DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

May 26, 2016

Luc Van Hove, M.D., Ph.D.
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Dear Dr. Van Hove:

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 the Idylla™ Ebola Virus Triage Test for the presumptive detection of Ebola Zaire virus[1] (detected in the West Africa outbreak in 2014) on the Idylla™ Instrument System (Idylla™ System) in EDTA venous whole blood specimens from individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors, 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 moderate complexity tests and by laboratories in the U.S. certified under CLIA to perform high complexity tests,[2] or in similarly qualified non-U.S. laboratories, by clinical laboratory personnel who have received specific training on the use of the Idylla™ Ebola Virus Triage Test on the Idylla™ System, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3).

On September 22, 2006, then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, determined, pursuant to section 319F-2 of the Public Health Service (PHS) Act (42 U.S.C. § 247d-6b), that the Ebola virus presents a material threat against the United States population sufficient to affect national security.[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 the Department of Health and Human Services (HHS) declared on August 5, 2014, that

[1] This assay is authorized for the presumptive detection of RNA from Ebola Zaire virus (detected in the West Africa outbreak in 2014). It may also detect RNA from *Sudan ebolavirus*; however, it does not distinguish between these different Ebola virus species.

[2] 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 moderate complexity tests and by laboratories in the U.S. certified under CLIA to perform high complexity tests, or in similarly qualified non-U.S. laboratories" together as "authorized laboratories."

[3] Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), the HHS Secretary's declaration that supports EUA issuance must be based on one of four determinations, including the identification by the DHS Secretary of a material threat pursuant to section 319F-2 of the PHS Act sufficient to affect national security or the health and security of United States citizens living abroad (section 564(b)(1)(D) of the Act).

circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection of Ebola virus, subject to the terms of any authorization issued under section 564(a) of the Act (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 Idylla™ Ebola Virus Triage Test (as described in the Scope of Authorization section of this letter (section II)) in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors (as described in the Scope of Authorization section of this letter (section II)) for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Idylla™ Ebola Virus Triage Test for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 Ebola Zaire virus (detected in the West Africa outbreak in 2014) can cause Ebola virus disease, a serious or life-threatening disease or condition to humans infected with this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the Idylla™ Ebola Virus Triage Test may be effective in diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection, and that the known and potential benefits of the Idylla™ Ebola Virus Triage Test for diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) 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 Idylla™ Ebola Virus Triage Test for diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection.[5]

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized Idylla™ Ebola Virus Triage Test by authorized laboratories for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

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[4] U.S. Department of Health and Human Services. *Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Ebola Virus*. 79 Fed. Reg. 47141 (August 12, 2014).

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

The Authorized Idylla™ Ebola Virus Triage Test

The Idylla™ Ebola Virus Triage Test is an automated test intended for the *in vitro* qualitative detection of Ebola Zaire virus RNA from EDTA venous whole blood specimens. The assay is performed on the Idylla™ System. A quick reference guide and Instructions for Use are included in the test kit.

The Idylla™ System consists of an instrument, a console, and a single-use test-specific cartridge. The Idylla™ Console is connected to one or more Idylla™ Instruments. Samples are inserted into the Idylla™ Cartridges which are processed, fully automated, on the Idylla™ System using application specific, encrypted software, called Test Type Packages (TTP). Driven by the Idylla™ Ebola specific software (Ebola TTP), the Idylla™ System covers the entire process from sample-to-result with fully integrated sample preparation (homogenization, cell lysis and RNA extraction) followed by real-time reverse transcription polymerase chain reaction (rRT-PCR) amplification, detection of target sequences, analysis of the obtained PCR data, and reporting of the results.

The Idylla™ Ebola Virus Triage Test is an rRT-PCR assay using TaqMan® probes for detection of Ebola virus in the Idylla™ Cartridge. Two hundred microliters (200 µl) of EDTA venous whole blood is dispensed into the Idylla™ Cartridge. All the reagents and controls required to perform the testing are contained within the Idylla™ Cartridge.

The user identifies the sample identifier and then initiates the Idylla™ Ebola Virus Triage Test request through the Idylla™ Console. The Idylla™ Cartridge containing the sample is inserted into an Idylla™ Instrument and the Idylla™ Instrument processes the specific assay test following the Ebola TTP.

The Idylla™ Cartridge contains five PCR chambers in which the rRT-PCR takes place. In four chambers, PCRs for the detection of Ebola RNA and a Sample Process Control take place; in the fifth chamber an Endogenous Control (RNase P) is amplified. Fluorescent labeled reporter dyes generated upon amplification are analyzed in each of the chambers and a software algorithm converts the data to a final reportable result. The Idylla™ Instrument executes the Ebola TTP. Test results are uploaded to the Idylla™ Console making the test report available to the user. The Idylla™ Cartridge can be safely disposed as biological waste after test completion.

To prevent erroneous reporting, each Idylla™ Cartridge contains the following controls:

- Sample Process Control (SPC): The SPC is an armored RNA that is dried onto the lysis pad of the Idylla™ Cartridge to verify adequate processing of the sample. The SPC is used as an internal process control for both the nucleic acid extraction and rRT-PCR reaction of the Ebola PCR. Additionally, this control detects specimen-associated inhibition of the RT-PCR reaction. The SPC should be positive in a negative sample and can be negative or positive in a positive sample. In the presence of high Ebola virus concentrations, the RT-PCR of the SPC may be competitively inhibited and can provide a negative or a positive result. In the absence of Ebola, the SPC must be positive to produce a valid negative result. The SPC is interpreted by the Ebola TTP software included data interpretation algorithm. A result will be provided only if the SPC passes the systems acceptance criteria; otherwise, the sample will be called invalid.

- Endogenous Control (EC): The EC amplifies the sample inherent RNase P gene and ensures that a human sample was correctly added to the test cartridge. The EC is interpreted by the Ebola TTP software included data interpretation algorithm. The EC passes if an RNase P signal is detected; otherwise, the sample will be called invalid.

The above described Idylla™ Ebola Virus Triage Test, when labeled consistently with the labeling authorized by FDA entitled "Idylla™ Ebola Virus Triage Test Instructions for Use" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by Biocartis NV 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, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described Idylla™ Ebola Virus Triage 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 and patients:

- Fact Sheet for Health Care Providers: Interpreting Idylla™ Ebola Virus Triage Test Results
- Fact Sheet for Patients: Understanding Results from the Idylla™ Ebola Virus Triage Test

As described in section IV below, Biocartis NV and any authorized distributor(s) are also authorized to make available additional information relating to the emergency use of the authorized Idylla™ Ebola Virus Triage 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 Idylla™ Ebola Virus Triage Test in the specified population, when used for presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014), 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 Idylla™ Ebola Virus Triage Test may be effective in the diagnosis of Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection 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 Idylla™ Ebola Virus Triage Test, when used to diagnose Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized Idylla™ Ebola Virus Triage 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 DHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the Idylla™ Ebola Virus Triage Test described above is authorized to diagnose Ebola Zaire virus

(detected in the West Africa outbreak in 2014) infection in individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors.

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 Idylla™ Ebola Virus Triage 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 Idylla™ Ebola Virus Triage 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

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

Biocartis NV and Any Authorized Distributor(s)

A. Biocartis NV and any authorized distributor(s) will distribute the authorized Idylla™ Ebola Virus Triage Test with the authorized labeling, as may be revised only by Biocartis NV in consultation with DMD/OIR/CDRH, to authorized laboratories.

B. Biocartis NV and any authorized distributor(s) will provide to authorized laboratories the authorized Idylla™ Ebola Virus Triage Test Fact Sheet for Health Care Providers and the authorized Idylla™ Ebola Virus Triage Test Fact Sheet for Patients.

C. Biocartis NV and any authorized distributor(s) will make available on their websites the authorized Idylla™ Ebola Virus Triage Test Fact Sheet for Health Care Providers and the authorized Idylla™ Ebola Virus Triage Test Fact Sheet for Patients.

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

E. Biocartis NV and any authorized distributor(s) will ensure that authorized laboratories using the authorized Idylla™ Ebola Virus Triage Test have a process in place for

reporting test results to health care providers and relevant public health authorities, as appropriate.[6]

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

G. Biocartis NV and any authorized distributor(s) will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which Biocartis NV and any authorized distributor(s) become aware.

H. Biocartis NV and any authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized Idylla™ Ebola Virus Triage Test that is consistent with, and does not exceed, the terms of this letter of authorization.

Biocartis NV

I. Biocartis NV will notify FDA of any authorized distributor(s) of the Idylla™ Ebola Virus Triage Test, including the name, address, and phone number of any authorized distributor(s).

J. Biocartis NV will provide any authorized distributor(s) with a copy of this EUA, and communicate to any 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. Biocartis NV may request changes to the authorized Idylla™ Ebola Virus Triage Test Fact Sheet for Health Care Providers or the authorized Idylla™ Ebola Virus Triage Test Fact Sheet for Patients. Such requests will be made by Biocartis NV in consultation with, and require concurrence of, DMD/OIR/CDRH.

L. Biocartis NV may request the addition of other specimen types for use with the authorized Idylla™ Ebola Virus Triage Test. Such requests will be made by Biocartis NV in consultation with, and require concurrence of, DMD/OIR/CDRH.

M. Biocartis NV may request that the Idylla™ Ebola Virus Triage Test be used for the presumptive detection of other species of the Ebola virus, including the Ebola Sudan virus. Such requests will be made by Biocartis NV upon submission of acceptable analytical and clinical data, and will be made in consultation with, and require concurrence of, DMD/OIR/CDRH.

N. Biocartis NV will track adverse events and report to FDA under 21 CFR part 803.

[6] For questions related to reporting Ebola test results to relevant public health authorities, it is recommended that Biocartis NV and authorized laboratories consult with the applicable country, state or territory health department(s). According to the U.S. Centers for Disease Control and Prevention (CDC), Ebola is a nationally notifiable condition. http://www.cdc.gov/vhf/ebola/.

Authorized Laboratories

O. Authorized laboratories will include with reports of the results of the Idylla™ Ebola Virus Triage Test the authorized Fact Sheet for Health Care Providers and the authorized Fact Sheet for Patients. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

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

Q. Authorized laboratories will collect information on the performance of the assay, and report to Biocartis NV and any authorized distributor(s) any suspected occurrence of false positive or false negative results of which they become aware.

R. All laboratory personnel using the assay will be appropriately trained on the use of the Idylla™ Ebola Virus Triage Test on the Idylla™ System and use appropriate laboratory and personal protective equipment when handling this test.

Biocartis NV, Any Authorized Distributors and Authorized Laboratories

S. Biocartis NV, any 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

T. All advertising and promotional descriptive printed matter relating to the use of the authorized Idylla™ Ebola Virus Triage Test 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.

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

U. All advertising and promotional descriptive printed matter relating to the use of the authorized Idylla™ Ebola Virus Triage 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 Ebola Zaire virus (detected in the West Africa outbreak in 2014), and any other Ebola virus species if so authorized; and
- This test is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of Ebola virus 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 Idylla™ Ebola Virus Triage Test may represent or suggest that this test is safe or effective for the diagnosis of Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection.

The emergency use of the authorized Idylla™ Ebola Virus Triage Test 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* diagnostics for detection of Ebola virus 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