March 4, 2016

Tiffany Miller, RAC
Director, Regulatory Affairs
OraSure Technologies, Inc.
220 East First Street
Bethlehem, PA 18015

Dear Ms. Miller:

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 OraQuick® Ebola Rapid Antigen Test[1] for the detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) [2] in cadaveric oral fluid swab specimens from individuals with epidemiological risk factors for Ebola virus infection and suspected to have died of Ebola. The test is intended to aid in diagnosing Ebola Zaire virus infection as the cause of death in order to inform decisions on safe and dignified burial procedures to prevent transmission of Ebola virus in the community. The test is to be used by personnel who are adequately equipped, trained, and capable of testing for Ebola infection, in laboratories, facilities, and in field surveillance and response teams acting under the direction of public health authorities ("covered personnel"), pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3). The OraQuick® Ebola Rapid Antigen Test for use with cadaveric oral fluid is not intended for use with oral fluid specimens from living individuals.

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

[1] For purposes of this authorization, the term "OraQuick® Ebola Rapid Antigen Test" includes, in addition to the OraQuick® Ebola Rapid Antigen Test Kit, the OraQuick® Ebola Rapid Antigen Test Kit Controls [quality control reagents intended for use only with the OraQuick® Ebola Rapid Antigen Test] and the OraQuick® Ebola Visual Reference Panel [intended to assist new operators in becoming proficient at reading specimens with antigen levels near the limit of detection of the device]. While the OraQuick® Ebola Rapid Antigen Test Kit Controls and OraQuick® Ebola Visual Reference Panel are both sold separately, under this authorization they must be used in conjunction with the OraQuick® Ebola Rapid Antigen Test Kit.

[2] This assay is intended for the qualitative detection of antigens from Ebola virus (species *Zaire ebolavirus,* detected in the West Africa outbreak in 2014), but may also detect antigens from *Sudan ebolavirus* and *Bundibugyo ebolavirus*; however, it does not distinguish between these different Ebola virus species.

[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).

Department of Health and Human Services (HHS) declared on August 5, 2014, that 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 OraQuick® Ebola Rapid Antigen Test (as described in the Scope of Authorization section of this letter (section II)) for use with cadaveric oral fluid swab specimens from individuals with epidemiological risk factors for Ebola virus infection and suspected to have died of Ebola, to aid in diagnosing Ebola Zaire virus infection as the cause of death in order to inform decisions on safe and dignified burial procedures to prevent transmission of Ebola virus in the community (as described in the Scope of Authorization section of this letter (section II)).

The OraQuick® Ebola Rapid Antigen Test was previously authorized on July 31, 2015, for the presumptive detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in venipuncture whole blood or fingerstick whole blood specimens from individuals with signs and symptoms of Ebola virus infection in conjunction with epidemiological risk factors (including geographic locations with high prevalence of Ebola infection), by laboratories and facilities adequately equipped, trained, and capable of testing for Ebola infection (including treatment centers and public health clinics) for circumstances when the use of a rapid Ebola virus test is determined to be more appropriate than the use of an authorized Ebola virus nucleic acid test (available at http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM456909.pdf).

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the OraQuick® Ebola Rapid Antigen Test for the 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 OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid may be effective as an aid in diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection as the cause of death to inform decisions on safe and dignified burial procedures to prevent transmission of Ebola virus infection in the community and that the known and potential benefits of the OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid as an aid in diagnosing Ebola Zaire

[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).

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 OraQuick® Ebola Rapid Antigen Test for use with cadaveric oral fluid as an aid in diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) infection as the cause of death to inform decisions on safe and dignified burial procedures to prevent transmission of Ebola virus in the community.[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 OraQuick® Ebola Rapid Antigen Test by covered personnel for the detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in cadaveric oral fluid swab specimens from individuals with epidemiological risk factors for Ebola virus infection and suspected to have died of Ebola. The test is intended to aid in diagnosing Ebola Zaire virus infection as the cause of death in order to inform decisions on safe and dignified burial procedures to prevent transmission of Ebola virus in the community. The authorized OraQuick® Ebola Rapid Antigen Test for use with cadaveric oral fluid is not intended for use with oral fluid specimens from living individuals.

The Authorized OraQuick® Ebola Rapid Antigen Test

The OraQuick® Ebola Rapid Antigen Test is a rapid single-use chromatographic lateral flow immunoassay contained within a rigid plastic device housing that is intended for the *in vitro* qualitative detection of antigens from the Ebola Zaire virus (detected in the West Africa outbreak in 2014) in authorized specimen types.

The OraQuick® Ebola Rapid Antigen Test utilizes a sandwich capture lateral flow immunoassay method to detect Ebola virus antigens. This lateral flow test is composed of an assay strip with several components: the flat pad, the blocker pad, the conjugate pad, the nitrocellulose membrane (with a Test Line ("T") and a Control ("C") line), and the absorbent pad. The clinical specimen is applied to the device followed by insertion of the device into the developer solution. The execution of the assay occurs as reagents are hydrated and liquid is transported along with the specimen across the strip towards the test zone.

If Ebola viral antigens are present in the specimen, then they will be bound by biotinylated anti-Ebola polyclonal antibodies eluting from the blocker pad. These complexed Ebola antigens will then form immunological sandwiches with signal generating colloidal gold labeled Ebola antibodies that are eluting from the conjugate pad. The immunological sandwich complex is subsequently captured through reaction of the biotinylated anti-Ebola antibody with the biotin binding protein streptavidin that is immobilized at the Test Line ("T") of the test strip.

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

The OraQuick® Ebola Rapid Antigen Test Kit is comprised of an OraQuick® Ebola Rapid Antigen Test device, a filled, capped and labeled Developer Vial, a device stand (used to hold the device during the running of the test following specimen collection), micropipettes, one quick reference guide for cadaveric oral fluid testing, and one package insert for cadaveric oral fluid testing. The OraQuick® Ebola Rapid Antigen Test Kit may also include one quick reference guide and one package insert for other currently authorized use(s). The OraQuick® Ebola Rapid Antigen Test device, the developer solution and the micropipettes to be used with the device are identical for both authorized test methods (i.e., use with whole blood from a living individual, and for cadaveric oral fluid); however, the instructions for use are different.

The test kit has a built-in procedural control that demonstrates assay validity. A purple line in the Control ("C") area of the Result Window indicates that the fluid migrated appropriately through the Test Device. The Control line will appear on all valid tests, whether or not the sample is positive (i.e., reactive) or negative (i.e., non-reactive).

The cadaveric oral fluid specimens to be tested with the above described OraQuick® Ebola Rapid Antigen Test are collected by swabbing the gum of the deceased individual. Swabbing can be performed directly with the Oraquick® Ebola Rapid Antigen Test device or with a validated and authorized swab that is subsequently stored in a validated and authorized viral transport media. Please refer to the Oraquick® Ebola Rapid Antigen Test - Instructions for Use - Cadaveric Oral Fluid for information on validated swabs and viral transport media.

The OraQuick® Ebola Rapid Antigen Test Kit Controls must be used with the OraQuick® Ebola Rapid Antigen Test. The OraQuick® Ebola Rapid Antigen Test Kit Controls contain two vials, one Ebola positive control vial (orange capped) and one Ebola negative control vial (white capped).

The OraQuick® Ebola Visual Reference Panel is intended to assist new operators in becoming proficient at reading specimens with antigen levels near the limit of detection of the device. It consists of three devices that have been specifically formulated and manufactured to represent positive results near the limit of detection, low positive, and negative test results. New operators must be able to correctly interpret all devices of the OraQuick® Ebola Visual Reference Panel prior to using the OraQuick® Ebola Rapid Antigen Test device.

The above described OraQuick® Ebola Rapid Antigen Test, when labeled consistently with the labeling authorized by FDA entitled "OraQuick® Ebola Rapid Antigen Test Instructions for Use - Cadaveric Oral Fluid" (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), which may be revised by OraSure Technologies, Inc. in consultation with FDA, is authorized to be distributed to laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola virus, and stakeholders working with such public health authorities, despite the fact that it does not meet certain requirements otherwise required by federal law.

The above described OraQuick® Ebola Rapid Antigen Test is authorized to be accompanied by the following information pertaining to the emergency use with cadaveric oral fluid, which is

authorized to be made available to response teams and relatives/caregivers of deceased individuals:

- Fact Sheet for Ebola Response Teams: Interpreting Results from the OraQuick® Ebola Rapid Antigen Test for use with Cadaveric Oral Fluid

- Fact Sheet for Relatives and Caregivers: Understanding Results from the OraQuick® Ebola Rapid Antigen Test

As described in section IV below, OraSure Technologies, Inc. and any authorized distributor(s) are also authorized to make available additional information relating to the emergency use of the authorized OraQuick® Ebola Rapid Antigen Test, when used with cadaveric oral fluid, which 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 OraQuick® Ebola Rapid Antigen Test in the specified population, when used for detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014) in cadaveric oral fluid swab specimens, 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 OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid may be effective as an aid in diagnosing 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 OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid to aid in diagnosing Ebola Zaire virus infection as the cause of death in order to inform decisions on safe and dignified burial procedures to prevent transmission of Ebola virus in the community, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid 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 OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid is authorized to aid in diagnosing Ebola Zaire virus (detected in the West Africa outbreak in 2014) as the cause of death in individuals with epidemiological risk factors for Ebola virus infection and suspected to have died of Ebola.

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 OraQuick® Ebola Rapid Antigen 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 OraQuick® Ebola Rapid Antigen 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:

OraSure Technologies, Inc. and Any Authorized Distributor(s)

A. OraSure Technologies, Inc. and any authorized distributor(s) will distribute the authorized OraQuick® Ebola Rapid Antigen Test with the authorized labeling, as may be revised by OraSure Technologies, Inc. in consultation with FDA, to laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities.

B. OraSure Technologies, Inc. and any authorized distributor(s) will provide to laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities, the authorized OraQuick® Ebola Rapid Antigen Test Fact Sheet for Response Teams and the authorized OraQuick® Ebola Rapid Antigen Test Fact Sheet for Relatives and Caregivers.

C. OraSure Technologies, Inc. and any authorized distributor(s) will make available on their websites the authorized OraQuick® Ebola Rapid Antigen Test Fact Sheet for Response Teams and the authorized OraQuick® Ebola Rapid Antigen Test Fact Sheet for Relatives and Caregivers.

D. OraSure Technologies, Inc. and any authorized distributor(s) will inform laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such

public health authorities, and any other relevant public health authority(ies), of this EUA, including the terms and conditions herein.

E. OraSure Technologies, Inc. and any authorized distributor(s) will ensure that first time users of the OraQuick® Ebola Rapid Antigen Test Kit will be informed about the requirement for use of the control material and the visual reference panel.

F. OraSure Technologies, Inc. and any authorized distributor(s) will ensure that laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities, using the authorized OraQuick® Ebola Rapid Antigen Test have a process in place for reporting test results to relevant public health authorities, as appropriate.

G. Through a process of inventory control, OraSure Technologies, Inc. and any authorized distributor(s) will maintain records of device usage.

H. OraSure Technologies, Inc. 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 OraSure Technologies, Inc. and any authorized distributor(s) become aware.

I. OraSure Technologies, Inc. and any authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized OraQuick® Ebola Rapid Antigen Test for use with cadaveric oral fluid that is consistent with, and does not exceed, the terms of this letter of authorization.

OraSure Technologies, Inc.

J. OraSure Technologies, Inc. will notify FDA of any authorized distributor(s) of the OraQuick® Ebola Rapid Antigen Test, including the name, address, and phone number of any authorized distributor(s).

K. OraSure Technologies, Inc. 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).

L. OraSure Technologies, Inc. only may request changes to the authorized OraQuick® Ebola Rapid Antigen Test Fact Sheet for Response Teams or the authorized OraQuick® Ebola Rapid Antigen Test Fact Sheet for Relatives and Caregivers. Such requests will be made only by OraSure Technologies, Inc. in consultation with, and require concurrence of, FDA.

M. OraSure Technologies, Inc. may request the addition of other specimen types for use with the authorized OraQuick® Ebola Rapid Antigen Test. Such requests will be made by OraSure Technologies, Inc. in consultation with, and require concurrence of, FDA.

N. OraSure Technologies, Inc. may request the addition of other cadaveric oral fluid collection methods, including other swab and/or viral transport media, for use with the authorized OraQuick® Ebola Rapid Antigen Test for use with cadaveric oral fluid. Such requests will be made by OraSure Technologies, Inc. in consultation with, and require concurrence of, FDA.

O. OraSure Technologies, Inc. will track adverse events and report to FDA under 21 CFR Part 803.

P. OraSure Technologies, Inc. will contact health care providers, public health authorities, and stakeholders working with such public health authorities in the event of any significant new findings that negatively impact the performance of the test and that are observed during the course of the emergency use of the OraQuick® Ebola Rapid Antigen Test when used with cadaveric oral fluid.

Q. OraSure Technologies, Inc. will submit additional data (i.e., an LOD study with cadaveric oral fluid swab specimens, a cross reactivity study for potential cross reacting organisms relevant to oral fluid and an interference study with potentially interfering substances relevant to oral fluid) to FDA no later than 6 months after authorization [September 4, 2016].

Laboratories, Facilities, and Public Health Authorities Overseeing Personnel Adequately Equipped, Trained, and Capable of Testing for Ebola Infection, and Stakeholders Working with Such Public Health Authorities

R. Laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities, will provide the authorized Fact Sheet for Response Teams to personnel performing the cadaveric oral fluid testing, and will include with reports of the OraQuick® Ebola Rapid Antigen Test results the authorized Fact Sheet for Relatives and Caregivers. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

S. Laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities, will have a process in place for the personnel performing the test to report test results back to the overseeing entity and to health care professionals, as appropriate.

T. Laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities, will collect information on the performance of the

assay, and report to OraSure Technologies, Inc. and any authorized distributor(s) any suspected occurrence of false positive or false negative results of which they become aware.

U. All covered personnel will be appropriately trained on the OraQuick® Ebola Rapid Antigen Test and use appropriate laboratory and/or personal protective equipment when handling this kit.

OraSure Technologies, Inc., Any Authorized Distributor(s), and Laboratories, Facilities, and Public Health Authorities Overseeing Personnel Adequately Equipped, Trained, and Capable of Testing for Ebola Infection, and Stakeholders Working with Such Public Health Authorities

V. OraSure Technologies, Inc., any authorized distributor(s), and laboratories, facilities, and public health authorities overseeing personnel adequately equipped, trained, and capable of testing for Ebola infection, and stakeholders working with such public health authorities, 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

W. All advertising and promotional descriptive printed matter relating to the use of the authorized OraQuick® Ebola Rapid Antigen 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.

X. All advertising and promotional descriptive printed matter relating to the use of the authorized OraQuick® Ebola Rapid Antigen 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 personnel who are adequately equipped, trained, and capable of testing for Ebola infection, in laboratories, facilities, and in field surveillance and response teams acting under the direction of public health authorities;
- This test has been authorized only for the detection of Ebola Zaire virus (detected in the West Africa outbreak in 2014); and
- This test has not been authorized for use with oral fluid from living individuals
- 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, whichever is sooner.

No advertising or promotional descriptive printed matter relating to the use of the authorized OraQuick® Ebola Rapid Antigen 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 OraQuick® Ebola Rapid Antigen 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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Robert M. Califf, M.D.
Commissioner of Food and Drugs

Enclosures