authorized Aptima® Zika Virus assay may represent or suggest that this test is safe or effective for the diagnosis of Zika virus infection.

The emergency use of the authorized Aptima® Zika Virus 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