

WHO Prequalification of In Vitro Diagnostics PUBLIC REPORT

Product: OraQuick HIV 1/2 Rapid Antibody Test WHO reference number: PQDx 0159-055-00

OraQuick HIV 1/2 Rapid Antibody Test with product codes **5x4-0010** and **5x4-0012**, manufactured in Thailand for **OraSure Technologies, Inc., rest-of-world regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 8 April 2016. This public report was amended on 14 June 2016, and then further amended on 2 February 2017.

Intended use:

OraQuick® HIV-1/2 Rapid Antibody Test is a qualitative, in vitro immunoassay. It detects antibodies to the human immunodeficiency virus types 1 and 2 (HIV-1/2) in human oral fluid, whole blood, serum or plasma. The assay is read visually, and is intended for the detection of such antibodies from individuals infected by HIV-1 or HIV-2.

Assay description:

OraQuick® HIV-1/2 is a visually read, qualitative immunochromatographic test for the detection of antibodies to HIV-1 and HIV-2. The flat pad that contacts the gums is treated with a mild surfactant, and no materials of viral origin are used in the manufacture of the test. One cannot become infected with HIV by taking this test.

The device is placed into the subject's mouth, so that the flat pad is between the cheek and the outer gums, then swabbed across the outer gum line. The device is then placed into a vial containing a premeasured amount of developer solution, and allowed to develop. The stand provided to hold the developer vial must be used. Fluid from the surface of the gums enters the device through the flat pad, then flows onto a test strip. As it migrates across the strip, it hydrates and mixes with a red-colored reagent (protein A bound to colloidal gold). IgG antibodies in the specimen bind to the reagent. In turn the bound IgG antibody recognizes synthetic HIV-1 or HIV-2 antigen immobilized on the strip enclosed in the housing, a colored line forms in the 'T' (test) area of the result window. If not, no line forms there. Further up the strip, the colored reagent encounters an immobilized biochemical that recognizes human antibodies. The line that forms in this 'C' area of the result window is the control line. It demonstrates assay validity, indicating that the oral fluid contains IgG, that the strip is functioning properly, and that fluid is migrating appropriately through the device.

Alternatively, a capillary or venous whole blood, serum or plasma specimen can be collected using the loop provided. The loop is immersed into the developer and stirred to

mix. Kit controls for OraQuick® HIV-1/2 Rapid Antibody Test are available separately. These serve to demonstrate that the test is maintaining adequate performance.

Test kit contents:

Component	100 tests (product code 5x4-0010)	500 tests (product code 5x4-0012)
Pouch containing 1 test device, 1 desiccant, 1 developer solution vial containing 1ml of phosphate buffer saline solution containing polymers and an antimicrobial agent.	100	500
Test stands	10	20
Specimen collection loops , 5µl	5	25
Instructions for use	1	1

Test kit controls contents:

Item	Product code
OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test Kit Controls 3 Vials Vial 1 - 1x HIV-1 positive control; Vial 2 - 1x HIV-2 positive control; and Vial 3 - 1x Negative control. Sufficient to run approximately 25 tests. Unopened expiry date: 12-months Opened expiry date: 8-weeks when stored at 2 – 8 °C).	1001-0077

Items required but not provided:

Item	Description
Consumables, for testing on fingerstick whole blood specimen	Alcohol swabs Sterile lancets
Equipment	Timer or watch

Storage:

The test kit should be stored at 2 to 30 °C.

- Store unused tests unopened at 2-30 °C. Do not open the foil pouch until you are ready to perform a test.
- This test should be performed at temperatures in the range of (15-37 °C). If stored refrigerated, ensure that the Divided Pouch is brought to operating temperature (15-37 °C) before performing testing.

- If the test kit is stored at temperatures outside of ambient temperature (2-27 °C), or used outside of the operating temperature (15-37 °C), use the Kit Controls to ensure performance of the test.

Shelf-life upon manufacture:

30 months.

Warnings:

- Handle specimens and materials contacting specimens as if potentially infectious biological materials in accordance with Universal Precautions. It has been reported that infectious HIV can be isolated from the oral fluid of some HIV infected individuals. When detectable in oral fluid, infectious virus is present at low levels compared with blood and may be inactivated by salivary inhibitors.
- Clean and disinfect any oral fluid- or blood-containing spills. Use a 0.5% sodium hypochlorite (1:10 household bleach) solution, or other appropriate disinfectant.
- Dispose of all potentially contaminated materials in accordance with local regulations for disposal of biohazardous materials.
- If an oral fluid test must be repeated (following the gum-swab procedure), wait 15 minutes and start the process over using a new test device, and use the whole blood test procedure.
- Use adequate lighting to visually check a test result. If two lines are present at any visible intensity, the test result is interpreted as reactive.
- Do not cover or otherwise obstruct the two small holes on the back of the test device. The flow of fluid can be impaired.
- Individuals infected with HIV-1 and/or HIV-2 who are receiving antiretroviral therapy (ART) may produce false negative results.
- Individuals undergoing preventive treatment for HIV may produce false negative results.
- Do not use the test beyond the expiration date printed on the Divided Pouch. Always check expiration date prior to testing.

Limitations

1. The OraQuick® HIV-1/2 Rapid Antibody Test must be used in accordance with these instructions to obtain an accurate result.
2. Oral fluid specimens for testing must be freshly collected, as detailed in the procedure. For blood-based testing, aged specimens or specimens which have undergone repeated freeze-thaw cycles may give incorrect results.
3. Blood-based specimens that have been heat or chemically inactivated may not give accurate results.
4. The test is not for use with body fluids not specified here, with oral fluid collected by other methods or with other commercially available oral fluid collectors, or with pooled specimens.

5. Clinical data has not been collected to demonstrate the performance of OraQuick® HIV-1/2 Rapid Antibody Test in persons under 13 years of age.
6. Do not use this test as the sole basis for a diagnosis of AIDS, ARC or HIV infection. Any reactive result should be confirmed.
7. For a reactive result, the intensity of the test line does not necessarily correlate to the titer of antibody in the specimen.
8. A non-reactive result does not preclude the possibility of exposure to HIV or infection by HIV. An antibody response to recent exposure may take some time to reach detectable levels.
9. If a red background in the result window makes it difficult to read the test at 20 minutes, wait until the background clears to read the result (but not more than 40 minutes total time).

Summary of WHO prequalification assessment for OraQuick HIV 1/2 Rapid Antibody Test

	Date	Outcome
PQ amended	14 June 2016, 2 February 2017	listed
PQ listing	8 April 2016	listed
Dossier review	26 January 2016	MR
Site inspection(s) of quality management system	8 January 2016	MR
Laboratory evaluation of performance and operational characteristics	28 January 2016	MR

MR: Meets requirements

N/A: Not applicable

Prioritization for prequalification

Based on the established criteria, OraQuick HIV 1/2 Rapid Antibody Test was given priority for WHO prequalification.

Product dossier assessment

The Manufacturer submitted a product dossier for OraQuick HIV 1/2 Rapid Antibody Test as per the "Instructions for compilation of a product dossier" (PQDx_018 v1). The information (data and documentation) submitted in the product dossier was reviewed by WHO staff and external technical experts (assessors) appointed by WHO.

The manufacturer's responses to the nonconformities found during dossier screening and assessment findings were accepted on 26 January 2016.

Based on the product dossier screening and assessment findings, the product dossier for OraQuick HIV 1/2 Rapid Antibody Test meets WHO prequalification requirements.

Manufacturing site inspection

A comprehensive inspection was performed at the site of manufacture (220 East First Street, Bethlehem, PA, 18015-1360, USA) of OraQuick HIV 1/2 Rapid Antibody Test, on 3-5 November 2014 as per the “Information for manufacturers on prequalification inspection procedures for the sites of manufacture of diagnostics” (PQDx_014 v1). In addition, an inspection was undertaken at a key supplier (Pacific Biotech, 42M004 Phetchabun Chalianglub Rd., Napa, Muang, Phetchabun 6700, Thailand). The inspections found that the manufacturer had an acceptable quality management system and good manufacturing practices in place that ensured the consistent manufacture of a product of good quality.

The manufacturer’s response to the nonconformities found at the time of the inspection were accepted on 8 January 2015.

Based on the site inspections and corrective action plan review, the quality management system for OraQuick HIV 1/2 Rapid Antibody Test meets WHO prequalification requirements.

Laboratory evaluation

OraQuick HIV-1/2 Rapid Antibody Test was evaluated by WHO in 2014 on serum/plasma specimens and in 2015 for oral fluid specimens. From this evaluation, we drew the following conclusions:

OraQuick HIV-1/2 Rapid Antibody Test is a qualitative rapid immunochromatographic test for the detection of antibodies to HIV 1/2 in oral fluid, whole blood, serum or plasma specimens. This type of assay requires no sophisticated equipment and can therefore be performed in laboratories with limited facilities and non-laboratory settings. Reading of the results can be done visually i.e. subjectively read.

Performance characteristics in comparison with an agreed reference standard: serum/plasma specimens (N=1118)		
	Initial (95% CI)	Final (95% CI)
Sensitivity %	99.1% (97.8% - 99.8%)	99.1% (97.8% - 99.8%)
Specificity %	99.8% (99.2% - 100%)	99.8% (99.2% - 100%)
Invalid rate %	0.1%	
Inter-reader variability %	0%	

Performance characteristics in comparison with an agreed reference standard: oral fluid specimens (N=596)		
	Initial (95% CI)	Final (95% CI)
Sensitivity %	*99.1% (94.8% - 100%)	Repeat testing was not conducted
Specificity %	100% (99.0% - 100%)	Repeat testing was not conducted
Invalid rate %	0.1%	
Inter-reader variability %	0.4%	

*For patients not on antiretroviral therapy (ART)

- The instructions for use includes a warnings that individuals infected with HIV-1 and/or HIV-2 who are receiving antiretroviral therapy (ART) may produce false negative results and individuals undergoing preventive treatment for HIV may produce false negative results.

Additional performance characteristics for serum/plasma evaluation	
Sensitivity during seroconversion on 8 seroconversion panels in comparison with a benchmark assay; Enzygnost Anti-HIV 1/2 Plus (Siemens Healthcare Diagnostics)	Seroconversion sensitivity index of + 1.375, therefore detection is 1.375 later than the benchmark assay.
Analytical sensitivity on a mixed titer panel in comparison with an agreed reference standard	24 of 25 specimens were correctly classified.
Lot to lot variation on a dilution panel	Acceptable

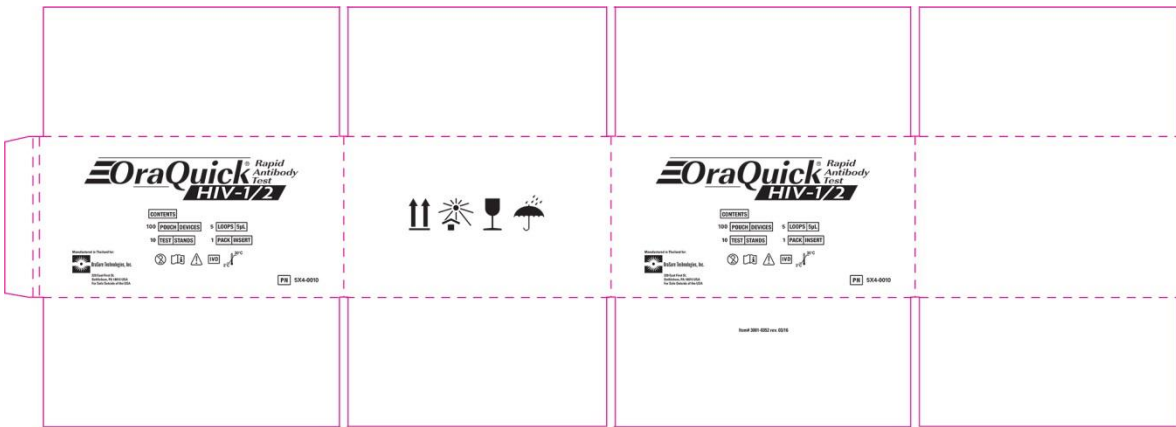
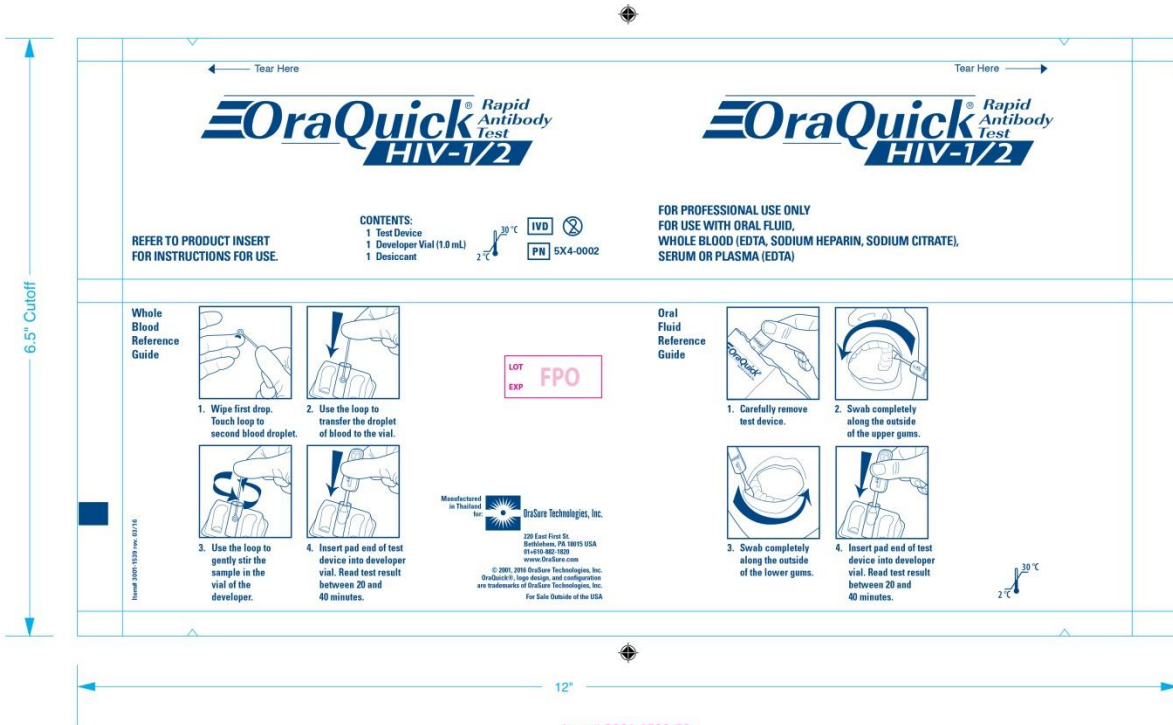
Key operational characteristics	
Validated specimen types	Serum, plasma (EDTA), venous whole blood (EDTA, Sodium heparin and sodium citrate), capillary whole blood, oral fluid
Number of steps	2, without precision required.
Time to result	20 minutes
Endpoint stability	20 minutes (no more than 40 minutes after specimen added to developer vial)
Internal QC	Yes, internal quality control in form of control line for detection of IgG.
In-use stability of reagents	The foil pouch should be opened just before use.

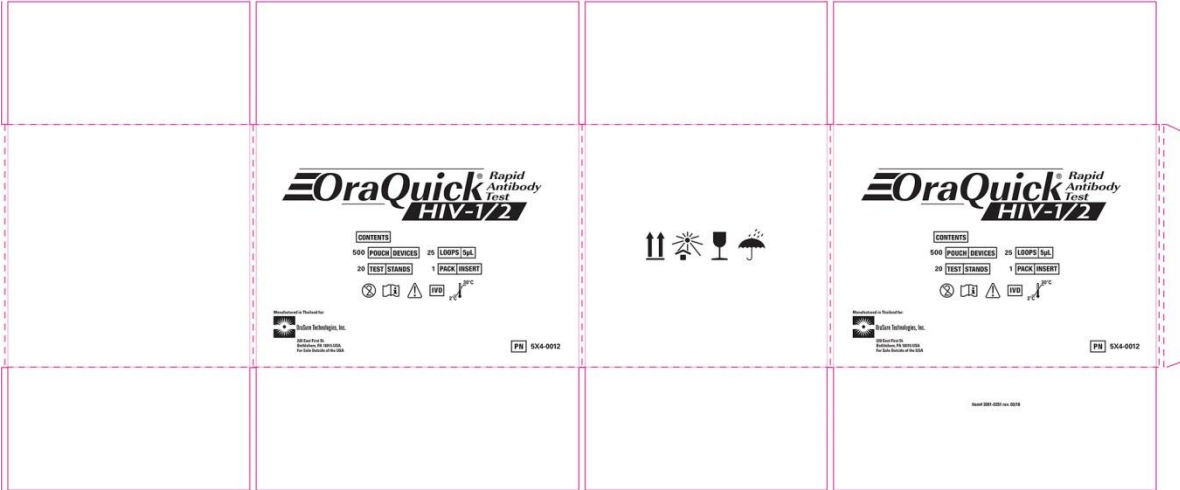
Change notification

In 2016, OraSure Technologies, Inc., submitted a change notification related changes made to changes to various raw materials, production and quality control processes. This change notification was assessed and product was found to meet WHO prequalification requirements.

Labelling

- 1. Labels**
- 2. Instructions for use**





Item# 3001-0351-70
rev. 03/16

OraQuick[®] Rapid Antibody Test

ADVANCE[®] HIV-1/2

KIT CTRLS

Prueba rápida de detección de anticuerpos anti VIH-1/2

For use only with the OraQuick ADVANCE[®] Rapid HIV-1/2 Antibody Test and the OraQuick[®] Rapid HIV-1/2 Antibody Test (for outside USA use only).
Para usar exclusivamente con la Prueba rápida OraQuick ADVANCE[®] para anticuerpos de VIH-1/2 y la Prueba rápida OraQuick[®] para anticuerpos de VIH-1/2 (para uso solo fuera de Estados Unidos).

IVD

REF

1001-0077

CONTENTS

 / CONTENIDO:

- HIV-1 Positive Control Vial (0.2 mL), Vial de Control Positivo de VIH-1 (0.2 ml)
- HIV-2 Positive Control Vial (0.2 mL), Vial de Control Positivo de VIH-2 (0.2 ml)
- Negative Control Vial (0.2 mL), Vial de Control Negativo (0.2 ml)
- Package Insert, Instructivo

OraSure Technologies, Inc.

220 East First Street, Bethlehem, PA 18015 USA

Item #3001-1203 rev. 03/16

LOT XXXXXXXX
 YYY-MM

OraQuick[®] Rapid Antibody Test

HIV-1/2

DEV SOL VIAL

REF

3001-1045

LOT

XXXXXX

IVD

YYY-MM

OraSure Technologies, Inc.

Bethlehem, PA 18015 USA

Qty: 1.0 mL

Item# 3001-1051 rev. 03/16B



Kit Controls

Read this package insert and the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit package insert completely before using the product. Follow the instructions carefully. Not doing so may result in inaccurate test results. Before performing testing, all operators **MUST** read and become familiar with Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other Blood-borne Pathogens in Health-Care Settings.^{1,2}

NAME AND INTENDED USE

The OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit Controls are quality control reagents for use only with the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test and the OraQuick® Rapid HIV-1/2 Antibody Test (for outside USA use only).

Run the Kit 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 2°- 27°C (36°- 80°F),
- if the temperature of the testing area falls outside of 15°- 37°C (59°- 99°F), and
- at periodic intervals as dictated by the user facility.

It is the responsibility of each laboratory using the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test or the OraQuick® Rapid HIV-1/2 Antibody Test (for outside USA use only) to establish an adequate quality assurance program to ensure the performance of the device under its specific locations and conditions of use.

SUMMARY AND EXPLANATION OF THE KIT CONTROLS

OraQuick *ADVANCE*® Kit Controls are human plasma-based reagents. 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 HIV-1 and HIV-2 Positive Controls will produce a Reactive test result and have been manufactured to produce a very faint Test ("T") line. The Negative Control will produce a non-reactive test result. 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 OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test.

MATERIALS PROVIDED

OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit Controls

Each Kit Control box contains a package insert and three vials (one HIV-1 positive control, one HIV-2 positive control and one negative control) as described below:

HIV-1 Positive Control

One black-capped vial containing 0.2 mL of photochemically inactivated human plasma positive for antibodies to HIV-1, diluted in a defibrinated pool of normal human plasma. Preservative: 2-methyl-4-isothiazolin-3-one. Negative for Hepatitis B surface antigen and Hepatitis C antibody.

HIV-2 Positive Control

One red-capped vial containing 0.2 mL of photochemically inactivated human plasma positive for antibodies to HIV-2, diluted in a defibrinated pool of normal human plasma. Preservative: 2-methyl-4-isothiazolin-3-one. Negative for Hepatitis B surface antigen and Hepatitis C antibody.

Negative Control

One white-capped vial containing 0.2 mL of defibrinated pool of normal human plasma negative for antibodies to HIV-1 and HIV-2. Preservative: 2-methyl-4-isothiazolin-3-one. Negative for Hepatitis B surface antigen and Hepatitis C antibody.

MATERIALS REQUIRED AND PROVIDED in the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit

Divided Pouches, each containing a Test Device, an Absorbent Packet, and a Developer Solution Vial
Reusable Test Stands
Specimen Collection Loops
Subject Information Pamphlets
OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Package Insert with Customer Letter

MATERIALS REQUIRED BUT NOT PROVIDED

Timer or watch capable of timing 20 to 40 minutes
Latex, vinyl or nitrile disposable gloves
Biohazard waste container
Clean, disposable, absorbent workspace cover

WARNINGS AND PRECAUTIONS**For *in vitro* Diagnostic Use**

1. Read this package insert and the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test package insert completely before using the product. Follow the instructions carefully. Not doing so may result in inaccurate test results.
2. Handle specimens, and materials contacting specimens, as if potentially infectious biological materials in accordance with "Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and Other Blood-borne Pathogens in Health-Care Settings".^{1,2}
3. Handle the Kit Controls, and materials contacting the Kit Controls, as if capable of transmitting infectious agents.
4. Do not drink, eat, or smoke in areas where the Kit Controls are being handled.
5. Wear disposable gloves while handling specimens. Wash hands thoroughly after performing each test. Dispose of gloves in a biohazard waste container after use.
6. Dispose of all Kit Controls and materials used in the test procedure in a biohazard waste container. The recommended method of disposal of biohazard waste is autoclaving for a minimum of 1 hour at 121°C. Disposable materials may be incinerated. Liquid wastes may be mixed with appropriate chemical disinfectants. A freshly prepared solution of 10% bleach (0.5% solution of sodium hypochlorite) is recommended. Allow 60 minutes for effective decontamination.
NOTE: Do not autoclave solutions that contain bleach. For additional information on biosafety, refer to "Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and Other Blood-borne Pathogens in Health-Care Settings".^{1,2}
7. Wipe all spills thoroughly with a freshly prepared solution of 10% bleach or other appropriate disinfectant.³
8. 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 *ADVANCE*® Rapid HIV-1/2 Antibody Test.

STORAGE INSTRUCTIONS

Store the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit Controls at 2°- 8°C (36°- 46°F). Do not use Kit Controls beyond the expiration date printed on the outer carton. Open the Kit Control vials only when you are performing tests. Recap and store the vials in their original container at 2°- 8°C (36°- 46°F) after use.

Dispose of unused portions of opened Kit Control vials after eight weeks.

DIRECTIONS FOR USE**General Test Preparation**

Perform procedures indicated in the *Set-Up Your Workspace* and *General Test Preparation* sections of the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test package insert or the Test Procedure sections of the OraQuick® Rapid HIV-1/2 Antibody Test package insert.

TEST PROCEDURE

1. Open a Kit Control vial containing the control reagent.
2. Insert the round end of an unused Specimen Collection Loop into the vial of control reagent. Visually inspect the loop to make sure that it is completely filled with the control reagent. **Use separate unused Specimen Collection Loops for each control reagent.**
NOTE: The Kit Control reagents are clear to straw-colored. Do not use if the reagent appears visually cloudy or discolored.
3. Immediately immerse the control-reagent-filled Specimen Collection Loop in the developer solution inside the Developer Solution Vial. Use the Specimen Collection Loop to stir the specimen in the developer solution. Remove the Specimen Collection Loop from the Developer Solution Vial and discard the used loop in a biohazard waste container.
4. Remove the Test Device from the Divided Pouch without touching the flat pad. Insert the Test Device, flat pad first, into the Developer Solution Vial containing the specimen. **Be sure that the result window faces forward and the flat pad touches the bottom of the Developer Solution Vial.**
5. Leave the Test Device in the Developer Solution Vial and start a timer. **Do not remove the Test Device from the vial until you have read the results.** Read the results after 20 minutes but not more than 40 minutes in a fully lighted area. Read the results as described in the *Test Result* and *Interpretation of Test Result* sections of the test kit product insert.
6. Dispose of the used Developer Solution Vial and the Test Device in a biohazard waste container.
7. Reseal the Kit Control reagent vials and store them in their original container at 2°- 8°C (36°- 46°F).

EXPECTED RESULTS**Negative Control:**

The Negative Control will produce a Non-Reactive test result. A line should be present in the Result Window in the area adjacent to only the triangle labeled "C." This indicates a Non-Reactive test result.

HIV-1 Positive Control:

The HIV-1 Positive Control will produce a Reactive test result and has been manufactured to produce a very faint Test ("T") line. A line should be present in the Result Window in the area adjacent to the triangle labeled "C" **and** a line should appear in the area adjacent to the triangle labeled "T." This indicates a Reactive test result. The lines will not necessarily be the same intensity.

HIV-2 Positive Control:

The HIV-2 Positive Control will produce a Reactive test result and has been manufactured to produce a very faint Test ("T") line. A line should be present in the Result Window in the area adjacent to the triangle labeled "C" **and** a line should appear in the area adjacent to the triangle labeled "T." This indicates a Reactive test result. The lines will not necessarily be the same intensity.













NOTE: If the test result for either the Negative Control or the HIV-1 Positive Control or the HIV-2 Positive Control is not as expected, the test should be repeated using a new Test Device, Developer Solution Vial and control specimen. If the test result for any of the controls is not as expected upon repeat testing, discontinue testing and contact OraSure Technologies Customer Service.

LIMITATIONS

The OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit Controls are quality control reagents for use only with the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test and the OraQuick® Rapid HIV-1/2 Antibody Test.

BIBLIOGRAPHY

1. CDC. Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. *MMWR* 1988; 37(24):377-388.
2. CDC. Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. *HICPAC* 2007; 12-93.
3. Sehulster LM, Hollinger FB, Dreesman GR, and Melnick JL. Immunological and biophysical alteration of hepatitis B virus antigens by sodium hypochlorite disinfection. *Appl Env Microbiol* 1981; 42:762-7.

EXPLANATION OF SYMBOLS	
 Batch Code	 <i>In Vitro</i> Diagnostic Medical Device
 Catalog Number	 Manufacturer
 Caution, Consult Accompanying Documents	 Temperature Limitation
 HIV Negative Control	 Use By
 HIV-1 Positive Control	 HIV-2 Positive Control
 Contents	 Kit Controls



OraSure Technologies, Inc.

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Item# 3001-1202-70
 rev. 03/16

Item# 3001-1202 rev. 03/16



**For Professional Use Only –
For Outside USA Use Only
In Vitro Diagnostic Use • Do Not Reuse**

Read this product insert completely before using the product. Follow the instructions carefully. Not doing so may give inaccurate test results. Not approved by the US Food and Drug Administration. For outside USA use only.

NAME AND INTENDED USE

OraQuick® HIV-1/2 is a qualitative, *in vitro* immunoassay. It detects antibodies to the human immunodeficiency virus types 1 and 2 (HIV-1/2) in human oral fluid, whole blood (EDTA, sodium heparin, sodium citrate), serum or plasma (EDTA). The assay is read visually, and is intended for the detection of such antibodies from individuals infected by HIV-1 or HIV-2.

SUMMARY AND EXPLANATION OF THE TEST

HIV-1 and HIV-2 are etiologic agents of the acquired immunodeficiency syndrome (AIDS) and related conditions. HIV has been isolated from patients with AIDS, AIDS related complex (ARC) and from healthy individuals at high risk for AIDS.¹⁻³ Clinical evidence of HIV infection may be obtained by testing for HIV antibodies in blood or oral fluid of individuals who may be at risk for HIV infection.⁴⁻⁶ The OraQuick® Rapid HIV-1/2 Antibody Test is a single-use, qualitative immunoassay to detect antibodies to Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2) in oral fluid, whole blood, serum and plasma specimens. The OraQuick® Rapid HIV-1/2 Antibody Test is intended for use as a point-of care test to aid in the diagnosis of infection with HIV-1 and HIV-2. This test is suitable for use in multi-test algorithms designed for statistical validation of rapid HIV test results. When multiple rapid HIV tests are available, this test should be used in appropriate multi-test algorithms. The OraQuick® Rapid HIV-1/2 Antibody Test is not approved for use to screen blood or tissue donors.

BIOLOGICAL PRINCIPLES OF THE TEST

OraQuick® HIV-1/2 is a visually read, qualitative immunochromatographic test for the detection of antibodies to HIV-1 and HIV-2. The flat pad that contacts the gums (see below) is treated with a mild surfactant, and no materials of viral origin are used in the manufacture of the test. One cannot become infected with HIV by taking this test.

The device (see figure below) is placed into the subject's mouth, so that the flat pad is between the cheek and the outer gums, then swabbed across the outer gum line (see oral fluid TEST PROCEDURE, below). The device is then placed into a vial containing a premeasured amount of developer solution, and allowed to develop. Use only the stand provided to hold the developer vial. Fluid from the surface of the gums enters the device through the flat pad, then flows onto a test strip. As it migrates across the strip, it hydrates and mixes with a red-colored reagent (protein A bound to colloidal gold). IgG antibodies in the specimen bind to the reagent. If in turn the bound IgG antibody recognizes synthetic HIV-1 or HIV-2 antigen immobilized on the strip enclosed in the housing, a colored line forms in the 'T' (test) area of the result window. If not, no line forms there.

Further up the strip, the colored reagent encounters an immobilized biochemical that recognizes human antibodies. The line that forms in this 'C' area of the result window is the control line. It demonstrates assay validity, indicating that the oral fluid contains IgG, that the strip is functioning properly, and that fluid is migrating appropriately through the device.

Alternatively, a whole blood, serum or plasma specimen can be collected using a loop. The loop is immersed into the developer and stirred to mix. See the test procedure for whole blood, serum or plasma below.

Kit controls for OraQuick® HIV-1/2 are available separately. These serve to demonstrate that the test is maintaining adequate performance (see Kit Control insert).

CONTENTS

OraQuick® HIV-1/2

500 pouched devices, 20 test stands, 25 loops, 1 product insert.
100 pouched devices, 10 test stands, 5 loops, 1 product insert.

Also available separately are:

Loop

Catalog number 1001-0144; package of 5.
Catalog number 1001-0145; package of 25.

Test Stand

Catalog number 004-0002; package of 5.

ACCESSORIES

OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Kit Controls, Catalog number 1001-0077 – package contains one (1) Negative Control (0.2mL), one (1) HIV-1 Positive Control (0.2mL), and one (1) HIV-2 Positive Control (0.2mL)

No accessories are required to run the oral fluid test. However, a timer or watch is needed to determine when to read the result.

When performing the test on a fingerstick whole blood specimen, an alcohol wipe and lancet (not supplied) are required.



WARNINGS AND PRECAUTIONS For *In Vitro* Diagnostic Use

- Handle specimens and materials contacting specimens as if potentially infectious biological materials in accordance with "Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other Blood-borne Pathogens in Health-Care Settings" (CDC, MMWR, June 24, 1988).⁷ It has been reported that infectious HIV can be isolated from the oral fluid of some infected patients. When detectable in oral fluid, infectious virus is present at low levels compared with blood and may be inactivated by salivary inhibitors.
- Clean and disinfect any oral fluid- or blood-containing spills. Use a 0.5% sodium hypochlorite (1:10 household bleach) solution, or other appropriate disinfectant.⁸
- Dispose of all potentially contaminated materials in accordance with local regulations for disposal of biohazardous materials.



- If an oral fluid test must be repeated (following the gum-swab procedure), wait 15 minutes and start the process over using a new test device.
- Use adequate lighting to visually check a test result. If two lines are present at any visible intensity, the test result is interpreted as reactive (see Interpretation of Results section).
- Do not cover or otherwise obstruct the two small holes on the back of the test device. The flow of fluid can be impaired.
- **Individuals infected with HIV-1 and/or HIV-2 who are receiving highly active antiretroviral therapy (HAART) or are undergoing preventive treatment for HIV may produce false negative results.**
- Do not use the test beyond the expiration date printed on the Divided Pouch. Always check expiration date prior to testing.

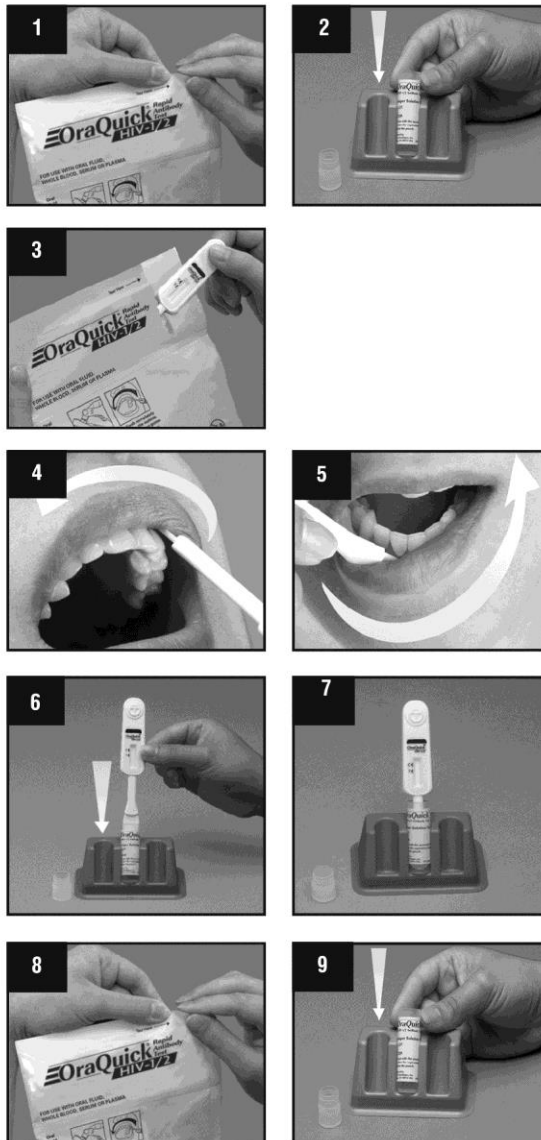
STORAGE

- Store unused OraQuick® HIV-1/2 tests unopened at 2-30 °C. Do not open the foil pouch until you are ready to perform a test.
- This test should be performed at temperatures in the range of (15-37 °C, 59-99 °F). If stored refrigerated, ensure that the Divided Pouch is brought to operating temperature (15-37 °C, 59-99 °F) before performing Testing.
- If the test kit is stored at temperatures outside of ambient temperature (2-30 °C, 36-86 °F), or used outside of the operating temperature (15-37 °C, 59-99 °F), use the Kit Controls to ensure performance of the test.

SPECIMEN COLLECTION and TEST PROCEDURE (oral fluid)

The administrator of the test should first instruct the subject about the test and how to collect an oral fluid sample. The test device is then offered to the subject. Instruct the subject to collect a sample, as outlined below.

1. Ensure prior to testing that the subject has not had anything to eat, drink or has chewed gum for at least 15 minutes. Have the subject wait for at least 30 minutes prior to testing if they have used any oral care products. Set the reusable stand on a flat, level surface. Tear open the foil pouch containing the test device and developer vial (see picture 1). Remove the developer vial. Carefully uncapped the vial by gently rocking the cap back and forth. Place the uncapped vial into the stand (see picture 2).
2. Have the subject grasp the test device and remove it from the foil pouch without touching the collection pad (see picture 3). **Check to see if absorbent packet is present. If no absorbent packet is present, discard the unit.**
3. Instruct the subject to swab completely around the **outer** gums with the test device, by gently wiping the **flat pad** completely across the **upper** and **lower** gums, one time around (see pictures 4 and 5).
4. When the subject has finished swabbing the gums, have the subject insert the **pad end** of the test device all the way down into the vial (see picture 6). Be sure the result window faces **forward** so it can be read (see picture 7). Start the timer, or note the time. Do not removed the device from the vial while the test is running.
5. **Read test results no sooner than 20 minutes but no later than 40 minutes after the device has been placed in the buffer vial.** Record the test result seen in the result window (refer to *Interpretation of Results and Limitations of the Procedure*, below), then dispose of the device and vial in a biohazardous waste container.



SPECIMEN COLLECTION and TEST PROCEDURE (whole blood, serum, plasma)

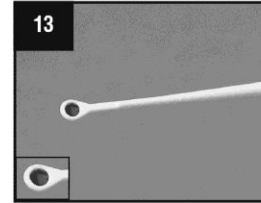
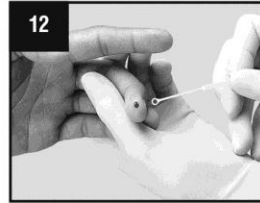
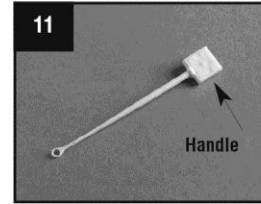
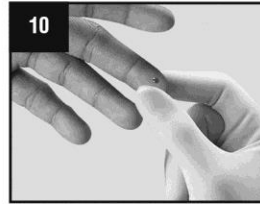
Please observe Universal Precautions* when performing blood testing procedures.

STEP 1.

Set the reusable stand on a flat, level surface. Tear open the foil pouch containing the test device and developer solution vial (see picture 8). Remove the vial. Carefully uncapped the vial by gently rocking the cap back and forth. Place the uncapped vial into the stand (see picture 9).

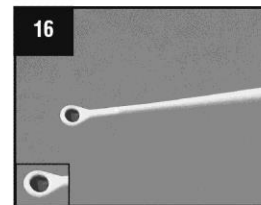
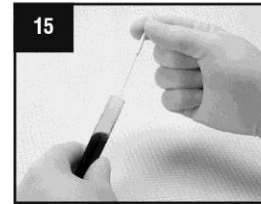
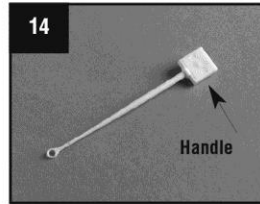
STEP 1.A: FINGERSTICK WHOLE BLOOD

- Using an antiseptic wipe, clean the finger of the person being tested. After cleansing the skin puncture site, allow the area to air dry, so the antiseptic action of the alcohol can take effect. Using a sterile lancet, puncture the skin just off the center of the finger pad. Hold the finger downward. Apply gentle pressure beside the point of the puncture. Avoid squeezing the finger to make it bleed (see picture 10). Wipe away this first drop of blood with a sterile gauze pad. Allow a new drop of blood to form.
- Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (see picture 11). Put the "rounded" end of the Loop on the drop of blood (see picture 12). Make sure that the Loop is completely filled with blood (see picture 13). NOTE: If the Loop is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new Loop for the collection of the blood sample.



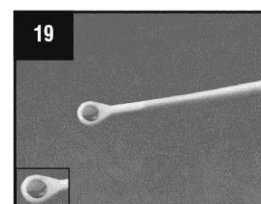
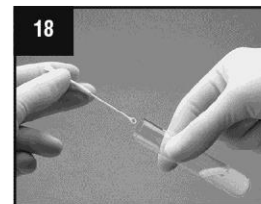
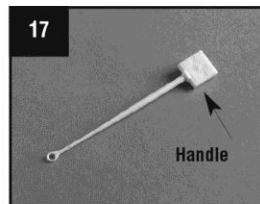
STEP 1.B: VENIPUNCTURE WHOLE BLOOD

- Using standard venous phlebotomy procedures, collect a whole blood sample using a tube containing any of the following anticoagulants: EDTA, sodium heparin, or sodium citrate. **Other anticoagulants have not been tested and may give an incorrect result.** If the specimens are not tested at the time of collection, the whole blood may be stored at 2°-30°C (36°-86°F) for up to 5 days. Prior to testing, mix the blood tube gently by inversion several times to ensure a homogeneous sample.
- Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (see picture 14). Put the "rounded" end of the Loop into the tube of blood (see picture 15). Make sure that the Loop is completely filled with blood (see picture 16). NOTE: If the Loop is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new Loop for the collection of the blood sample.



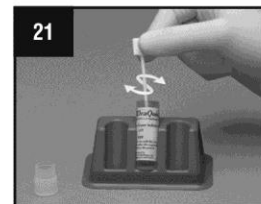
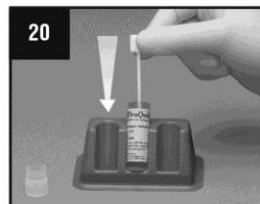
STEP 1.C: PLASMA

- Using standard venous phlebotomy procedures, collect a whole blood sample using a tube containing EDTA anticoagulant. **Other anticoagulants have not been tested and may give an incorrect result.** If the specimens are not tested at the time of collection, the specimen may be stored as whole blood for up to 5 days at 2°-30°C (36°-86°F) or as plasma for up to 7 days at 2°-8°C (36°-46°F).
- Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (see picture 17). Put the "rounded" end of the Loop into the tube of plasma (see picture 18). Make sure that the Loop is completely filled with plasma (see picture 19). NOTE: If the Loop is dropped or comes in contact with any other surface, discard it in a biohazard waste container. Get a new Loop for the collection of the plasma sample.



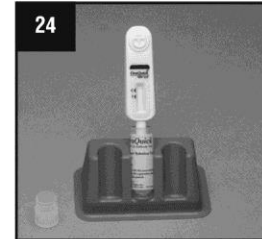
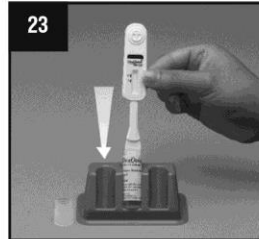
STEP 2. MIX

- Immediately insert the blood-filled end of the Loop all the way into the Vial (see picture 20). Use the Loop to stir the blood sample in the Developer Solution ("Solution") (see picture 21). Remove the used Loop from the Solution. Throw the used Loop away in a biohazard waste container.



STEP 3. TEST

1. Grasp the test device and remove it from the foil pouch without touching the collection pad (see picture 22). **Check to see if absorbent packet is present. If no absorbent packet is present, discard the unit.** Insert the **pad end** all the way down into the vial (see picture 23). Be sure the result window faces **forward** so it can be read (see picture 24). Start the timer, or note the time. Do not remove the device from the vial while the test is running.
2. **Read test results no sooner than 20 minutes but no later than 40 minutes after the device has been placed in the buffer vial.** Record the test result seen in the result window (refer to *Interpretation of Results and Limitations of the Procedure*, below), then dispose of the device and vial in a biohazardous waste container.



QUALITY CONTROL

A control line in the 'C' area of the result window indicates a valid result. A valid result indicates a suitable sample was collected and the test functioned properly. The control line will appear on all valid tests, whether or not the result is reactive. (refer to *Interpretation of Results*, below).

Kit control reagents are available separately. These are used to verify adequate test performance. Kit controls should be run once per shift by the test administrator, and whenever changing to a different lot of tests. Refer to the Kit Control product insert when using these reagents.

INTERPRETATION OF RESULTS – Refer to the result window

NON-REACTIVE – only the control line appears

If a single line appears on the test strip in the area adjacent to the triangle labeled 'C', the result is **non-reactive**. The diagram at the right shows a non-reactive result. It suggests the **absence** of anti-HIV antibodies in the specimen.

Note: using the **Negative Kit Control** gives this result (see insert for OraQuick *ADVANCE*® HIV-1/2 Kit Controls).



NON-REACTIVE

REACTIVE – two lines appear

If two lines appear on the test strip, adjacent to the 'T' and 'C' triangles, respectively, the result is considered **reactive**. One of these lines may be darker than the other. At the right are examples of reactive results, which suggest the **presence** of anti-HIV antibodies in the specimen.

Reactive results should be confirmed by another method.

Note: using the **HIV-1 Kit Control** or **HIV-2 Kit Control** gives a result like the one shown in the center panel (see insert for OraQuick *ADVANCE*® HIV-1/2 Kit Controls).



REACTIVE



REACTIVE



REACTIVE

INVALID – no line present in 'C' area of window

If there is no line in the area labeled 'C', the result is **invalid**. An invalid test should be repeated with a new test device. If the invalid test was obtained with an oral fluid specimen, use the blood test procedure for repeat testing. At the right are examples of invalid results. If a test must be repeated, use a new Collection Loop, new Test Device and new Developer Vial.



INVALID



INVALID



INVALID

LIMITATIONS OF THE PROCEDURE

1. The OraQuick® HIV-1/2 test kit must be used in accordance with these instructions to obtain an accurate result.
2. Oral fluid specimens for OraQuick® HIV-1/2 testing must be freshly collected, as detailed in the procedure. For blood-based testing, aged specimens or specimens which have undergone repeated freeze-thaw cycles may give incorrect results.
3. Blood-based specimens that have been heat or chemically inactivated may not give accurate results.
4. The test is not for use with body fluids not specified here, with oral fluid collected by other methods or with other commercially available oral fluid collectors, or with pooled specimens.
5. Clinical data has not been collected to demonstrate the performance of OraQuick® HIV-1/2 in persons under 13 years of age.
6. Do not use this test as the sole basis for a diagnosis of AIDS, ARC or HIV infection. Any reactive result should be confirmed.
7. For a reactive result, the intensity of the test line does not necessarily correlate to the titer of antibody in the specimen.
8. Reactive results should be verified using other assays to confirm the HIV diagnosis.
9. A non-reactive result does not preclude the possibility of exposure to HIV or infection by HIV. An antibody response to recent exposure may take some time to reach detectable levels.
10. If a red background in the result window makes it difficult to read the test at 20 minutes, wait until the background clears to read the result (but not more than 40 minutes total time).
11. Patients on anti-retroviral (ARV) therapy may have low levels of antibodies to HIV resulting in false non-reactive results when testing the oral fluid.

PERFORMANCE CHARACTERISTICS

Sensitivity and Specificity with 95% Confidence Intervals

A sensitivity study was performed at 3 clinical trials sites using freshly obtained oral fluid, whole blood and plasma specimens collected from 1000 individuals at high risk for HIV infection, with a documented diagnosis of HIV infection or AIDS, or blood donors with no recognized risk for HIV infections. Of the 1000 subjects, 779 were HIV seronegative and 219 were positive. 778 were concordant negative and 1 was incorrectly identified as positive by OraQuick® and EIA, but negative by western blot. A total of 778 matched samples were OraQuick® non-reactive in oral fluid, whole blood and plasma. Specificity of the OraQuick® HIV-1/2 test was 99.87% (778/779). Of the 219 positive subjects, all had repeatedly reactive serum EIA results and were reactive with the OraQuick® test in oral fluid, whole blood and plasma. Sensitivity of the OraQuick® HIV-1/2 test was 100.0% (219/219). Two subjects were not included in the analysis as their HIV status was indeterminate. The results of the study are summarized in the table below.

Sample Type	Sensitivity (N=219)		Specificity (N=779)	
	True Positive	Proportion (95% CI)	True Negative	Proportion (95% CI)
Plasma	219/219	100.0% (98.3%, 100.0%)	779/779	100.0% (99.5%, 100.0%)
Whole Blood	219/219	100.0% (98.3%, 100.0%)	779/779	100.0% (99.5%, 100.0%)
Oral Fluid	219/219	100.0% (98.3%, 100.0%)	778/779	99.87% (99.29%, 100.0%)

Reactivity with HIV-1 Seroconversion Panels

Commercially available Seroconversion (SC) panels are created by conducting longitudinal studies, where bleeds are collected to determine at which point the individual is determined as HIV positive in different tests. A total of 20 HIV-1 Seroconversion Panels were tested with the OraQuick® Test and compared to results from a licensed 3rd generation Anti-HIV EIA. Of these 20 panels, eight (8) SC panels produced concordant results, eleven (11) SC panels were detected earlier by the EIA and one (1) SC panel was detected earlier by the OraQuick® Test. On average, EIA detected reactive results at 35.45 days from day 0 of collection and the OraQuick® Test produced reactive results at 36.55 days from day 0 of collection. Day 0 of collection is unlikely to be the date of HIV infection. The delay in days presented in the table shows that the OraQuick® Test is comparable to licensed EIAs.

# of SC Panels	# of SC Panel Concordant Results	# SC Panels Detected Earlier by 3 rd gen EIA	# SC Panels Detected Earlier by OraQuick®	Average Days 3 rd gen EIA	Average Days OraQuick®	Delay Days (OraQuick®-3 rd gen EIA)
20	10	8	2	35.45	36.55	1.10 95% C.I. (-0.43 to 2.63)

INTERFERING SUBSTANCES AND UNRELATED MEDICAL CONDITIONS

To assess the impact of unrelated medical conditions or interfering substances on the specificity of the OraQuick® Rapid HIV-1/2 Antibody Test, 321 serum/plasma specimens from a variety of medical conditions unrelated to HIV infection and 119 specimens with interfering substances were analyzed. The results of this study are shown in the table below. One specimen from subjects known to be positive for EBV, for HBV, or for rheumatoid factor, one from a multiparous woman, and three specimens from known HAV infected subjects gave false positive results.

In addition, a study was performed to assess the potential effect of anticoagulants on assay specificity. Venipuncture whole blood was collected from 24 HIV negative subjects, in each of 3 tubes containing one of the following anticoagulants: EDTA, sodium heparin, and sodium citrate. The samples were then aliquoted and stored either refrigerated (2°-8°C), at room temperature (18°C) or at elevated temperatures (30-33°C) and tested over a 7-day period. There was no anticoagulant-specific effect observed on assay performance with samples held up to 5 days at 2-30°C.

Medical Conditions Producing Reactive Results					
Condition	R	NR	Condition	R	NR
Multiparous women	1 ²	14	Hepatitis A virus (HAV)	3 ¹	17
Rheumatoid factor	1 ²	17	Hepatitis B virus (HBV)	1	16
Epstein Barr virus (EBV)	1 ²	14			

Medical Conditions Producing Non-Reactive Results		
Anti-nuclear antibody (ANA) n=17	Lupus n=15	Multiple transfusions n=10
Cytomegalovirus (CMV) n=15	Rubella n=15	Herpes Simplex virus n=5
Hepatitis C virus (HCV) n=15	Syphilis n=15	Dialysis patient n=4
Human T-cell Lymphotropic virus Type I (HTLV-I) n=15	Influenza n=10	Anti-scl or anti-rnp antibody n=3
Human T-cell Lymphotropic virus Type II (HTLV-II) n=15	Hemophilia n=10	Breast cancer n=1
IgG gammopathies n=13	Cirrhosis n=5	Anti-DNA antibody n=1
IgM gammopathies n=12	Colon cancer n=4	Gonorrhea n=1
Toxoplasmosis n=15	HTLV I/II n=2	
Tuberculosis n=15	Chlamydia n=3	
Interfering Substances producing Non-Reactive Results		
Elevated Hemoglobin	Elevated Protein	Elevated Bilirubin
Elevated Triglycerides	Icteric	Sodium Heparin ³
Visual Hemolysis (hemolytic)	Lipemic	Sodium Citrate ³
Bacterially Contaminated	EDTA ³	

¹ A total of 3 of the 20 HAV specimens were OraQuick® false reactive. Two of the 3 specimens were OraQuick® non-reactive at the first read time and reactive at the second read time. The remaining specimen was reactive at both read times.

² One of the specimens was OraQuick® non-reactive at the first read time and reactive at the second read time.

³ The OraQuick® assay maximum read time for these specimens was 40 minutes. Based upon specimen storage for 5 days at 2-30°C.

As part of the oral fluid clinical studies, information was collected from the participants regarding concurrent diseases or medical conditions, oral pathologies, non-HIV viral infections, and other factors (e.g., use of tobacco products, mouthwash within 24 hours of testing, concomitant medications, dental fixtures, and food or drink immediately prior to testing). None of these disease states, medical conditions or other factors interfered with test specificity. In a separate study of 40 individuals, consumption of alcohol, brushing of teeth, use of mouthwash or smoking tobacco 5 minutes prior to testing, were shown to have no effect on test specificity. Nonetheless, it is recommended that subject observes a wait period prior to oral fluid collection, according to the Oral Fluid Collection Procedure of this package insert.

REPRODUCIBILITY

The reproducibility of the OraQuick® Rapid HIV-1/2 Antibody Test was tested at 3 sites using 3 lots of the device on 3 different days with 9 operators (3 per site). A blind-coded panel was tested that consisted of 5 contrived blood specimens (4 antibody-positive and 1 antibody-negative). Test results were recorded at two read times. A total of 405 tests were performed (135/site), with a total of 81 tests per panel member. The overall reproducibility of the OraQuick® Rapid HIV-1/2 Antibody Test was 405/405 = 100%. Concordance between the specified assay read time limits was 99.8% (404/405); a single HIV-1 low positive panel member that was non-reactive at the first read was reactive at the second read.

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8. Sehulster LM, Hollinger FB, Dreesman GR, and Melnick JL. Immunological and biophysical alteration of hepatitis B virus antigens by sodium hypochlorite disinfection. *Appl Env Microbiol* 1981; 42:762-7.

EXPLANATION OF SYMBOLS		
This Way Up	Temperature Limitation	Caution, Consult Accompanying Documents
Avoid Prolonged Exposure to Sunlight	Catalog Number	Tests
Fragile, Handle With Care	5µL Specimen Collection Loop	Part Number
Keep Dry	Loops 5µL	Contents
Batch Code	Do Not Reuse	Pouched Devices
In Vitro Diagnostic Medical Device	Use By	Test Stands

Manufactured in Thailand for



OraSure Technologies, Inc.

220 East First Street
Bethlehem, PA 18015 USA
(001) 610-882-1820
www. OraSure.com

Item# 204-7052-70
rev. 10/16

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