OraSure Technologies, Inc.

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OraQuick® Ebola Rapid Antigen Test
Customer Letter

Dear Customer,

Thank you for deciding to use the OraQuick® Ebola Rapid Antigen Test. The sale, distribution, and use of this product is restricted as described in the product insert. By purchasing this device, you are doing so as an agent of a clinical laboratory and agree that you or any of your consignees will abide by the following restrictions on the sale, distribution, and use of the device:

- **U.S. hospitals or clinical laboratories concerned about a patient with potential Ebola virus exposure should contact their local and/or state public health authorities. These agencies will work with CDC to determine whether a patient is or is not a person under investigation (PUI); only PUI should be tested for Ebola.**
- **Follow CDC recommendations on collection, testing and transport when testing with the OraQuick Ebola Rapid Antigen Test.**
- **Testing with the OraQuick® Ebola Rapid Antigen Test for whole blood and cadaveric oral fluid MUST not be performed unless the patient meets clinical and epidemiologic criteria for testing suspect specimens.**
- **The test is not intended for general Ebola infection screening, such as airport screening or contact tracing of individuals without sign and symptoms of Ebola infection.**
- **Sale of the OraQuick® Ebola Rapid Antigen Test for whole blood and cadaveric oral fluid is restricted to laboratory professionals or healthcare workers that are adequately equipped, trained, and capable of such testing.**
  - **These laboratories and facilities MUST have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.**
  - **All personnel from laboratories and facilities using the assay MUST be appropriately trained on the OraQuick® Ebola Rapid Antigen Test and use appropriate laboratory and personal equipment when handling this kit.**
- **Negative results do not preclude Ebola virus infection and should not be used as the sole basis for patient management decisions. The definitive identification of Ebola virus disease requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reporting is required. The diagnosis of Ebola virus disease must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of Ebola virus.**
- **Read times below 30 minutes significantly affect performance of the device with low positive samples. It is therefore critical that - unless samples are clearly positive - samples are not read prior to the 30 minutes. Reducing the read time below 30 minutes can prevent correct identification of low positive samples. Therefore, all negative result MUST be read at 30 minutes.**

READER PROFICIENCY: As a laboratory or facility planning to use the OraQuick® Ebola Rapid Antigen Test, you are required to use the OraQuick® Ebola Kit Controls and the OraQuick® Ebola Visual Reference Panel. All new operators MUST be able to correctly interpret all deices provided within the OraQuick® Ebola Visual Reference Panel prior to using the OraQuick® Ebola Rapid Antigen Test. The clinical performance of this device was established based on an operator's ability to read visual intensities at the "T" line at all levels including very weak bands representing low antigen levels.

Refer to the package insert for the OraQuick® Ebola Rapid Antigen Test for warnings, precautions, information on how the test works, how to use the device, interpretation of the results, and limitations of the test, the meaning of a positive or negative result, or for circumstances in which the OraQuick® Ebola Kit Controls should be run.

If you have any questions, please call (800) ORASURE (800-672-7873) within the United States or +(001) 610-882-1820 for outside the United States. You can also go to **www.OraSure.com.**

Sincerely,

OraSure Technologies Inc.

220 East First Street, Bethlehem, PA 18015
Phone 610-882-1820 • Fax 610-882-2275
www.OraSure.com

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OraQuick® Rapid Antigen Test EBOLA

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Instructions for Use

For *in-vitro* diagnostic use

COMPLEXITY: High

NAME AND INTENDED 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.

SPECIAL LIMITATIONS (Please see additional Limitations on page 8)

- **U.S. hospitals or clinical laboratories concerned about a patient with potential Ebola virus exposure should contact their local and/or state public health authorities. These agencies will work with CDC to determine whether a patient is or is not a person under investigation (PUI); only PUI should be tested for Ebola.**
- **Follow CDC recommendations on collection, testing and transport when testing with the OraQuick Ebola Rapid Antigen Test.**
- **Testing with the OraQuick® Ebola Rapid Antigen Test for whole blood and cadaveric oral fluid MUST not be performed unless the patient meets clinical and epidemiologic criteria for testing suspect specimens.**
- **The test is restricted for general Ebola infection screening, such as airport screening or contact tracing of individuals without sign and symptoms of Ebola infection.**
- **Sale of the OraQuick® Ebola Rapid Antigen Test for whole blood and cadaveric oral fluid is restricted to laboratory professionals or healthcare workers that are adequately equipped, trained, and capable of such testing.**
  - **These laboratories and facilities MUST have a process in place for reporting test results to health care professionals and relevant public health authorities, as appropriate.**
  - **All personnel from laboratories and facilities using the assay MUST be appropriately trained on the OraQuick® Ebola Rapid Antigen Test and use appropriate laboratory and personal equipment when handling this kit.**
- **Negative results do not preclude Ebola virus infection and should not be used as the sole basis for patient management decisions. The definitive identification of Ebola virus disease requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reporting is required. The diagnosis of Ebola virus disease must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of Ebola virus.**

SUMMARY AND EXPLANATION OF THE TEST

Ebola hemorrhagic fever is a severe, often-fatal disease in humans and nonhuman primates that has appeared sporadically since its initial recognition in 1976. Ebola virus is one of three genera of the family of RNA viruses called the Filoviridae. There are four species of Ebola virus affecting humans: Bundibugyo virus (BDBV), Sudan virus (SUDV), Taï Forest virus (TAFV), and Ebola virus (EBOV) strains. The presence of Ebola virus antigens indicate that the individual may be currently infected and capable of transmitting the virus.

The OraQuick® Ebola Rapid Antigen Test utilizes a sandwich capture lateral flow immunoassay method to detect Ebola virus antigens. Ebola antigens are captured and visualized by colloidal gold labeled with Ebola antibodies generating a visible line in the test zone for a positive sample.

PRINCIPLES OF THE TEST

The OraQuick® Ebola Rapid Antigen Test is a manually performed, visually read immunoassay for the qualitative detection of Ebola virus in human venipuncture whole blood, fingerstick whole blood, and cadaveric oral fluid. The OraQuick® Ebola Rapid Antigen Test is comprised of both a single-use test device and vial containing a pre-measured amount of a buffered developer solution. The test consists of a sealed pouch with two separate compartments for each component. The OraQuick® Ebola Rapid Antigen Test utilizes a proprietary lateral flow immunoassay procedure.

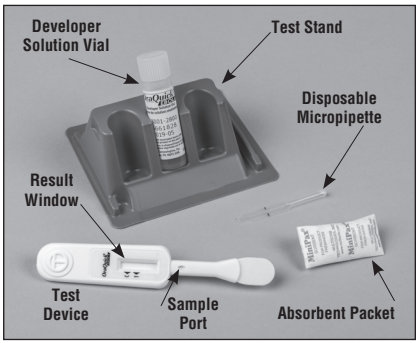
The assay test strip, which can be viewed through the test device result window, is comprised of a series of components: the blocker pad, the conjugate pad, the nitrocellulose membrane, and finally the absorbent pad. The performance of the assay occurs by hydration and transport of reagents as they interact with the specimen across the strip via chromatographic lateral flow. The conjugate pad contains salts, buffers, and a signal generating reagent consisting of Ebola antibodies conjugated to colloidal gold. Ebola antigens in the sample are captured by Ebola antibodies at the Test (T) Zone, which become immobilized on the nitrocellulose membrane and visualized by colloidal gold labeled with Ebola antibodies. The Control (C) Zone immobilized onto the nitrocellulose membrane is visualized by colloidal gold ensuring component elution, reagent activity, and adequate device performance.

A fingerstick or venipuncture whole blood specimen is collected using a plastic micropipette or calibrated lab pipette and transferred to the device, followed by the insertion of the device into the developer vial. For cadaveric oral fluid specimens, there are two ways to collect specimens: 1.) swab the gum line or the soft pallet tissue in the back of the throat with the flat pad of the device and then insert the device directly into the developer solution or 2.) swab the gum line or the soft pallet tissue in the back of the throat with a recommended swab and insert into recommended viral transport media. When using viral transport media, the specimen is collected from the transport media tube using a calibrated lab pipette and transferred to the device, followed by the insertion of the device into the developer vial. The developer solution facilitates the capillary flow of the specimen into the device and onto the assay strip. As the specimen flows through the device, antigens from the specimen are bound by the Ebola antibody labeled gold colorimetric reagent present on the assay strip. If the specimen contains Ebola antigens, the resulting labeled complexes bind to the Test (T) Zone resulting in a red to purple line. If the specimen does not contain Ebola virus, the labeled complexes do not bind at the Test Zone and no line is observed. The intensity of the line color is not directly proportional to the amount of virus present in the specimen. The remaining colloidal gold is transported and bound to the Control (C) Zone. This procedural control serves to demonstrate that the fluid has migrated adequately through the device. A red to purple line will appear at the Control (C) Zone during the performance of all valid tests whether or not the sample is positive or negative for Ebola virus (refer to the *Test Result and Interpretation of Test Result* section on page 8 of in this package insert). Positive results may be interpreted as soon as red to purple lines are visible at the Test (T) Zone and Control (C) Zone. Negative results MUST be read 30 minutes after inserting the device into the Developer Vial.

MATERIALS PROVIDED

The OraQuick® Ebola Rapid Antigen Test Kit is available in the following packaging configuration:

Components of Kit Catalog Number	25 Count Kit 1001-0509
Divided Pouch Each containing: Test Device (1) Absorbent Packet (1) Developer Soltuion Vial (1) (each vial contains 1.0 mL of a buffered saline solution with an antimicrobial agent)	25
Test Stands	25
Plastic Micropipettes	30
Instructions for Use	1
Cadaveric Oral Fluid Quick Reference Guide	1
Whole Blood Quick Reference Guide	1
Fact Sheet for Patients	30
Fact Sheet for Relatives and Caregivers	30



MATERIALS REQUIRED AND AVAILABLE AS AN ACCESSORY TO THE KIT

OraQuick® Ebola Rapid Antigen Oral Fluid Test Kit Controls 1001-0508

Ebola Positive Control (1 vial, orange cap, 0.25 mL)
Ebola Negative Control (1 vial, white cap, 0.25 mL)
Package Insert

OraQuick® Ebola Visual Reference Panel 1001-0537
Ebola Limit of Detection (1 device)
Ebola Low Positive (1 device)
Ebola Negative (1 device)
Package Insert

Foil Transfer Pouch 1001-0494

MATERIALS REQUIRED BUT NOT PROVIDED

Timer or watch capable of timing 30 minutes
Biohazard waste container
Materials required for venipuncture whole blood specimen collection or
Materials required to obtain a fingerstick whole blood specimen

OPTIONAL MATERIALS NOT PROVIDED WITH KIT

Calibrated lab pipette capable of dispensing 20µL
Disposable pipette tips
BD Universal Viral Transport for Viruses, Chlamydia, Mycoplasmas and Ureaplasmas (220258)
∑-Virocult® System (MW951S)

WARNINGS AND PRECAUTIONS

- **For prescription use only.**
- **All testing MUST be conducted under appropriate biosafety conditions in accordance with applicable country, state and local laws and with CDC and/or WHO guidelines.**
- **Specimens MUST always be treated as infectious and/or biohazardous. The use of all possible universal precautions is highly recommended when handling specimens with this test.**
- **Use personal protective equipment (PPE) consistent with current guidelines including safety goggles and / or face shields, masks or respiratory equipment, disposable gowning, boots, and gloves. Users performing this test MUST be appropriately trained of the donning and doffing of personal protective equipment.**
- **All personnel conducting testing MUST read and be familiar with Universal Precautions[1], Infection Control for Viral Hemorrhagic Fevers in the African Health Care Setting[2] and in Information for Healthcare Worker in the United States (http://www.cdc.gov/vhf/ebola/healthcare-us/index.html) depending upon their location of testing.**
- **For information on the transport of Ebola virus suspected positive samples, please refer to CDC Guidance for Collection, Transport, and Submission of Specimens for Ebola Virus Testing (http://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/specimens.html), and the WHO Guidance on regulations for the transportation of infectious substances 2017-1018 (www.who.int/csr/disease/ebola/training/laboratory/en/).**
- **All equipment and biohazardous waste MUST be discarded in accordance with country, state, and local laws and policies.**
- **This test kit is for use with venipuncture and fingerstick whole blood specimens and cadaveric oral fluid swab specimens only.**
- **Read times below 30 minutes significantly affect performance of the device with low positive samples. It is therefore critical that - unless samples are clearly positive - samples are not read prior to the 30 minutes. Reducing the read time below 30 minutes can prevent correct identification of low positive samples. Therefore, all negative result MUST be read at 30 minutes.**
- **Samples MUST NOT be pre-diluted. Such pre-dilution can result in false negative results.**
- **This test is not intended to be used as a screening test on patients without signs & symptoms of Ebola infection or to monitor individuals who are undergoing treatment.**
- **Do not smoke, eat, or drink in areas where specimens or kit reagents are handled.**
- **This package insert must be read completely before using the product.**
- **Follow the instructions carefully when performing the OraQuick® Ebola Rapid Antigen Test. Failure to do so may cause an inaccurate test result.**
- **This test should be performed at temperatures in the range of 15°-40°C (59°-104°F). If stored refrigerated, ensure that the divided pouch is brought to operating temperature (15°-40°C, 59°-104°F) before performing testing.**
- **Do not use this test beyond the expiration date printed on the divided pouch. Always check expiration date prior to testing.**
- **Individuals who have received an Ebola vaccine may produce false results.**

Device Handling Precautions

- Use all micropipettes, pipette tips, test stands, test devices, and developer solution vials only once and dispose of properly (see *Warnings and Precautions*). **Do not reuse any test components.**
- Inspect the divided pouch. If the divided pouch has been damaged, discard the divided pouch and its contents and select a new divided pouch for testing.
- Do not interchange test devices and developer solution vials from kits with different lot numbers.
- Avoid microbial contamination and exercise care in handling the kit components.
- Adequate lighting is required to read a test result.

STORAGE INSTRUCTIONS

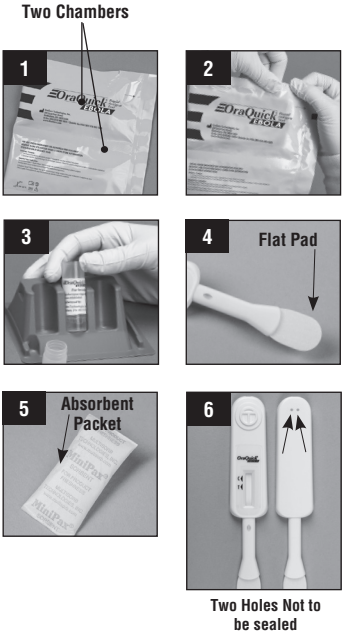
Store unused OraQuick® Ebola Rapid Antigen Tests unopened at 5°- 30°C (41°- 86°F). Do not open the divided pouch until you are ready to perform a test. If stored refrigerated, ensure that the divided pouch is brought to operating temperature (15°- 40°C, 59°- 104°F) before opening.

DIRECTIONS FOR USE

GENERAL TEST PREPARATION

1. Follow the *Warnings and Precautions* section in this instruction for use.
2. Gather the materials you will need.
3. Allow the OraQuick® Ebola Rapid Antigen Tests to come to operating temperature (15°- 40°C, 59°- 104°F) before use. Refer to the External Quality Control section in this package insert to determine when the Kit Controls should be run.
4. Set an OraQuick® Test Stand at your workspace, using only the stand provided.
5. Open the two chambers of the OraQuick® Divided Pouch ("Pouch") by tearing at the notches on the top of each side of the Pouch (*see pictures 1 and 2*).
6. Remove the Developer Solution Vial ("Vial") from the Pouch. Hold the Vial firmly in your hand. Carefully remove the cap from the Vial by gently rocking the cap back and forth while pulling it off. Set the cap on your workspace cover.
7. Slide the Vial into the top of one of the slots in the Stand. **DO NOT** force the vial into the Stand from the front of the slot as splashing may occur. Make sure the Vial is pushed all the way to the bottom of the slot in the Stand (*see picture 3*).
8. Remove the Device from the Pouch. Handle the device by the plastic housing, **NOT** the Flat Pad (*see picture 4*). Place the device on a flat clean surface. Check to make sure that an Absorbent Packet is included with the Device (*see picture 5*). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.

   NOTE: DO NOT seal the two holes in the back of the Device with labels or other materials. Doing so may cause an Invalid result (*see picture 6*).



SPECIMEN COLLECTION AND TESTING PROCEDURE

The OraQuick® Ebola Rapid Antigen Test can be used for testing venipuncture whole blood and fingerstick whole blood specimens or cadaveric oral fluid specimens. Refer to the specific testing procedures below.

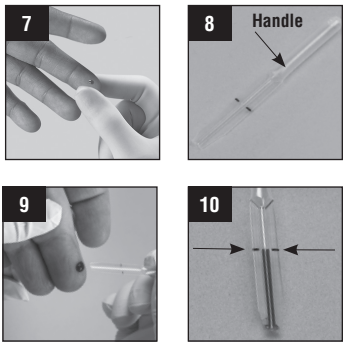
FINGERSTICK WHOLE BLOOD AND VENIPUNCTURE PROCEDURE

STEP 1: COLLECT

STEP 1A: FINGERSTICK WHOLE BLOOD

1. Using an antiseptic wipe, clean the finger of the person being tested. Allow the finger to dry thoroughly or wipe dry with a sterile gauze pad. Using a sterile lancet, puncture the skin just off the center of the finger pad and perpendicular to the fingerprint ridges. Apply slight pressure beside the point of the puncture (*see picture 7*). Avoid aggressive squeezing of the finger to make it bleed. Wipe away this first drop of blood with a sterile gauze pad. Allow a new drop of blood to form.
2. Pick up an unused plastic micropipette by the handle (*see picture 8*). Hold the micropipette horizontally and touch the tip to the drop of blood (*see picture 9*). Filling of the micropipette is automatic, never squeeze the micropipette while sampling. To prevent bubbles, the tip of the pipette must maintain uninterrupted contact with the blood sample until filled. Make sure that the micropipette is filled up to the indicator line with blood and there are no bubbles present (*see picture 10*). If a bubble is present, discard collected sample and obtain a new sample using a new micropipette.

   NOTE: If the micropipette is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new micropipette for the collection of the blood sample.

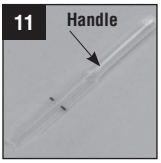


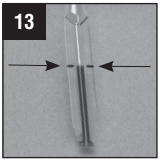
STEP 1B: VENIPUNCTURE WHOLE BLOOD

1. Using standard venous phlebotomy procedures collect a whole blood sample using a tube containing EDTA (lavender top) anticoagulant. If the specimens are not tested at the time of collection, the specimen may be stored at 2°- 30°C (36°- 86°F) for up to 24 hours.
2. Prior to testing, mix the blood tube gently by inversion several times to ensure a homogeneous sample.

3a. Pick up an unused micropipette by the handle (*see picture 11*). Place the tip of the micropipette in the blood tube. Filling of the micropipette is automatic, never squeeze the micropipette while sampling *(see picture 12*). To prevent bubbles, the tip of the pipette must maintain uninterrupted contact with the blood sample until filled. Make sure that the micropipette is filled up to the indicator line with blood and there are no bubbles present (*see picture 13*). If a bubble is present, discard collected sample and obtain a new sample using a new micropipette.
NOTE: If the micropipette is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new micropipette for the collection of the blood sample.

3b. A calibrated lab pipette, capable of dispensing 20µL with a disposable tip, may be used in place of the micropipette. After drawing up the sample, inspect the tip for bubbles (*see picture 14*). If a bubble is present, discard the collected sample and obtain a new sample using a new tip.





STEP 2: TEST

1. Deposit the blood sample through the sample port on the device by compressing the micropipette or releasing the sample from the calibrated pipette directly above the sample port (*see pictures 15-16*). **Samples MUST only be applied directly to the device and must NOT be pipetted into the Developer Vial.**
2. Insert the Flat Pad of the Device all the way into the Developer Vial (*see picture 17*). Make sure that the Flat Pad touches the bottom of the Vial. The Result Window on the Device should be facing towards you (*see picture 18*).
3. Start timing the test (*see picture 19*). **DO NOT** remove the Device from the Vial while the test is running. Red fluid will appear and travel up the Result Window. The red fluid may gradually lighten as the test develops (*see picture 20*). Read the results in a fully lighted area. Positive results may be interpreted as soon as lines are visible at the Test (T) Zone and Control (C) Zone and have been observed as early as 4 minutes. **All negative results MUST be read at 30 minutes after inserting the device into the Developer Vial. Read times less than 30 minutes significantly affect the performance of the device and prevent the correct identification of low positive samples**.
4. Refer to the *Test Result and Interpretation of Test Result* section on page 8 of in this package insert.

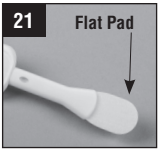
CADAVERIC ORAL FLUID PROCEDURE – DIRECT COLLECTION

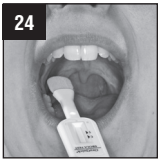
STEP 1: COLLECT

1. Remove the Device from its Pouch. Handle the device by the plastic housing, **NOT** the Flat Pad (*see picture 21*). Check to make sure that an Absorbent Packet is included with the Device (see picture 22). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
2. Open the mouth of the cadaver and collect a sample from the posterior oral cavity by swiping the flat pad around the back of the soft palate (*see pictures 23 and 24*). If collection in this manner is not feasible due to rigor mortis, collection of cadaveric oral fluid can be taken from the gum line. To obtain a sample from the gum line, swipe the flat pad once around the top and once around the bottom of the gum line (*see pictures 25 and 26*).
   NOTE: Both sides of the Flat Pad may be used during this procedure.
3. If the device cannot be placed immediately in the Developer Vial for Testing (Step 2 below), the device may be placed in a foil Transfer Pouch. **Only those pouches provided by OraSure Technologies as an accessory as part number (1001-0494) should be used to ensure proper stability of the sample.**
4. Sealed Transfer Pouch may be stored at 15°- 40°C (59°- 104°F) for 60 minutes or at 2°- 8°C (36°- 46°F) for up to 22 hours prior to testing.

STEP 2: TEST

1. If testing samples that were stored on ice, remove the Transfer Pouch from storage and allow it to come to room temperature for 15 minutes prior to testing.
2. Insert the Flat Pad of the Device all the way into the Vial (*see picture 27*). Make sure that the Flat Pad touches the bottom of the Vial. The Result Window on the Device should be facing towards you (*see picture 28*).
3. Start timing the test (*see picture 29*). DO NOT remove the Device from the Vial while the test is running. Purple fluid will appear and travel up the Result Window. The purple fluid will gradually disappear as the test develops (*see picture 30*). Positive results may be interpreted as soon as lines are visible at the Test (T) Zone and Control (C) Zone. Negative results have to be read 30 minutes after inserting the device into the Developer Vial.
4. Refer to the *Test Result and Interpretation of Test Result* section on page 8 of this Package Insert.





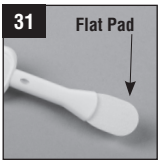
CADAVERIC ORAL FLUID PROCEDURE – TRANSPORT MEDIA

STEP 1: COLLECT

1. Cadaveric oral fluid specimens should be collected and handled following the instructions for use of the swab/viral transport media. Once a swab specimen is collected, it should be placed in the transport media vial. Specimens may be stored at 2°- 40°C (36°- 104°F) for up to 24 hours. If the sample cannot be tested within 24 hours of collection, the transport media can be frozen at - 70°C (- 94°F) with a maximum of 3 freeze/thaw cycles.

STEP 2: TEST

1. Prior to testing, mix the transport media tube gently by inversion several times to ensure a homogeneous sample. Remove the collection swab from the tube.
2. Remove the Device from the Pouch. Handle the device by the plastic housing, NOT the Flat Pad (s*ee picture 31).* Place the device on a flat clean surface. Check to make sure that an Absorbent Packet is included with the Device (*see picture 32*). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
   NOTE: DO NOT cover the two holes in the back of the Device with labels or other materials. Doing so may cause an Invalid result (*see picture 33*).



Two Holes Not to be sealed

3. Using a calibrated laboratory pipette with disposable tip, slowly draw up 20µL of sample from the viral transport media tube (*see picture 34*). Inspect the tip for bubbles in the sample (*see picture 35*). If a bubble is present, discard the sample and obtain a new sample using a new pipette tip.
4. Deposit the cadaveric sample into the sample port on the device by inserting the pipette tip directly above the sample port (*see picture 36*) and releasing the sample.
5. Insert the Flat Pad of the Device all the way into the Vial (*see picture 37*). Make sure that the Flat Pad touches the bottom of the Vial. The Result Window on the Device should be facing towards you (*see picture 38*).
6. Start timing the test (*see picture 39*). **DO NOT** remove the Device from the Vial while the test is running. Purple fluid will appear and travel up the Result Window. The purple fluid will gradually disappear as the test develops (*see picture 40*). Positive results may be interpreted as soon as lines are visible at the Test (T) Zone and Control (C) Zone. Negative results have to be read 30 minutes after inserting the device into the Developer Vial.
7. Refer to the *Test Result and Interpretation of Test Result* section on page 8 of this Package Insert.

GENERAL TEST CLEAN-UP

1. Dispose of the used test materials in a biohazard waste container. All equipment and biohazardous waste should be discarded in accordance with country, state, and local laws and policies.
2. Change your gloves between each test to prevent contamination. Throw away the used gloves in a biohazard waste container.
3. Use a freshly prepared 10% solution of bleach to clean up any spills.

QUALITY CONTROL PROCEDURES

Built-in Control Features

The OraQuick® Ebola Rapid Antigen Test has a built-in procedural control that demonstrates assay validity. A red to purple line in the Control (C) zone 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 or negative for Ebola Antigens. (Refer to the *Test Result and Interpretation of Test Result* section on page 8 of this package insert).

External Quality Control

OraQuick® Ebola Rapid Antigen Test Kit Controls must be used with the OraQuick® Ebola Rapid Antigen Test. The Kit Controls are specifically formulated and manufactured to ensure performance of the Test, and are used to verify your ability to properly perform the test and interpret the results. The Ebola Positive Control will produce a positive test result andthe Ebola Negative Control will produce a negative test result (Refer to the *Test Result and Interpretation of Test Result* section on page 8 of this package insert). Use of kit control reagents manufactured by any other source may not produce the required results, and therefore, will not meet the requirements for an adequate quality assurance program for the OraQuick® Ebola Rapid Antigen Test. If external controls do not produce expected results, patient testing should not be performed. Contact OraSure Technologies' Customer Care if the Kit Control reagents do not produce the expected results.

Run the External Controls under the following circumstances:

- Each new operator prior to performing testing on patient specimens,
- When opening a new test kit lot,
- Whenever a new shipment of test kits is received,
- If the temperature of the test kit storage area falls outside of 5°- 30°C (41°- 86°F), and
- At periodic intervals as dictated by local, state and country laws and by the user facility.

Test Procedure for External Controls:

Refer to the OraQuick® Ebola Rapid Antigen Test Kit Control package insert for full instruction on the use of these reagents. It is the responsibility of each laboratory using the OraQuick® Ebola Rapid Antigen Test to establish an adequate quality assurance program to ensure the performance of the device under its specific locations and conditions of use.

Qualification for New Operators

The OraQuick® Ebola Visual Reference Panel is available separately for use with the OraQuick® Ebola Rapid Antigen Test. OraQuick® Ebola Visual Reference Panel includes potential test results including negative, low positive, and the limit of detection of the device. New operators must be able to correctly interpret all devices in the OraQuick® Ebola Visual Reference Panel prior to using the OraQuick® Ebola Rapid Antigen Test device with patient samples. Failure to read at low intensities can result in the inability to detect specimens near the limit of detection of the OraQuick® Ebola Rapid Antigen Test and may result in false negative results.

TEST RESULT AND INTERPRETATION OF TEST RESULT

Positive results may be interpreted as soon as lines are visible in the Test (T) Zone and the Control (C) Zone and have been observed as early as 4 minutes. Negative results have to be read 30 minutes after inserting the device into the Developer Vial.

NEGATIVE

A test is **Negative** if:

A red to purple line appears in the C Zone and NO line appears next to the T Zone (*see pictures 41a/b*)

A Negative test result is interpreted as Ebola antigen not detected in the specimen. The cadaver is presumed negative for Ebola antigen.

A Negative result does not preclude Ebola virus infection.

POSITIVE

A test is **Positive** if:

A red to purple line appears in the C Zone and a red to purple line appears in the T Zone. Lines may vary in intensity. The test is positive regardless of how faint these lines appear (*see pictures 42a/b, 43a/b, and 44a/b*).

A Positive test result is interpreted as Ebola antigen detected in the specimen. The patient/cadaver is presumed positive for Ebola antigen. Definitive identification of EVD requires additional testing and confirmation procedures in consultation with public health and/or other authorities to whom reporting is required.

In accordance with CDC and WHO recommendations cadavers with a positive result should be subjected to safe and dignified burial procedures and contacts of an Ebola positive cadaver should be identified. Follow up testing of possible contacts should be conducted in accordance with, EMERGENCY GUIDELINE Implementation and management of contact tracing for Ebola virus disease (http://apps.who.int/iris/bitstream/10665/185258/1/WHO_EVD_Guidance_Contact_15.1_eng.pdf?ua=1) issued by the World Health Organization (WHO) and the Centers for Disease Control (CDC).

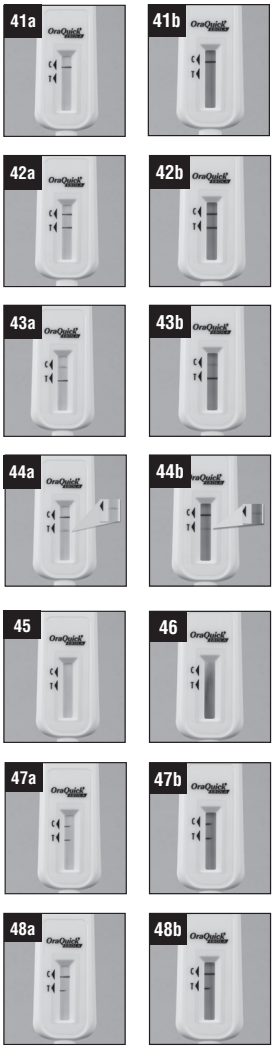
INVALID

A test is **Invalid** if any of the following occurs:

- **NO** red to purple line appears in the C Zone (*see picture 45*), or
- A red to purple background in the Result Window makes it difficult to read the result at 30 minutes (*see picture 46*), or
- Any partial line on one side of the C or T Zones (*see picture 47a/b and 48a/b*).

An Invalid test result means that there was a problem running the test, related either to the specimen or to the Test Device. **An Invalid result cannot be interpreted. An invalid test result needs to be repeated with a fresh sample and a new device. Please contact OraSure Technologies' Customer Care if you are unable to obtain a valid test result upon repeat testing.**

To report a device problem, contact OraSure Technologies Customer Service (1-800-orasure) within the United States or +(001) 610-882-1820 for outside the United States. You can also go to http://www.orasure.com/contact/contact-customer-service.asp.



LIMITATIONS OF THE TEST

1. Weak positive samples may take longer to develop and can take the entire 30 minutes for a test line to be present. Therefore, all negative test results MUST be read 30 minutes after inserting the device in the Developer Vial. Negative test result must not be reported prior to reading the device at 30 minutes.
2. Reading any test result after 30 minutes may yield inaccurate test results.
3. Testing with the OraQuick® Ebola Rapid Antigen Test should not be performed unless the patient meets clinical and epidemiologic criteria for testing suspect specimens.
4. Assay results are for the presumptive identification of Ebola virus. The definitive identification of Ebola virus requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reporting is required. The diagnosis of Ebola virus must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of Ebola virus.
5. Negative results do not preclude Ebola virus infection and should not be used as the sole basis for patient management decisions. The definitive identification of Ebola Virus Disease (EVD) requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reporting is required.
6. Potential cross reactivity of the OraQuick® Ebola Rapid Antigen Test with Ebola vaccines or therapeutics has not been evaluated. Specimens from patients who have received therapeutics or vaccines against Ebola virus may exhibit false positive or other confounding test results.
7. Testing of whole blood samples with concentrations of Rheumatoid Factor above 1050 IU/mL may result in false positive results.
8. Testing cadaveric oral fluid samples with concentrations of mucin above 15mg/mL may result in false positive results.
9. Cross-reactivity with organisms other than those tested in the cross-reactivity study have not been assessed.

PERFORMANCE CHARACTERISTICS
WHOLE BLOOD CLINICAL PERFORMANCE

Performance of the device with Ebola virus positive fingerstick whole blood was established in a non-human primate model.

i. Sierra Leone Study

A total of 75 retrospective, remnant whole blood samples collected from patients in West Africa (Sierra Leone) during the 2014-2015 Ebola outbreak were tested with the OraQuick® Ebola Rapid Antigen Test. These samples were tested in West Africa using an U.S. FDA Emergency Use authorized (EUA) Ebola Virus Real-time RT-PCR Assay. The whole blood samples were stored frozen thereafter until testing with the OraQuick® Ebola Rapid Antigen Test. Testing was performed in a randomized, blinded manner. OraQuick® Ebola Rapid Antigen Test performance in comparison to the results generated by the EUA Ebola Virus Real-time RT-PCR Assay (the Comparator) were calculated based on OraQuick® Ebola Rapid Antigen Test results that were read at 30 minutes.

Percent Agreement against the RT-PCR comparator – overall and stratified by Ct

	PCR Ct Ranges	Percent Agreement	95% CI[1]
PPA	15 – 23	100% (16/16)	79.41% - 100.0%
	24 – 34[2]	44.4% (4/9)	13.70% - 78.80%
	15 – 34 (overall)	84.0% (21/25)	63.92% - 95.46%
NPA	>40	98.0% (49/50) [3]	89.35% - 99.95%

[1] Calculated using Clopper-Pearson exact method. [2] Cts in this range are representative for Ebola concentrations around and below the LoD of the OraQuick® Ebola Rapid Antigen Test. [3] This false positive sample tested repeat positive in a re-test.

OraQuick® Ebola Rapid Antigen Test compared to the Comparator

		Comparator RT-PCR Results										Comparator RT-PCR Results	
		15- 20		21-24		25-29		30-34		Overall		Ebola not detected	
		+	-	+	-	+	-	+	-	+	-	+	-
OQ Ebola Results	+	7		9		3		2		21			1
	-		0		0	2	0	2	0	4	0	0	49

No samples were tested with a Ct value of 24 or 29.

ii. Ebola Positive Contrived Blood Samples

Twenty-Five (25) venous whole blood samples from febrile individuals (> 100.4°F) were collected and spiked with Gamma Irradiated Zaire Ebola Virus, Mayinga (BEI, NR-31807) to make contrived positive samples. Twelve (12) samples were spiked at 1.5 x Limit of Detection (LoD), and thirteen (13) were spiked at 5 x LoD. Positive percent agreement (PPA) for the venous whole blood samples was 100% (95% CI 86.28% - 100.00%). Results are summarized in the table below.

Sample Type	Positive Percent Agreement (n/N)	95% CI*
Venous Whole Blood	100% (25/25)	86.28% - 100.00%
nn = number in agreement, N = sample size *Confidence Interval (CI) calculated using Clopper-Pearson (exact) method.		

iii. Performance in a Non-Endemic Population

To support a fingerstick whole blood claim, a specificity study was conducted on 26 subjects in the United States. Data from one individual was excluded due to out of window reads. In another study, a total of 493 individuals were enrolled across 4 sites in the United States. Of these, 38 individual's samples were used to contrive positive samples for blinding purposes, 1 individual withdrew consent and 4 individual samples were excluded from the analysis due to deviations. The remaining 450 individuals were included in the analysis of which 226 were venous whole blood samples and 224 were fingerstick blood samples. A sub-set of the individuals enrolled were febrile (> 100.4°F). A summary of all results are provided in the table below.

Sample Type	Negative Percent Agreement (n/N)	95% CI*
Venous Whole Blood - febrile	100% (21/21)	83.89% - 100.00%
Venous Whole Blood - non-febrile	100% (205/205)	98.22% - 100.00%
Fingerstick Whole Blood - febrile	100% (21/21)	83.89% - 100.00%
Fingerstick Whole Blood - non-febrile	99.6% (227/228)	97.59% - 99.99%
n = number in agreement, N = sample size *Confidence Interval (CI) calculated using Clopper-Pearson (exact) method.		

iv. Fingerstick Whole Blood Performance

Performance of the device with Ebola virus positive fingerstick whole blood was established in a non-human primate (NHP) model. The purposes of the NHP study was to evaluate (1) concordance of the OraQuick® Ebola Rapid Antigen Test results between venous whole blood (venous) and capillary blood (fingerstick) and (2) concordance of OraQuick® Ebola Rapid Antigen Test results with a reference RT-PCR assay under EUA.

The table below summarizes the results of the animal matched venous whole blood and fingerstick whole blood tested on the OraQuick device, along with the RT-PCR results. NPA of the OraQuick Ebola Rapid Antigen Test was calculated using the animal's baseline samples prior to viral challenge. NPA was 100% (10/10 samples) for venous whole blood and fingerstick.

	PPA (compared to Infected Status)		PPA (compared to PCR)	
	Fingerstick	**Venous**	**Fingerstick**	**Venous**
Day 3	20% (1/5)	0 % (0/5)	N/A	N/A
Day 5	100% (5/5)	60% (3/5)	100% (5/5)	60% (3/5)
Day 7 to 8	100% (4/4)	100% (5/5)	100% (4/4)	100% (5/5)

v. Performance with WHO International Reference Panel for Ebola Virus VP40 Antigen

The WHO recombinant VP40 reference material was evaluated to determine the dilutional sensitivity of the OraQuick® Ebola Rapid Antigen Test with an independent standardized material. This material (1st Reference Reagent 2016, lyophilized Ebola VP40 Antigen; Item #2016.2302, Sample 3) was obtained from National Institute for Biological Standards and Control (NIBSC). Sample 3 was reconstituted per manufacturer's instructions, pooled, and serial dilutions prepared in whole blood. Five sets of dilutions were prepared using the same whole blood sample. The dilutions and results are displayed in the table below.

		Rep 1	**Rep 2**	**Rep 3**	**Rep 4**	**Rep 5**
Undiluted	**0**	R	R	R	R	R
Dilution	**1:3**	NR	NR	R	R	R
	1:6	NR	NR	NR	NR	NR
	1:9	NR	NR	NR	NR	NR
	1:12	NR	NR	NR	NR	NR
	1:24	NR	NR	NR	NR	NR
	1:48	NR	NR	NR	NR	NR

R: Reactive. NR: Non-Reactive. R and NR results are equivalent to Positive and Negative results, respectively.

WHOLE BLOOD ANALYTICAL SENSITIVITY

WHOLE BLOOD LIMIT OF DETECTION

A Limit of Detection (LoD) range finding study in venous whole blood identified 1.64x106 TCID50/mL as the tentative LoD for Zaire Ebola Inactivated Virus (Virus Stock: Ebola Zaire Mayinga ZZXDK901 / 812094 / VSP / 2.5x108 TCID50/mL). This tentative LoD was confirmed as the LoD by 19 out of 20 replicates testing positive with the same Ebola Inactivated Virus at this concentration.

Additionally, a LoD range finding study was performed using recombinant VP40 antigen spiked into pooled venous whole blood. This LoD range finding study determined the tentative LoD of the OraQuick® Ebola Rapid Antigen Test in venous whole blood with recombinant antigen to be 53,000 pg/mL or 1.06 ng/test. This tentative LoD was confirmed as the LoD by 20 out of 20 replicates testing positive with the same recombinant VP40 antigen at this concentration.

WHOLE BLOOD ANALYTICAL REACTIVITY (INCLUSIVITY)

Analytical reactivity of the OraQuick® Ebola Rapid Antigen Test was evaluated for additional strains of the Ebola virus. Testing of three (3) replicates was performed using negative venous whole blood as the testing sample matrix. The OraQuick® Ebola Rapid Antigen Test also reacts with E. Sudan and E. Bundibugyo in addition to reacting with E. Zaire.

Ebola Strain	Inactivated or Live	Concentration Tested	Reactivity (Positive (P)/Negative (N))
Ebola Zaire Mayinga ZZXDK901/812094/VSP	Inactivated	$1.5x10^6$ $TCID_{50}$/mL	P[B]
Ivory Coast (COTE D'IVOIRE 11/27/94)	Inactivated	Unknown (1:10 dilution) Unkown (1:1 dilution)	N N
Reston (119876 Pennsylvania)	Inactivated	3.16×10^6 PFU/mL 3.16×10^7 PFU/mL	N N
Sudan (BONEFACE)	Inactivated	10^5 PFU/mL 5×10^5 PFU/mL	N P[A]
Sudan[E] (200011676 GULU)	Inactivated	5.6×10^4 PFU/mL 2.8×10^5 PFU/mL	P[A] P
Bundibugyo[F] (200706291 UGANDA prototype)	Inactivated	3.98×10^4 PFU/mL 1.99×10^5 PFU/mL	P P
Sudan Gulu[E] (2000011676)	Inactivated	3.25×10^5 PFU/ml 5.95×10^5 PFU/mL 1.19×10^6 PFU/mL 1.79×10^6 PFU/mL	N N P P[C]
Bundibugyo[F] (Uganda)	Inactivated	3.73×10^4 PFU/mL 6.83×10^4 PFU/mL 1.37×10^5 PFU/mL 2.05×10^5 PFU/mL	N N[D] P P
Taï Forest (aka Ivory Coast)	Inactivated	1.36×10^7 VP/mL 7.5×10^7 VP/mL	N N
Reston (aka H28)	Inactivated	5.83×10^5 PFU/mL	N

[A] Two of three replicates tested Positive and acceptance criteria met.

[B] Testing completed in LoD study.

[C] A 4th replicate was added to confirm original non-reactive results for one replicate – 3 out of 4 replicates reactive.

[D] One of three replicates was reactive and criteria was not met.

[E,F] The two tested materials from the same strain have been obtained from a different source. Differences in preparation methods can lead to differences in the number of plaque forming units even if the starting material is the same.

WHOLE BLOOD HIGH DOSE HOOK EFFECT

A high-dose hook effect is a false negative result due to very high concentrations of the target analyte. Antigen at excessive concentrations could quench the specific antibodies in the assay decreasing complexes between the antibody on the gold conjugate and the biotinylated antibody. Insufficient binding of the gold conjugate could occur at the test line and the result interpreted as a false negative result. An analytical study was conducted and the results demonstrate acceptable performance of the OraQuick® Ebola Rapid Antigen Test when evaluating samples at excessive antigen concentrations. There is no decrease in visual intensity at the test line for a VP40 antigen concentration up to 10,000 times the established LoD.

WHOLE BLOOD ANALYTICAL SPECIFICITY

WHOLE BLOOD INTERFERING SUBSTANCES

The OraQuick® Ebola Rapid Antigen Test was evaluated with the following interfering substances present in negative whole blood and whole blood spiked with recombinant antigen (rAg) at 2.0 X the LoD in order to assess their potential effect on the assay performance as per CLSI guidelines EP7-A2[3]. For Bilirubin, Hemoglobin, Protein and HAMA testing was completed on three (3) whole blood samples tested at n=2 replicates for each condition. Rheumatoid Factor testing was performed on three serum samples, that were each tested in two dilutions with n=2 replicates. The concentrations of Rheumatoid Factor that were tested ranged from 525 IU/mL to 11,900 IU/mL. The remaining substances were tested on four (4) whole blood samples at n=3 replicates. Those interfering substances that produced occasional false negative results in the low positive rAg spiked samples (2.0 X LoD) were repeated in the presence of slightly higher rAg concentration (4 X LoD) to distinguish random statistical distribution of measurements on a low positive sample from true interference of the test substance.

Interfering Substance	Target Testing Concentration	n	Negative Samples		Positive rAG Spiked Samples	
			Positive	Negative	Positive	Negative
Bilirubin	25 mg/dL	6	0	6 (100%)	6 (100%)	0
Hemoglobin	20 g/dL	6	0	6 (100%)	6 (100%)	0
Protein	5 g/dL	6	0	6 (100%)	6 (100%)	0
HAMA	2464 ng/mL	6	0	6 (100%)	6 (100%)	0
Rheumatoid Factor (serum)	1050 IU/mL	2	0	2 (100%)	2 (100)	0
	2920 IU/mL	2	2 (100%)	0	2 (100%)	0
Rheumatoid Factor (serum in whole blood)	525 IU/mL	4	0	4 (100%)	3 (75%)	1 (25%)
	1460 IU/mL	4	4 (100%)	0	4 (100%)	0
Rheumatoid Factor (plasma)	11,900 IU/mL	6	6 (100%)	0	6 (100%)	0
Rheumatoid Factor (plasma in whole blood)	2000 IU/mL	6	5 (83%)	1 (17%)	6 (100%)	0
Cholesterol	13 mmol/L	12	0	12 (100%)	12 (100%)	0
Antinuclear Antibodies	1:160 titer	12	0	12 (100%)	11 (91.7%)	1 (8.3%)
	1:120 titer	3			3 (100%)	0
	1:160 titer at 4.0 x LoD	12			12 (100%)	0
Acetylsalicylic Acid	3.62 mmol/L	12	0	12 (100%)	12 (100%)	0
Salicylic Acid	4.34 mmol/L	12	0	12 (100%)	12 (100%)	0
Sulfamethoxazole	1.58 mmol/L	12	0	12 (100%)	12 (100%)	0
Ribavirin	11.04 µg/mL	12	0	12 (100%)	11 (91.7%)	1 (8.3%)
	5.52 µg/mL	3			3 (100%)	0
	11.04 µg/mL at 4.0 x LoD	12			12 (100%)	0
Emtricitabine	7.5 µg/mL	12	0	12 (100%)	11 (91.7%)	1 (8.3%)
	3.75 µg/mL	3			3 (100%)	0
	7.5 µg/mL at 4.0 x LoD	12			12 (100%)	0
Efavirenz	16.6 µg/mL	12	0	12 (100%)	12 (100%)	0
Ritonavir	33.6 µg/mL	12	0	12 (100%)	10 (83.3%)	2 (16.7%)
	16.8 µg/mL	6			6 (100%)	0
	33.6 µg/mL at 4.0 x LoD	12			12 (100%)	0
Elvitegravir	5.61 µg/mL	12	0	12 (100%)	12 (100%)	0
Chloroquine	17.95 µg/mL	12	0	12 (100%)	12 (100%)	0
Atovaquone / Proguanil	89.1/2.8 µg/mL	12	0	12 (100%)	12 (100%)	0
Ibuprofen	2425 µmol/L	12	0	12 (100%)	12 (100%)	0
Acetaminophen	1324 µmol/L	12	0	12 (100%)	12 (100%)	0
Quinine	148 µmol/L	12	0	12 (100%)	11 (91.7%)	1 (8.3%)
	74 µmol/L or 24 µg/mL	3			3 (100%)	0
	148 µmol/L at 4.0 x LoD	12			12 (100%)	0
Rifampin	78.1 µmol/L	12	0	12 (100%)	12 (100%)	0
Amoxicillin	206 µmol/L	12	0	12 (100%)	12 (100%)	0

Tetracycline	34 µmol/L	12	0	12 (100%)	12 (100%)	0
Erythromycin	81.6 µmol/L	12	0	12 (100%)	12 (100%)	0
Biotin	3.6 µg/mL	12	0	12 (100%)	12 (100%)	0

Rheumatoid Factor caused false positive results in the OraQuick® Ebola Rapid Antigen Test at all tested concentrations greater than 1050 IU/mL. Concentrations of Rheumatoid Factor equal or less than 1050 IU/mL do not cause interference in the assay.

WHOLE BLOOD CROSS REACTIVITY

Cross reactivity of the OraQuick® Ebola Rapid Antigen Test was evaluated by testing additional viral, bacterial, and parasitic pathogens. In this study three (3) replicates were tested with the pathogens spiked into venous whole blood at the concentrations listed below. None of the tested organisms produced false positive results in the OraQuick® Ebola Rapid Antigen Test at the concentration tested.

Virus/Bacteria/Parasite	Inactived or Live	Type/Strain	Concentration Tested	Reactivity
Marburg	Inactivated	RAVN Musoke Lake Victoria (aka Musoke) 2005011379 Angola VOEGE	Log 5.53 $TCID_{50}$/mL 3.16 x 10^6 PFU/mL 3.73 x 10^6 PFU/mL 1.44 x 10^6 PFU/mL 3.6 x 10^6 PFU/mL	None None None None None
Crimean Congo Hemorrhagic Fever	Inactivated	OMAN199809166 #811466	5.6 x10^4 $TCID_{50}$/mL	None
Lassa	Inactivated	Josiah Josiah Macenta (aka Z-136) Pinneo	3.16 x 10^5 PFU/mL 1.88 x 10^5 PFU/mL 1.19 x 10^7 PFU/mL 2.00 x 10^6 PFU/mL	None None None None
Rift Valley Fever	Inactivated	ZH-501 ZH-501	3 x10^6 PFU/mL 5.43 x 10^6 PFU/mL	None None
Yellow Fever	Inactivated	Vaccine Strain #806588 Asibi	Unknown 1.88 x 10^6 PFU/mL	None None
Chikungunya virus	Live	ATCC VR-64	3.0 x 10^8 LD_{50}/mL	None
Influenza A	Live	A/Wisconsin/10/1998	2.3 x 10^5 $TCID_{50}$/mL	None
Influenza B	Live	B/Florida/04/06	4.6 x 10^5 $TCID_{50}$/mL	None
Rotavirus	Live	ATCC VR-899	6.4 x 10^6 $TCID_{50}$/mL	None
Adenovirus	Live	Type 5 ATCC VR-5	2.0 x 10^5 $TCID_{50}$/mL	None
RSV	Live	ATCC VR-26	9.0 x 10^5 $TCID_{50}$/mL	None
Enterovirus	Live	Enterovirus 71 ATCC VR-1432	5.1 x 10^5 $TCID_{50}$/mL	None
Salmonella	Live	S. enterica ATCC 10708	3.8 x 10^7 CFU/mL	None
Salmonella typhi	Live	S. typhi ATCC 6539	5.4 x 10^5 CFU/mL	None
Shigella	Live	S. dysenteriae ATCC 9361	4.0 x 10^6 CFU/mL	None
Pseudomonas aeruginosa	Live	P. aeruginosa ATCC 15442	3.4 x 10^8 CFU/mL	None
Vibrio Cholera	Live	V. cholera ATCC 39050	6.7 x 10^5 CFU/mL	None
Streptococcus pneumonia	Live	S. pneumonia ATCC 6303	2.1 x 10^8 CFU/mL	None
Hemophilus influenza (meningitis)	Live	H. influenzae ATCC 33930	3.0 x 10^7 CFU/mL	None
Leptospira genus	Live	L. biflexa ATCC 23582	~ 9.1 x 10^4 CFU/mL	None
Neisseria meningitides	Live	N. meningitides ATCC 13090	3.5 x 10^6 CFU/mL	None
Yersinia enterocolitica	Live	Y. enterocolitica ATCC 23715	7.0 x 10^6 CFU/mL	None
Plasmondium vivax (malaria)	Live	P. falciparum ATCC 30932	0.26% parasitemia	None
Trypanosoma	Live	P. vivax ATCC 30151	6.8 x 10^5 cells/mL	None
Rickettsia	Protein Only	R. africae (protein) BEI NR-42992	11.6 mg/mL	None
Dengue	Inactivated	Serotype 1, strain WP74 Serotype 2, strain 16803 Serotype 3, strain CH53489 Serotype 4, strain 341750	6.20 x 10^4 PFU/mL 7.18 x 10^5 PFU/mL 1.52 x 10^4 PFU/mL 2.12 x 10^5 PFU/mL	None None None None

Virus/Bacteria/Parasite	Inactived or Live	Type/Strain	Concentration Tested	Reactivity
Bacteroides fragilis	Live	VPI 2553 [EN-2; NCTC 9343] ATCC 25285	1.0 x 10^8 CFU/mL	None
Klebsiella pneumoniae	Live	[CIP 104216, NCIB 10341] ATCC 4352	5.8 x 10^7 CFU/mL	None
Enterococcus faecium	Live	NCTC 7171 [DSM 20477, JCM 8727, NCDO 942] ATCC 19434	7.6 x 10^7 CFU/mL	None
Escherichia coli	Live	AMC 198 ATCC 11229	4.5 x 10^7 CFU/mL	None
Vesicular Stomatitis Virus	Live	Rhabdovirus Indiana Lab [V-520-001-522] ATCC VR-158	7.9 x 10^6 $TCID_{50}$/mL	None
Human Immunodeficiency Virus-1	Live	Clinical Sample ZeptoMetrix 022117B1D	5.1 x 10^6 $TCID_{50}$/mL	None
Hepatitis A Virus	Live	Clinical Sample University of Ottawa 021916B1C-1D	4.5 x 10^7 $TCID_{50}$/mL	None
Cytomegalovirus	Live	Herpesviridae AD-169 ATCC VR-1788	2.9 x 10^5 $TCID_{50}$/mL	None
Epstein-Barr Virus	Live	Herpesviridae, Lymphocryptovirus P-3 ATCC VR-602	1.44 10^5 copies/mL*	None
Hepatitis B Virus	Live	Clinical Sample DLS13-01459	1.2 x 10^7 IU/mL	None
West Nile Virus	Live	Flaviviridae, Flavivirus B 956 [V-554-001-522] ATCC VR-1267	2.3 x 10^8 $TCID_{50}$/mL	None
Hepatitis C Virus	Live	Clinical Sample DLS14-08008	4.7 x 10^6 IU/mL	None
Mumps Virus	Live	Flaviviridae, Flavivirus B 956 [V-554-001-522] ATCC VR-1267	7.1 x 10^5 TCI_{D50}/mL	None
Measles	Live	Paramyxoviridae, Morbillivirus Edmonston ATCC VR-24	1.5 x 10^6 $TCID_{50}$/mL	None
Rubella	Live	Togaviridae, Rubivirus M33 ATCC VR-315	1.5 x 10^5 $TCID_{50}$/mL	None
Streptococcus pneumoniae	Live	Slovakia 14-10 [29055] ATCC 700677	4.6 x 10^4 CFU/mL	None
Borrelia hermsii	Live	HS1 Serotype 26 ATCC BAA-2821	1:11 Dilution	None
Yersinia pseudotuberculosis	Live	IP2666 BEI NR-4371	1:11 Dilution	None
Rickettsia australis	Live	JC BEI NR-10454	8.1 x 10^5 $TCID_{50}$/mL	None

*Concentration determined in plasma.

WHOLE BLOOD REPRODUCIBILITY

The reproducibility of the OraQuick® Ebola Rapid Antigen Test was tested at 3 sites using 3 lots of test devices twice a day for 5 days with 9 operators (3 per site). Three whole blood panel member types (negative, low positive - 2x limit of detection (LoD), and moderate positive – 5x LoD) were tested. Panel members were blinded per operator, run, and device lot to ensure that the results of the panel member types were unpredictable to the operator. Overall concordance across operators, sites, and device lots was 99.6% (95% CI 98.9-99.9%) for the negative specimen, 99.9% (95% CI 99.3-100.0%) for the low positive specimen and 100.0% (95% CI 99.5-100.0%) for the moderate positive specimen.

CADAVERIC ORAL FLUID CLINICAL PERFORMANCE

i. WHO Study

A total of 277 retrospective cadaveric specimens (collected in VTM) were tested in a study conducted by the World Health Organization; all samples were originally tested with a PCR test. Prior to testing with the OraQuick® Ebola Rapid Antigen Test, all samples were re-tested with an EUA PCR test to confirm the original Ebola PCR result.

A total of 222 specimens negative with the original RT-PCR were re-tested on the EUA PCR. Of these specimens, 29 gave an invalid result, possibly because of a failure of the human gene target internal control due to poor specimen quality, and were excluded. Therefore, a total of 193 PCR negative specimens were included in the RDT evaluation.

Of the 55 specimens positive with the original RT-PCR and re-tested on the EUA PCR, 51 specimens passed as positive; 3 were negative and 1 gave an invalid result and were therefore excluded. Of the 51 positive specimens, 16 were tested in a manner inconsistent with the instructions for use and were therefore excluded from the study. A total of 35 positive specimens were included in the performance evaluation.

The performance of the OraQuick® Ebola Rapid Antigen Test when compared to the EUA PCR is shown in the following table:

	Comparator PCR	
	Positive Percent Agreement (PPA) (95% CI)	**Negative Percent Agreement (NPA) (95% CI)**
OraQuick® Ebola Rapid Antigen Test	34/35 97.1% (85.5 - 99.5)	193/193 100.00% (98.1 - 100)

Note: The study also included testing of 16 samples that were diluted 1:4 in distilled water. The OraQuick® Ebola Rapid Antigen test correctly detected 14 out of these 16 samples as positive. The two samples that were incorrectly detected as being negative had high PCR Ct values representative of Ebola virus concentrations below the assay's LOD. These diluted samples are not included in the performance calculation.

ii. CDC Study – Sierra Leone

CDC in collaboration with the Ministry of Health (MOH) has conducted a Field Evaluation of New Rapid Diagnostic Tests for Ebola Virus Disease in Sierra Leone that included the testing of cadavers. A total of 50 samples were tested with the OraQuick® Ebola Rapid Antigen Test according to the instructions for use with cadaveric oral fluid using the direct sampling method. The 50 samples tested by OraQuick® RDTs were all negative by PCR. One sample initially produced an invalid result and was re-tested according to the instructions for use; the sample re-tested as negative. The following table includes a summary of the field study data:

Date of testing	**Region**	**RDTs tested**	**Positive**	**Negative**	**Invalid**	**PCR**
January 10, 2016	Kenema	50	0	50[A]	0	50[B]

A) The control line on the OraQuick® device was not visualized and the test was interpreted as invalid. Upon repeat testing the; OraQuick® test was negative. A swab for PCR was collected and the samples were negative by PCR.

B) In the West African Outbreak PCR was performed in conjunction with the OraQuick® tests for all cadavers. The 50 samples tested by OraQuick® RDTs were all negative by PCR.

This study provided a Negative Percent Agreement (NPA) for the OraQuick® Ebola Rapid Antigen Test of 50/50 = 100% with a 95% Confidence Interval of 93 - 100%.

iii. CDC Study – Guinea

In Guinea 334 oral swab samples were taken from cadavers and tested in parallel with PCR and with the OraQuick® Ebola Rapid Antigen Test. Samples were collected between June 2015 and August 2015. All samples were negative by PCR and also tested negative by the OraQuick® Ebola Rapid Antigen Test.

iv. CDC Study – Liberia

Additionally, 97 specimens from cadavers in Liberia were tested with the OraQuick® Ebola Rapid Antigen Test. Samples were parallel tested with either the CDC or the DOD EUA PCR. Samples were collected between May and June 2015 and tested with the OraQuick® Ebola Rapid Antigen Test according to the instructions for use with cadaveric oral fluid. All samples tested were negative by PCR; three of these PCR negative samples resulted in an invalid test result with the OraQuick® Ebola Rapid Antigen Test. The samples were not retested with the OraQuick® Ebola Rapid Antigen Test and were therefore excluded from the performance calculation below. All other PCR negative samples also resulted in a negative OraQuick® Ebola Rapid Antigen Test result. This study provided a Negative Percent Agreement (NPA) for the OraQuick® Ebola Rapid Antigen Test of 94/94 = 100% with a 95% Confidence Interval of 96.1 to 100%.

v. OraSure Technologies Inc. Study – Ebola Positive Contrived Oral Fluid Samples

The performance of the device was evaluated using twenty (20) Ebola contrived positive saliva samples as a surrogate for direct collect oral fluid and spiking the sample onto the device collection pad. Samples were contrived positive using gamma-irradiated Zaire ebolavirus, Mayinga, NR-31807 from BEI Resources. Ebola negative samples were included in the blinded test reads to control for bias. Percent Positive Agreement was 95%. One contrived positive sample at the 1.5 x LoD level was recorded as a negative result. The negative samples yielded expected results with 100% concordance. This study provided a Positive Percent Agreement (PPA) of 19/20 = 95% with a 95% Confidence Interval of 75.13 to 99.87%.

vi. OraSure Technologies Inc. Study - Cadaver Oral Fluid Samples in Viral Transport Media (VTM)

The specificity performance of the OraQuick® Ebola Rapid Antigen Test in cadaveric oral fluid samples collected in Becton Dickinson (BD) Universal Viral Transport for Viruses, Chlamydiae, Mycoplasmas and Ureaplasmas and ∑-Virocult® Swab and Virus Transport Medium for the Collection of Virus Specimens was evaluated with 63 negative cadaveric oral fluid samples blinded with contrived positive oral fluid samples. OraQuick® Ebola Rapid Antigen Test results were negative for all cadaveric oral fluid samples tested in both the BD VTM and ∑-Virocult VTM. All contrived samples were correctly identified as positive by the operators. The Negative Percent Agreement (NPA) for the OraQuick® Ebola Rapid Antigen Test was determined to be 63/63 = 100% with a 95% Confidence Interval of 94.3 to 100.0% in both the BD VTM and ∑-Virocult VTM.

CADAVERIC ORAL FLUID LIMIT OF DETECTION – LIVING DONORS

A Limit of Detection (LoD) range finding study was conducted with oral fluid collected from living donors with the BD Universal Transport System (3mL medium), the ∑-Virocult Transport System (1mL medium), and directly collected with the OraQuick® Ebola Rapid Antigen Test. For the direct collection with the OraQuick® Ebola Rapid Antigen Test recombinant VP40 antigen was spiked directly on to the collection pad of the OraQuick® Ebola Rapid Antigen Test after oral fluid collection and prior to insertion in to the Developer Vial. Recombinant VP40 antigen was spiked on the swab of the respective transport system after oral fluid collection and prior to placement in the transport medium. A total of 20µL was then placed in the sample port of the OraQuick® Ebola Rapid Antigen Test prior to insertion of the device into the Developer Vial.

The tentative LoD for oral fluid directly collected from living donors with the OraQuick® Ebola Rapid Antigen Test was 0.53 ng/test with a VP40 antigen concentration in oral fluid of 7.6 ng/mL. This concentration was confirmed as the LoD by 19 out of 20 replicates testing positive with the same recombinant VP40 antigen at this concentration.

The tentative LoD for oral fluid collected from living donors with the BD Universal Transport System was 0.217 ng/test with a VP40 antigen concentration in oral fluid of 465 ng/mL. This concentration was confirmed as the LoD by 20 out of 20 replicates testing positive with the same recombinant VP40 antigen at this concentration.

The tentative LoD for oral fluid collected from living donors with the ∑-Virocult® Transport System was 3.2 ng/test with a VP40 antigen concentration in oral fluid of 3200 ng/mL. This concentration was confirmed as the LoD by 20 out of 20 replicates testing positive with the same recombinant VP40 antigen at this concentration.

Collector	LoD/Test [Amount of rAG per Test]	LoD [Concentration of rAG in Oral Fluid[B]]
Direct Collection OraQuick®	0.53 ng/test[A]	7.6 ng/mL
BD Universal Viral Transport for Viruses	0.217 ng/test	465 ng/mL
∑-Virocult® Transport System	3.20 ng/test	3200 ng/mL

[A] Recombinant antigen, live and inactivated virus were tested in parallel with the OraQuick® Ebola Rapid Antigen Test for use with whole blood. With whole blood the LoD of 0.53ng/test corresponded to an LoD of 1.64 x 10^6 TCID50/mL

[B] LoD concentration in oral fluid was calculated using the average volumes of oral fluid that is absorbed by each of the swabs/devices (i.e., 70 µl for the OraQuick® Ebola Rapid Antigen Test flat pad, 70 µl for the BD swab diluted into 3 mL of VTM and 50µl for the ∑-Virocult® swab diluted in 1 mL VTM) and the subsequent volume of 20µl of the VTM solution that was transferred to the device.

Additional testing has established that the analytical LoD in cadaveric oral fluid and live donor derived oral fluid is equivalent

CADAVERIC ORAL FLUID CROSS REACTIVITY

Cross reactivity of the OraQuick® Ebola Rapid Antigen Test was evaluated by testing additional viral and bacterial pathogens. In this study, three (3) replicates were tested with the pathogens spiked into Ebola negative oral fluid (saliva as surrogate) at the concentrations listed below. None of the tested organisms produced false positive results in the OraQuick® Ebola Rapid Antigen Test at the concentration tested.

Virus/Bacteria	Inactivated or Live	Type/Strain	Concentration Tested	Reactivity
Herpes Simplex Virus Type 1	Live	ATCC VR-260	2.7 x 10^6 $TCID_{50}$/mL	None
Herpes Simplex Virus Type 2	Live	ATCC VR-734	1.0 x 10^6 $TCID_{50}$/mL	None
Actinomyces viscosus	Live	ATCC 43146	2.9 x 10^6 CFU/mL	None
Candida albicans	Live	ATCC 18804	6.1 x 10^6 CFU/mL	None
Staphylococcus aureus	Live	ATCC 6538	3.6 x 10^7 CFU/mL	None
Staphylococcus epidermis	Live	ATCC 12228	3.9 x 10^6 CFU/mL	None
Streptococcus pyogenes	Live	ATCC 19615	1.4 x 10^7 CFU/mL	None
Streptococcus salivarius	Live	ATCC 7073	7.7 x 10^6 CFU/mL	None
Streptococcus mutans	Live	ATCC 25175	2.0 x 10^6 CFU/mL	None
Lactobacillus johnsonii	Live	ATCC 33200	1.9 x 10^6 CFU/mL	None
Porphyromonas gingivalis	Live	ATCC 49417	1.7 x 10^6 CFU/mL	None
Mycobacterium tuberculosis	Live	ATCC 25177	1.0 x 10^6 CFU/mL	None
Moraxella catarrhalis	Live	Ne 11 [CCUG 353, LMG 11192, NCTC 11020] ATCC 25238	2.7 x 10^7 CFU/mL	None
Corynebacterium diphteriae	Live	5159 ATCC 13812	8.4 x 10^6 CFU/mL	None
Nocardia sp.	Live	N1408 [QN360] ATCC 700034	5.4 x 10^5 CFU/mL	None
Bacteroides oralis	Live	VPI D27B-24 [NCTC 11459] ATCC 33269	5.1 x 10^5 CFU/mL	None
Chlamydolphia pneumoniae	Live	AR-39 ATCC 53592	2.6 x 10^6 IFU/mL	None
Mycoplasma pneumonia	Live	FH strain of Eaton Agent [NCTC 10119] ATCC 15531	2.6 x 10^6 IFU/mL	None
Bordetella pertussis	Live	Tohama I ATCC BAA-589	6.9 x 10^6 IFU/mL	None

Additional cross reactivity with the following organisms was performed for the OraQuick® Ebola Rapid Antigen Test for use with whole blood and no cross reactivity was observed at the tested concentration: Marburg, Crimean Congo Hemorrhagic Fever, Lassa, Rift Valley Fever, Yellow Fever (Vaccine Strain), Chikungunya virus, Influenza A, Influenza B, Rotavirus, Adenovirus, RSV, Enterovirus, Salmonella enterica, Salmonella typhi, Shigella dysenteriae, Pseudomonas aeruginosa, Vibrio cholera, Streptococcus pneumonia, Haemophilus influenza (meningitis), Leptospira, Neisseria meningitides, Yersinia enterocolitica, Plasmodium falciparum (malaria), Plasmodium vivax (malaria), Trypanosoma cruzi, Rickettsia africae (protein), Bacteroides fragilis, Klebsiella pneumoniae, Enterococcus faecium. E. Coli, Vesicular Stomatitis Virus, HIV-1, Hepatitis A, Hepatitis B, Hepatitis C, Cytomegalovirus, Epstein-Barr Virus, West Nile, Mumps, Measles, Rubella, Borrelia hermsii, Yersinia pseudotuberculosis, Rickettsia australis, Dengue. However, the test reacts with Ebola Sudan and Ebola Bundibugyo.

CADAVERIC ORAL FLUID INTERFERING SUBSTANCES

The OraQuick® Ebola Rapid Antigen Test was evaluated with the following interfering substances present in negative oral fluid and oral fluid spiked with recombinant antigen (rAg) at 2.0 X the LoD in order to assess their potential effect on the assay performance as per CLSI guidelines EP17-A2[4]. For Toothpaste, Mucin and Leukocytes testing was completed on three (3) oral fluid samples each tested at n=2 replicates for each condition.

The concentration for toothpaste could not be analytically quantified, but duration of interference use was two (2) minutes and then a thirty (30) minute wait before direct collection with the OraQuick® Ebola Rapid Antigen Test. At the Mucin 20mg/mL test concentration there was one (1) false positive in negative oral fluid test group and (1) false negative in the rAg spiked oral fluid test group. No interference was noted at the 15mg/mL test concentration.

Interfering Substances	Target Testing Concentration	Reactivity
Toothpaste	n/a	None
Mucin	20 mg/mL	Reactive
	15 mg/mL	None
Leukocytes	6.12 x 10 cells / L	None

CADAVERIC ORAL FLUID REPRODUCIBILITY

The reproducibility of the OraQuick® Ebola Rapid Antigen Test was tested at 3 sites using 3 lots of test devices twice a day for 5 days with 9 operators (3 per site). Three VTM Oral Fluid (live donor saliva as surrogate) panel member types (negative, low positive - 2x limit of detection (LoD), and moderate positive – 5x LoD) were tested. Panel members were blinded per operator, run, and device lot to ensure th 0at the results of the panel member types were unpredictable to the operator. Overall concordance across operators, sites, and device lots for VTM oral fluid was 99.9% (95% CI 99.3-100.0%) for the negative specimen, 99.8% (95% CI 99.1-100.0%) for the low positive specimen and 100.0% (95% CI 99.5-100.0%) for the moderate positive specimen.

Three Direct Collect Oral Fluid (live donor saliva as surrogate) panel member types (negative, low positive - 2x limit of detection (LoD), and moderate positive – 5x LoD) were also tested. Panel members were blinded per operator, run, and device lot to ensure that the results of the panel member types were unpredictable to the operator. Overall concordance across operators, sites, and device lots for direct collect oral fluid was 98.1% (95% CI 97.0-99.0%) for the negative specimen, 95.2% (95% CI 93.5-96.5%) for the low positive specimen and 99.4% (95% CI 98.6-99.8%) for the moderate positive specimen.

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3. *EMERGENCY GUIDELINE Implementation and management of contact tracing for Ebola virus disease* (http://apps.who.int/iris/bitstream/10665/185258/1/WHO_EVD_Guidance_ Contact_15.1_eng.pdf?ua=1) issued by the World Health Organization (WHO) and the Centers for Disease Control (CDC).

EXPLANATION OF SYMBOLS

LOT	Batch Code	IVD	*In Vitro* Diagnostic Medical Device
REF	Catalog Number		Manufacturer
	Caution, Consult Accompanying Documents	PN	Part Number
	Use By		Temperature Limitation
		Rx	Medical Prescription

For Technical or Customer Service within the United States, phone (800) ORASURE (800-672-7873).
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Critical reagents in the OraQuick® Ebola Rapid Antigen Test are being supplied by:

- the Viral Hemorrhagic Fever Consortium, or "VHFC" (www.VHFC.org). The VHFC reagents were developed with the support of the National Institute of Allergy and Infectious Diseases of the National Institutes of Health ("NIH/NIAID"). VHFC members Autoimmune Technologies LLC and Zalgen Labs LLC manufacture the critical reagents.
- the Biological Defense Research Directorate at the United States Navy Medical Research Center (NMRC).

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