DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

April 5, 2017

Mari Meyer
Vice President, Regulatory and Clinical Affairs, North America
DiaSorin Incorporated
1951 Northwestern Avenue
Stillwater, MN 55082

Dear Ms. Meyer:

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 DiaSorin Incorporated's ("DiaSorin") LIAISON® XL Zika Capture IgM Assay for the presumptive qualitative 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 or moderate complexity tests, or by similarly qualified non-U.S. laboratories,[1] pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3). Specimens used with the LIAISON® XL Zika Capture IgM Assay should be collected between 8 days and 10 weeks after onset of symptoms or risk of exposure. Where there are presumptive Zika IgM positive and presumptive recent Zika positive results from the LIAISON® XL Zika Capture IgM Assay, confirmation of the presence of anti-Zika 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 testing algorithms 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.[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

[1] 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 or moderate 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.

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

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 LIAISON® XL Zika Capture IgM Assay (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 qualitative 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 LIAISON® XL Zika Capture IgM Assay for the presumptive qualitative detection of Zika virus 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 LIAISON® XL Zika Capture IgM Assay may be effective in diagnosing recent Zika virus infection, and that the known and potential benefits of the LIAISON® XL Zika Capture IgM Assay for diagnosing Zika virus infection outweigh the known and potential risks of such product, when, for presumptive Zika IgM positive and presumptive recent Zika 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 testing algorithms 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 LIAISON® XL Zika Capture IgM Assay for 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 LIAISON® XL Zika Capture IgM Assay by authorized laboratories for the presumptive qualitative detection of Zika virus 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

[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).

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

epidemiological criteria for which Zika virus testing may be indicated) when, for presumptive Zika IgM positive and presumptive recent Zika positive results, additional testing (as described in the Instructions for Use document) is performed[5] and/or test results for other patient-matched specimens (using the latest CDC testing algorithms for the diagnosis of Zika virus infection) are considered.

The Authorized LIAISON® XL Zika Capture IgM Assay

The LIAISON® XL Zika Capture IgM Assay is an automated immunoassay utilizing chemiluminescent detection technology for the *in vitro* presumptive qualitative detection of Zika virus 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 and IgG antibodies from the patient specimen using magnetic particles functionalized with either anti-human-IgM antibody or anti-human-IgG antibody followed by the addition of Zika virus specific NS1 antigen and detector conjugate. The IgG result is used as an aid in the identification of a recent Zika viral infection when the IgM result falls in the dual cut-off zone as outlined in the LIAISON® XL Zika Capture IgM Assay Instructions for Use.

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 IgM positive or presumptive recent Zika positive results, 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 testing algorithms for the diagnosis of Zika virus infection, is therefore required to confirm Zika virus infection.

The automated assay uses two separate reagent packs (ZIKV-M and ZIKV-C Reagent Integrals) which contain magnetic beads coated with either a monoclonal anti-human-IgM antibody or a monoclonal anti-human-IgG antibody. Calibrators, patient sera or controls are then incubated with both reagent packs during the LIAISON® XL Zika Capture IgM Assay procedure and either human IgM antibodies or human IgG antibodies are captured by the appropriate magnetic particles. Following a wash cycle, the magnetic particles are then incubated with a recombinant Zika virus NS1 antigen-isoluminol conjugate, washed and reagents added to induce chemiluminescence that can be measured by the LIAISON® XL Analyzer or other instruments that may be authorized. The LIAISON® XL Zika Capture IgM Assay requires both the ZIKV-M and ZIKV-C Reagent Integrals to be calibrated under specific conditions described in the authorized LIAISON® XL Zika Capture IgM Assay Instructions for Use.

The LIAISON® XL Zika Capture IgM Assay includes the following materials, or other authorized materials:

- **ZIKV-M Reagent Integral:**

[5] As discussed in the Instructions for Use document, the additional testing for presumptive Zika IgM positive or presumptive recent Zika positive results is to be performed using the latest CDC testing algorithms for the diagnosis of Zika virus infection.

  - Magnetic Particles – coated with a mouse monoclonal antibody to human IgM
  - Calibrator 1 - Human serum/defibrinated plasma containing Zika virus IgM
  - Calibrator 2 - Human serum/defibrinated plasma containing Zika virus IgM
  - Specimen Diluent
  - Assay Buffer

- **ZIKV-C Reagent Integral:**
  - Magnetic Particles – coated with a mouse monoclonal antibody to human IgG
  - Specimen Diluent
  - Assay Buffer

- **Additional components not on the Reagent Integrals:**
  - ZIKV-M Conjugate Lyophilized – recombinant Zika virus NS1 antigen conjugated to an isoluminol derivative
  - ZIKV-C Conjugate Lyophilized – recombinant Zika virus NS1 antigen conjugated to an isoluminol derivative
  - ZIKV-C Calibrator 1- Human serum/defibrinated plasma containing Zika virus IgG
  - ZIKV-C Calibrator 2- Human serum/defibrinated plasma containing Zika virus IgG

The LIAISON® XL Zika Capture IgM Assay requires the following control materials or other authorized control materials, which are not provided with the test:

- **LIAISON® XL Zika Capture IgM Control Set:** The positive control aids in verifying the validity of the kit.

Controls listed above must be performed once per day of use, or according to the guidelines or requirements of local regulations or accredited organizations. Controls must generate expected results in order for patient results to be considered valid.

The LIAISON® XL Zika Capture IgM Assay also requires the use of additional materials and ancillary reagents commonly used in clinical laboratories and that are described in the authorized LIAISON® XL Zika Capture IgM Assay Instructions for Use.

The above described LIAISON® XL Zika Capture IgM Assay, when labeled consistently with the labeling authorized by FDA entitled "LIAISON® XL Zika Capture IgM Assay Instructions for Use" (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 DiaSorin 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 LIAISON® XL Zika Capture IgM Assay is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Interpreting LIAISON® XL Zika Capture IgM Assay Results

- Fact Sheet for Patients: Understanding Results from the LIAISON® XL Zika Capture IgM Assay

Other Fact Sheets developed by DiaSorin 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 LIAISON® XL Zika Capture IgM Assay and to be made available to healthcare providers and patients.

As described in Section IV below, DiaSorin is also authorized to make available additional information relating to the emergency use of the authorized LIAISON® XL Zika Capture IgM 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 LIAISON® XL Zika Capture IgM Assay in the specified population, when used for presumptive qualitative detection of Zika virus 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 LIAISON® XL Zika Capture IgM Assay may be effective in the diagnosis of recent 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 LIAISON® XL Zika Capture IgM Assay, 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.

The emergency use of the authorized LIAISON® XL Zika Capture IgM 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 LIAISON® XL Zika Capture IgM Assay 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 LIAISON® XL Zika Capture IgM 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 LIAISON® XL Zika Capture IgM 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:

DiaSorin and Its Authorized Distributor(s)

A. DiaSorin and its authorized distributor(s) will distribute the authorized LIAISON® XL Zika Capture IgM Assay with the authorized labeling only to authorized laboratories. DiaSorin may request changes to the authorized labeling. Such requests will be made by DiaSorin in consultation with, and require concurrence of, DMD/OIR/CDRH.

B. DiaSorin and its authorized distributor(s) will provide to authorized laboratories the authorized LIAISON® XL Zika Capture IgM Assay Fact Sheet for Healthcare Providers and the authorized LIAISON® XL Zika Capture IgM Assay Fact Sheet for Patients, and any additional LIAISON® XL Zika Capture IgM Assay Fact Sheets for Healthcare Providers and Patients that OCET/OCS/OC and DMD/OIR/CDRH may authorize.

C. DiaSorin and its authorized distributor(s) will make available on their websites the authorized LIAISON® XL Zika Capture IgM Assay Fact Sheet for Healthcare Providers and the authorized LIAISON® XL Zika Capture IgM Assay Fact Sheet for Patients, and any additional LIAISON® XL Zika Capture IgM Assay Fact Sheets for Healthcare Providers and Patients that OCET/OCS/OC and DMD/OIR/CDRH may authorize.

D. DiaSorin 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. DiaSorin and its authorized distributor(s) will ensure that authorized laboratories using the authorized LIAISON® XL Zika Capture IgM Assay have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.[6]

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

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

H. DiaSorin and its authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized LIAISON® XL Zika Capture IgM Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

DiaSorin

I. DiaSorin will notify FDA of any authorized distributor(s) of the LIAISON® XL Zika Capture IgM Assay, including the name, address, and phone number of any authorized distributor(s).

J. DiaSorin 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. DiaSorin may request changes to the authorized LIAISON® XL Zika Capture IgM Assay Fact Sheet for Healthcare Providers and the authorized LIAISON® XL Zika Capture IgM Assay Fact Sheet for Patients. DiaSorin may also develop new LIAISON® XL Zika Capture IgM Assay Fact Sheets for Healthcare Providers 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 DiaSorin in consultation with, and require concurrence of, OCET/OCS/OC and DMD/OIR/CDRH.

L. DiaSorin may request the addition of other instruments for use with the authorized LIAISON® XL Zika Capture IgM Assay. Such requests will be made by DiaSorin in consultation with, and require concurrence of, DMD/OIR/CDRH.

M. DiaSorin may request the addition of other ancillary reagents for use with the authorized LIAISON® XL Zika Capture IgM Assay. Such requests will be made by DiaSorin in

[6] For questions related to reporting Zika test results to relevant public health authorities, it is recommended that DiaSorin 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/).

consultation with, and require concurrence of, DMD/OIR/CDRH.

N. DiaSorin may request the addition of other specimen types for use with the authorized LIAISON® XL Zika Capture IgM Assay. Such requests will be made by DiaSorin in consultation with, and require concurrence of, DMD/OIR/CDRH.

O. DiaSorin may request the addition of other control materials for use with the authorized LIAISON® XL Zika Capture IgM Assay. Such requests will be made by DiaSorin in consultation with, and require concurrence of, DMD/OIR/CDRH.

P. DiaSorin may request substitution for or changes to the authorized materials used in the detection process of the human anti-Zika IgM and human anti-Zika IgG in the specimen. Such requests will be made by DiaSorin in consultation with, and require concurrence of, DMD/OIR/CDRH.

Q. DiaSorin will track adverse events and report to FDA under 21 CFR Part 803.

R. DiaSorin will evaluate the performance of the LIAISON® XL Zika Capture IgM Assay with any 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, DiaSorin will update its labeling, in consultation with, and with concurrence of, DMD/OIR/CDRH, to reflect the additional testing.

S. DiaSorin will assess traceability[7] of the LIAISON® XL Zika Capture IgM Assay with any FDA-recommended reference material(s). After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, DiaSorin will update its labeling to reflect the additional testing.

T. DiaSorin will track the performance of the LIAISON® XL Zika Capture IgM Assay and report to DMD/OIR/CDRH on a semi-annual basis.

Authorized Laboratories

U. Authorized laboratories will include with reports of the results of the LIAISON® XL Zika Capture IgM Assay the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients, and any additional LIAISON® XL Zika Capture IgM Assay Fact Sheets for Healthcare Providers 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.

V. Authorized laboratories will perform the LIAISON® XL Zika Capture IgM Assay on serum or with other authorized specimen types.

W. Authorized laboratories will perform the LIAISON® XL Zika Capture IgM Assay on the LIAISON® XL Analyzer or on other authorized instruments.

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

X. Within the United States and its territories, authorized laboratories will report all presumptive Zika IgM positive and presumptive recent Zika positive results to DiaSorin.

Y. Authorized laboratories will have a process in place to assure that, for presumptive Zika IgM positive and presumptive recent Zika 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 testing algorithms for the diagnosis of Zika virus infection, are considered.

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

AA. Authorized laboratories will collect information on the performance of the assay and report to DMD/OIR/CDRH (*via* email CDRH-EUA-Reporting@fda.hhs.gov) and DiaSorin any suspected occurrence of false negative and false positive results and significant deviations from the established performance characteristics of which they become aware.

BB. All laboratory personnel using the assay must be appropriately trained in performing and interpreting immunoassay techniques, use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the algorithm used for the interpretation of results of the LIAISON® XL Zika Capture IgM Assay.

DiaSorin, Its Authorized Distributor(s), and Authorized Laboratories

CC. DiaSorin, 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

DD. All advertising and promotional descriptive printed matter relating to the use of the authorized LIAISON® XL Zika Capture IgM Assay 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.

EE. All advertising and promotional descriptive printed matter relating to the use of the authorized LIAISON® XL Zika Capture IgM 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;

[8] For questions related to reporting Zika test results to relevant public health authorities, it is recommended that DiaSorin 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/).

- 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 LIAISON® XL Zika Capture IgM 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 LIAISON® XL Zika Capture IgM 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,

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Stephen M. Ostroff, M.D.
Acting Commissioner of Food and Drugs

Enclosures