



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

October 10, 2019

Re: DEN190025

Trade/Device Name: OraQuick Ebola Rapid Antigen Test

Regulation Number: 21 CFR 866.4002

Regulation Name: Device to detect antigens of biothreat microbial agents in human clinical specimens

Regulatory Class: Class II

Product Code: QID

Dated: May 10, 2019

Received: May 13, 2019

Dear Tiffany Miller:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the OraQuick Ebola Rapid Antigen Test, a prescription device with the following indications for use:

The OraQuick Ebola Rapid Antigen Test is an in vitro diagnostic single-use immunoassay for the qualitative detection of antigens from viruses within the *Ebolavirus* genus but does not differentiate between these viruses. Testing with the OraQuick Ebola Rapid Antigen Test must only be performed when public health authorities have determined the need for this test. Testing for Ebola Virus Disease (EVD) must be performed in accordance with current guidelines provided by the appropriate public health authorities that address appropriate biosafety conditions, interpretation of test results, and coordination of testing, results and patient management with public health authorities. The OraQuick Ebola Rapid Antigen Test is intended for use with specimens from:

- individuals with epidemiological risk factors with signs and symptoms of EVD or
- recently deceased individuals with epidemiological risk factors who are suspected to have died of EVD.

EVD is a nationally notifiable condition and must be reported to public health authorities in accordance with local, state, and federal regulations.

The OraQuick Ebola Rapid Antigen Test is intended for use with venipuncture whole blood and fingerstick whole blood specimens as an aid in diagnosis of EVD in patients suspected of and with signs or symptoms consistent with EVD who have epidemiological risk factor(s) for *Ebolavirus* exposure (e.g., contact with a known or suspected case, travel to a geographic location at a time when

Ebolavirus transmission was known or suspected to have occurred). Performance of the device with *Ebolavirus* positive fingerstick whole blood was established in a non-human primate model.

The OraQuick Ebola Rapid Antigen Test is intended for use with cadaveric oral fluid collected from recently deceased individuals with epidemiological risk factors who are suspected to have died of EVD. Cadaveric oral fluid should be collected directly with the device or collected with oral swabs in viral transport media. The OraQuick Ebola Rapid Antigen Test is intended as an aid in the determination of EVD as the cause of death to inform decisions on safe handling of cadavers to prevent disease transmission.

The OraQuick Ebola Rapid Antigen Test results are presumptive, definitive identification of EVD requires performing additional testing and confirmation procedures in consultation with public health and/or other authorities to whom reporting is required.

Negative results were observed in individuals with low levels of circulating virus, therefore negative results do not preclude infection with viruses within the *Ebolavirus* genus.

The level of *Ebolavirus* antigens that would be present in EVD clinical specimens from individuals with early systemic infection is unknown. Test performance of the OraQuick Ebola Rapid Antigen Test is associated with the level of *Ebolavirus* antigens in the patient; therefore, the test is not intended for use in an asymptomatic population for mass-screening purposes (e.g., as the sole means of EVD control at airports or border-crossings) or for testing of individuals at risk of exposure without observable signs of infection.

The OraQuick Ebola Rapid Antigen Test is intended for use by experienced personnel who have documented device specific training offered by OraSure Technologies Inc., training in the correct use of recommended personal protective equipment (PPE) and expertise in infectious disease diagnostic testing, including the safe handling of clinical specimens potentially containing *Ebolavirus*. The test is intended for use by laboratory professionals or healthcare workers who have demonstrated availability of biosafety equipment, access to patient containment facilities, and established procedures (e.g., SOP) for coordinating testing, results and patient management with public health authorities consistent with state, local and federal recommendations and guidelines.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov. FDA concludes that this device should be classified into Class II. This order, therefore, classifies the OraQuick Ebola Rapid Antigen Test, and substantially equivalent devices of this generic type, into Class II under the generic name Device to detect antigens of biothreat microbial agents in human clinical specimens.

FDA identifies this generic type of device as:

Device to detect antigens of biothreat microbial agents in human clinical specimens. A device to detect antigens of biothreat microbial agents in human clinical specimens is identified as an in vitro diagnostic device intended for the detection of antigens of microbial agents in specimens collected from patients with signs and symptoms of infection with biothreat microbial agents and who have

been exposed to these agents or are suspected or at risk of exposure. The device can include antibodies for immobilization and detection of the analyte. This device may also be used for cadaver testing to prevent human diseases for which cadavers constitute a source of human-to-human transmission.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On May 13, 2019, FDA received your De Novo requesting classification of the OraQuick Ebola Rapid Antigen Test. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the OraQuick Ebola Rapid Antigen Test into class I or II, it is necessary that the proposed class has sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the OraQuick Ebola Rapid Antigen Test can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health	Mitigation Measures
Risk of false results	Certain analytical performance data, clinical performance data, Certain device information in labeling, Certain limitations on distribution, Certain validation procedures and studies, Collection device specification
Failure to correctly interpret test results	Certain device information in labeling, Certain limitations on distribution, Certain results interpretation information in labeling, Certain risk mitigation strategies and end user trainings, Certain validation procedures and studies
Failure to correctly operate the device	Certain results interpretation information, Certain device description, Certain device information in labeling, Certain limitations on distribution, Certain risk mitigation strategies and end user trainings, Certain validation procedures and studies

In combination with the general controls of the FD&C Act, the Device to detect antigens of biothreat microbial agents in human clinical specimens is subject to the following special controls:

1. The distribution of these devices is limited to laboratories that follow public health guidelines that address appropriate biosafety conditions, interpretation of test results, coordination of testing, results and patient management with public health authorities and that have personnel that have completed device specific training required under paragraph (b)(5)(vi) of this section.
2. If sample collection devices are used, any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt (standalone or as part of a test system) for the collection of human specimens; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.
3. Labeling must include an intended use statement that includes the following:
 - i. What the device detects;
 - ii. The type of results provided to the user;
 - iii. The sample types with which it is intended for use;
 - iv. Whether the measurement is qualitative, semi-quantitative, or quantitative;
 - v. The clinical indications appropriate for the test use; e.g., in conjunction with patient history, epidemiological information, clinical observations, and other laboratory evidence to make patient management decisions;
 - vi. The intended use population(s) (e.g., signs and symptoms and epidemiological risk factors);
 - vii. If applicable, that use of the device is limited to an outbreak, suspected exposure of the subject, or to a situation where public health authorities have determined the need for the test;
 - viii. A statement that testing should be performed and reported in accordance with current guidelines provided by the appropriate public health authorities;
 - ix. A statement that use of this device is limited to laboratories, laboratory professionals or healthcare workers that follow public health guidelines that address appropriate biosafety conditions, interpretation of test results and coordination of testing, results and patient management with public health authorities, and that consist of personnel who completed device specific training provided by [insert name of the manufacturer].

4. The labeling required under 21 CFR 809.10(b) must include:
 - i. A detailed explanation of the interpretation of results, including acceptance criteria for evaluating the validity of results.
 - ii. For any devices intended solely for the presumptive identification of an antigen(s) of biothreat microbial agents, a warning statement that the test results alone do not conclusively establish infection and that additional testing and confirmation procedures may be necessary in consultation with the appropriate public health or other authorities to whom reporting is required.
 - iii. Limiting statements indicating, as applicable:
 - a. Situations where the device has been demonstrated to fail or may not perform at its expected performance level (e.g., any disease specific circumstances or circumstances identified by human factors or robustness studies);
 - b. That device results are intended to be followed up according to the latest professional guidelines (e.g., recommendations from the Centers for Disease Control and Prevention);
 - c. That specimens can result in false negative results if collected outside of the indicated window for testing as recommended by public health authorities;
 - d. A statement that this is a nationally notifiable disease or other condition caused by a biothreat microbial agent that should be reported to public health authorities in accordance with local, state, and federal law.
 - e. Any specific circumstances that pose significant risk to public health, and for which the device has not been validated, including testing of matrices and patient populations that are not identified in the intended use such as individuals without signs and symptoms of infection including mass infection screening (such as airport or border screening) that is not limited to individuals who have signs and symptoms and who have been exposed to biothreat microbial agents or are suspected or at risk of such exposure.
 - f. A description of the recommended training for safe use of the device and to minimize the risk of false results.
 - iv. For any devices intended for use in a point of care setting, labeling must include a brief reference sheet for healthcare professionals that accompanies the device and that includes, at a minimum, the name and intended use of the test, step-by-step instructions of all control and sample testing procedures for the claimed sample types, the result(s) interpretation, warning and limitation statements, and information for troubleshooting or technical assistance with the device.

5. Design verification and validation must include, as applicable:
 - i. A detailed device description, including the principle of device operation and test methodology from obtaining a sample to the test result, all pre-analytical methods for specimen processing, and a rationale for target selection and selection of reagents.
 - ii. Detailed documentation and results from analytical performance studies, including: Limit of Detection (LoD), analytical sensitivity determined using a standardized reference material that FDA has determined is appropriate (e.g., a World Health Organization reference material or international standard), analytical reactivity (i.e., species and/or strain inclusivity), analytical specificity (cross-reactivity and microbial interference), interference of endogenous and exogenous substances, specimen stability, reproducibility, precision, and other studies as applicable to the technology (e.g., linearity). Results for multiple lots must be included in the LoD study and in the precision or reproducibility studies.
 - iii. For any devices intended for use in a point of care setting, detailed documentation and results that demonstrate the robustness of the device, including the entire testing procedure from sampling to result interpretation (e.g., human factors or flex studies).
 - iv. For any devices that detect the presence of an analyte directly from specimen, detailed documentation and results from a shelf-life assessment that includes panel members formulated in the most complex clinical matrix identified in the device's intended use.
 - v. Detailed documentation and results from either a clinical study or, when determined to be acceptable by FDA, a study with an equivalent data set. Documentation from this study must include study reports, testing results, and results of all statistical analyses, including line data of all test samples, and, if applicable, an appropriate justification describing how the sample set is representative of the intended use population. This study must compare the device performance to results obtained from a reference or comparator method that FDA has determined is appropriate and must be conducted with multiple reagent lots. If applicable, this study must use prospectively (sequentially) collected samples for each indicated specimen type that are collected from subjects representative of the intended use population (if the number of prospective clinical samples is insufficient to characterize the performance of the device, as determined by FDA, then additional characterized clinical samples must be evaluated to supplement the study). This study must include specimens that contain relevant organism concentrations applicable to the indicated specimen type(s) and the targeted analyte(s), if applicable.
 - vi. As part of the risk management activities, an appropriate device specific end user training program must be offered as an effort to mitigate the risks of false results, failure to correctly operate the device, and failure to correctly interpret test results, and as applicable, operator exposure to biothreat microbial agents that may be present in test specimens and control materials.
 - vii. As part of the risk management activities, if the labeling includes hyperlinks to documents

from public health authorities regarding sampling, sample shipment, sample testing or clinical management of patients suspected of being infected; or if the labeling includes direct contact information for any such public health authority, then the hyperlinks and contact information must be reviewed at least annually and updated to reflect any changes to those hyperlinks or contact information.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the Device to detect antigens of biothreat microbial agents in human clinical specimens they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD & C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD & C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Silke Schlottmann at 301-796-9551.

Sincerely,

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
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