U.S. FOOD & DRUG ADMINISTRATION

September 27, 2017

Thomas D. Ippolito
Vice President, Clinical and Regulatory Affairs
Chembio Diagnostic Systems, Inc.
3661 Horseblock Road
Medford, NY 11763

Dear Mr. Ippolito:

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 Chembio Diagnostic Systems, Inc.'s ("Chembio") DPP Zika IgM Assay System for the presumptive qualitative detection of Zika virus IgM antibodies in human serum (plain or separation gel) and fingerstick whole blood, EDTA venous whole blood, or EDTA plasma (each collected alongside a patient-matched serum specimen) specimens 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 from symptomatic patients or returning travelers from endemic areas should not be collected prior to 8 days after onset of symptoms or risk of exposure, respectively. Where there are reactive results (i.e., presumptive Zika IgM positive), from the DPP Zika IgM Assay System, 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.[2]

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

[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] Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html (last updated on July 24, 2017).

national security or the health and security of United States citizens living abroad and that involves Zika virus.[3] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostic tests for detection of Zika virus and/or diagnosis of Zika virus infection, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).[4]

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 DPP Zika IgM Assay System (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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System may be effective in diagnosing recent Zika virus infection, and that the known and potential benefits of the DPP Zika IgM Assay System for diagnosing Zika virus infection outweigh the known and potential risks of such product, when, for reactive results (i.e., presumptive Zika IgM positive), 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 DPP Zika IgM Assay System for diagnosing Zika virus infection.[5]

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[3] As amended by the Pandemic and All-Hazards Preparedness Reauthorization Act, Pub. L. No. 113-5, under section 564(b)(1)(C) of the Act, the Secretary may make a determination of a public health emergency, or of a significant potential for a public health emergency.

[4] 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).

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

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 DPP Zika IgM Assay System 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 epidemiological criteria for which Zika virus testing may be indicated) when, for reactive results (i.e., presumptive Zika IgM positive), additional testing (as described in the Instructions for Use document) is performed[6] 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 DPP Zika IgM Assay System

The DPP Zika IgM Assay System is a single-use immunochromatographic lateral flow assay for the *in vitro* presumptive qualitative detection of Zika virus IgM antibodies in human serum (plain or separation gel) and fingerstick whole blood, EDTA venous whole blood, or EDTA plasma (each collected alongside a patient-matched serum specimen) specimens 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 DPP Zika IgM Assay System employs a dual path platform technology and consists of a sample path that distributes sample onto a reagent strip containing a TEST (T) area and a CONTROL (C) area in the test-control window of the test device. The reagent strip is for the detection of ZIKV IgM antibodies. The test procedure is based on capturing human IgM antibodies from the patient specimen in the TEST (T) area that is functionalized with Zika NS1 antigens followed by the addition of an antibody-binding colored conjugate. The patient specimen is collected and then diluted with sample buffer before being applied to the SAMPLE+BUFFER Well#1 of the DPP Zika Test Device. The specimen migrates along the sample path membrane and is delivered to the TEST (T) area of the reagent strip, where Zika NS1 antigens are immobilized. Zika-specific antibodies, if present in the sample, bind to the immobilized NS1 antigens in the TEST (T) area, while non-specific antibodies bind to the Protein A in the CONTROL (C) area. Running buffer is then added into the BUFFER Well #2, which hydrates the dried antibody-binding colored conjugate causing it to migrate to the TEST area. ZIKV IgM antibodies bound to the TEST (T) area will capture the antibody-binding colored conjugate and detection is performed using the Chembio DPP Micro Reader, or other authorized instruments, that uses assay-specific algorithms to verify the presence of the control line and measure color intensity in the TEST (T) area position; it interprets the results using

[6] As discussed in the Instructions for Use document, the additional testing for reactive results (i.e., presumptive Zika IgM positive) is to be performed using the latest CDC testing algorithms for the diagnosis of Zika virus infection.

assay-specific cut-off values, and reports a reactive, nonreactive, or invalid result along with a numerical intensity value for the IgM test line.

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 reactive results (i.e., presumptive Zika IgM positive), 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 DPP Zika IgM Assay System includes use of the DPP Zika Test Device kit and the DPP Micro Reader kit which are comprised of the following materials and instruments, or other authorized materials and instruments:

- The DPP Zika Test Device kit: individually pouched DPP Zika Test Devices each with a desiccant pouch, Microsafe tubes, sample vials, transfer pipets, DPP Zika IgM Sample Buffer- BLUE Cap, DPP Zika IgM Running Buffer – YELLOW Cap, product insert (authorized Instructions for Use) and a quick reference guide.
- The DPP Micro Reader kit: DPP Micro Reader, holder case, USB cable and user manual.

The DPP Zika IgM Assay System requires the following control materials or other authorized control materials, which are not provided with the test:

- DPP Zika IgM Assay Control Pack: DPP Zika Reactive Control, DPP Nonreactive Control and product insert. The assay controls are used to verify and assess the assay performance and verify the user's ability to properly perform the test and to interpret the results.

Quality control requirements should be followed in conformance with local, state, and federal regulations or accreditation requirements and the user laboratory's standard quality control procedures.

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

The above described DPP Zika IgM Assay System, when labeled consistently with the labeling authorized by FDA entitled "DPP Zika IgM Assay System," "DPP Micro Reader," "DPP Zika IgM Assay Control Pack," and "DPP Zika IgM Assay System Quick Reference Instructions," (available at http://www.fda.gov/MedicalDevices/Safety/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 Chembio 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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System Results
- Fact Sheet for Patients: Understanding Results from the DPP Zika IgM Assay System

Other Fact Sheets developed by Chembio 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 DPP Zika IgM Assay System and to be made available to healthcare providers and patients.

As described in Section IV below, Chembio is also authorized to make available additional information relating to the emergency use of the authorized DPP Zika IgM Assay System 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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System, 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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System 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 DPP Zika IgM Assay System.

- 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:

Chembio and Its Authorized Distributor(s)

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

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

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

D. Chembio 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. Chembio and its authorized distributor(s) will ensure that authorized laboratories using the authorized DPP Zika IgM Assay System have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.[7]

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

G. Chembio and its authorized distributor(s) will collect information on the performance of the assay. Chembio 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 Chembio becomes aware.

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

I. Chembio and its authorized distributor(s) will make available the DPP Zika IgM Control Pack control material or other authorized control materials for purchase at the same time as the DPP Zika IgM Assay System.

Chembio

J. Chembio will notify FDA of any authorized distributor(s) of the DPP Zika IgM Assay System, including the name, address, and phone number of any authorized distributor(s).

K. Chembio 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).

L. Chembio may request changes to the authorized DPP Zika IgM Assay System Fact Sheet for Healthcare Providers and the authorized DPP Zika IgM Assay System Fact Sheet for Patients. Chembio may also develop new DPP Zika IgM Assay System 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 Chembio in consultation with, and require concurrence of, OCET/OCS/OC and DMD/OIR/CDRH.

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

M. Chembio may request the addition of other instruments for use with the authorized DPP Zika IgM Assay System. Such requests will be made by Chembio in consultation with, and require concurrence of, DMD/OIR/CDRH.

N. Chembio may request the addition of other ancillary reagents for use with the authorized DPP Zika IgM Assay System. Such requests will be made by Chembio in consultation with, and require concurrence of, DMD/OIR/CDRH.

O. Chembio may request the addition of other specimen types for use with the authorized DPP Zika IgM Assay System. Such requests will be made by Chembio in consultation with, and require concurrence of, DMD/OIR/CDRH.

P. Chembio may request the addition of other control materials for use with the authorized DPP Zika IgM Assay System. Such requests will be made by Chembio in consultation with, and require concurrence of, DMD/OIR/CDRH.

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

R. Chembio will track adverse events and report to FDA under 21 CFR Part 803.

S. Chembio will evaluate the performance of the DPP Zika IgM Assay System 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, Chembio will update its labeling, in consultation with, and with concurrence of, DMD/OIR/CDRH, to reflect the additional testing.

T. Chembio will assess traceability[8] of the DPP Zika IgM Assay System with any FDA-recommended reference material(s). After submission to FDA and DMD/OIR/CDRH's review of and concurrence with the data, Chembio will update its labeling to reflect the additional testing.

U. Chembio will track the performance of the DPP Zika IgM Assay System and report to DMD/OIR/CDRH on a semi-annual basis.

Authorized Laboratories

V. Authorized laboratories will include with reports of the results of the DPP Zika IgM Assay System the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients, and any additional DPP Zika IgM Assay System 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

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

these Fact Sheets may be used, which may include mass media.

W. Authorized laboratories will perform the DPP Zika IgM Assay System on only human serum (plain or separation gel) and fingerstick whole blood, EDTA venous whole blood, or EDTA plasma (each collected alongside a patient-matched serum specimen) specimens or with other authorized specimen types.

X. If non-serum specimens are used with the DPP Zika IgM Assay System, authorized laboratories responsible for collecting the patient specimen must collect a patient-matched serum specimen, or if this is not possible, an additional serum specimen must be collected soon after the original specimen. This is to facilitate any additional testing that may be required, using the latest CDC testing algorithms for the diagnosis of Zika virus infection, to confirm Zika virus infection.

Y. Authorized laboratories must read the results of the DPP Zika IgM Assay System on the DPP Micro Reader or on other authorized instruments. Authorized laboratories must not attempt to interpret the results of the DPP Zika IgM Assay System visually.

Z. Within the United States and its territories, authorized laboratories will report all reactive results (i.e., presumptive Zika IgM positive) to Chembio.

AA. Authorized laboratories will have a process in place to ensure that, for reactive results (i.e., presumptive Zika IgM positive), 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.

BB. Authorized laboratories will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.[9]

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

DD. All laboratory personnel using the assay must be appropriately trained in performing and interpreting immunochromatographic 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 interpretation of results of the DPP Zika IgM Assay System.

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

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

EE. Chembio, 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

FF. All advertising and promotional descriptive printed matter relating to the use of the authorized DPP Zika IgM Assay System 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.

GG. All advertising and promotional descriptive printed matter relating to the use of the authorized DPP Zika IgM Assay System 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 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 DPP Zika IgM Assay System may represent or suggest that this test is safe or effective for the diagnosis of Zika virus infection.

The emergency use of the authorized DPP Zika IgM Assay System 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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Rachel Sherman, M.D., M.P.H.
Principal Deputy Commissioner

Enclosures