**NAME AND INTENDED USE**

The OraQuick® ADVANCE 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, fingerstick whole blood, venipuncture whole blood and plasma specimens. The OraQuick® ADVANCE 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.

**RESTRICTIONS**

- Sale of the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test is restricted to clinical laboratories
  - that have an adequate quality assurance program, including planned systematic activities to provide adequate confidence that requirements for quality will be met; and
  - where there is assurance that operators will receive and use the instructional materials.
- The OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test is approved for use only by an agent of a clinical laboratory.
- Test subjects must receive the "Subject Information" pamphlet prior to specimen collection and appropriate information when test results are provided.
- The OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test is not approved for use to screen blood or tissue donors.

**SUMMARY AND EXPLANATION OF THE TEST**

Acquired Immune Deficiency Syndrome (AIDS), AIDS-related complex (ARC) and pre-AIDS are thought to be caused by the Human Immunodeficiency Virus (HIV). The first AIDS-related virus, HIV-1 (also known as HTLV-III, LAV-1, and ARV) has been isolated from patients with AIDS and from healthy persons at high risk for AIDS. A closely related but distinct second type of pathogenic human immunodeficiency retrovirus, designated HIV-2 (formerly LAV-2), has been isolated from West African patients with AIDS. HIV-2 has been shown to share a number of conserved sequences with HIV-1, but serological cross-reactivity between HIV-1 and HIV-2 has been shown to be highly variable from sample to sample.

HIV is known to be transmitted by sexual contact, by exposure to blood (including sharing contaminated needles and syringes) or by contaminated blood products, or it may be transmitted from an infected mother to her fetus during the perinatal period. Individuals infected with HIV produce antibodies against the HIV viral proteins. Testing for the presence of antibodies to HIV in bodily fluids (e.g., blood, oral fluid, and urine) is an accurate aid in the diagnosis of HIV infection. However, the implications of seropositivity must be considered in a clinical context. For example, in neonates, the presence of antibodies to HIV is indicative of exposure to the virus. An antibody response to a recent exposure may take several months to reach detectable levels. HIV has been isolated from asymptomatic, seronegative individuals presumably before seroconversion following exposure.

The standard laboratory HIV testing algorithm used in the United States consists of screening with an enzyme immunoassay (EIA) and confirmation of repeatedly reactive EIA samples using a Western blot test. Results are typically reported within 48 hours to 2 weeks, making these standard screening and supplemental tests inadequate to meet the need for rapid HIV diagnosis. The OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test is a point-of-care test to aid in the diagnosis of infection with HIV-1 and HIV-2.

Using a rapid HIV test increases the number of HIV-infected persons who may be diagnosed. The Centers for Disease Control and Prevention (CDC) estimates that nearly one third of the estimated 900,000 HIV-infected persons in the United States do not know their HIV status. As a result, they cannot benefit from early intervention with effective antiviral therapy. Rapid HIV testing addresses this
issue by providing results during the initial visit and enabling immediate counseling. Additionally, for pregnant women who do not know their HIV status at the time of delivery, rapid HIV testing permits therapy to be initiated for these mothers during labor, and to their infants post partum, substantially reducing the chance that the infants will become infected with HIV. Likewise, rapid HIV testing is instrumental in the decision to initiate treatment for health care workers after accidental exposures to body fluids from infected individuals. In the U.S., it is estimated that 600,000 to 1,000,000 "needlestick injuries" occur each year. Critical decisions about treatment depend on the availability of accurate, rapid HIV test results.

**BIOLGICAL PRINCIPLES OF THE TEST**

The OraQuick ADVANCE Rapid HIV-1/2 Antibody Test is a manually performed, visually read, 20 minute immunoassay for the qualitative detection of antibodies to HIV-1 and HIV-2 in human oral fluid, whole blood obtained from a finger puncture or a venipuncture, and plasma. The OraQuick ADVANCE rapid test is comprised of a single-use test device and a single-use vial containing a pre-measured amount of a buffered developer solution. Each component is sealed in separate compartments of a single pouch to form the test. The OraQuick ADVANCE rapid test utilizes a proprietary lateral flow immunassay procedure. The device plastic housing holds an assay test strip comprised of several materials that provide the matrix for the immunochromatography of the specimen and the platform for indication of the test results.

The assay test strip, which can be viewed through the test device result window, contains synthetic peptides representing the HIV envelope region and a goat anti-human IgG procedural control immobilized onto a nitrocellulose membrane in the Test (T) zone and the Control (C) zone, respectively.

An oral fluid specimen is collected using the flat pad on the test device, followed by the insertion of the test device into the vial of developer solution. A fingerstick whole blood, venipuncture whole blood or plasma specimen is collected and transferred into the vial of developer solution, followed by the insertion of the test device. The developer solution facilitates the flow of the specimen into the device and onto the test strip. As the diluted specimen flows through the device, it rehydrates antibodies that react with the antigens immobilized on the nitrocellulose membrane, a reddish-purple line will appear, qualitatively indicating the presence of antibodies to HIV-1 and/or HIV-2 in the specimen. The intensity of the line color is not directly proportional to the amount of antibody present in the specimen.

Further up the assay strip, the sample will encounter the C zone. This built-in procedural control serves to demonstrate that a specimen was added to the vial and that the fluid has migrated adequately through the test device. A reddish-purple line will appear in the C zone during the performance of all valid tests, whether or not the sample is positive or negative for antibodies to HIV-1 and/or HIV-2 (refer to the Test Result and Interpretation of Test Result section below).

The test results are interpreted after 20 minutes but not more than 40 minutes after the introduction of the test device into the developer solution containing the test specimen. No precision pipetting, the device and onto the test strip. As the diluted specimen flows through the device, it rehydrates antibodies that react with the antigens immobilized on the nitrocellulose membrane, a reddish-purple line will appear, qualitatively indicating the presence of antibodies to HIV-1 and/or HIV-2 in the specimen. The intensity of the line color is not directly proportional to the amount of antibody present in the specimen.

**Materials Provided**

OraQuick ADVANCE Rapid HIV-1/2 Antibody Test Kits are available in the following packaging configurations:

<table>
<thead>
<tr>
<th>Kit Size</th>
<th>100 Count</th>
<th>25 Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divided Pouches, each containing</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>Test Device (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absorbent Packet (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developer Solution Vial (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(each vial contains 1 mL of a phosphate buffered saline solution containing polymers and an antimicrobial agent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reusable Test Strips</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Specimen Collection Loops</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>Subject Information Pamphlets</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>Package Insert</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Customer Letter</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Materials Required and Available as an Accessory to the Kit**

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

Package contains HIV-1 Positive Control (1 vial, black cap, 0.2 mL), HIV-2 Positive Control (1 vial, red cap, 0.2 mL) and Negative Control (1 vial, white cap, 0.2 mL), and a Package Insert.

**Materials Required but Not Provided**

- Timer or watch capable of timing 20 to 40 minutes
- Clean, disposable, absorbent wipe container
- Biohazard waste container
- Additional items required for fingerstick and venipuncture whole blood collection, and plasma specimens:
  - Antiseptic wipe
  - Sterile lancet to obtain a fingerstick whole blood specimen, or materials required to obtain a venipuncture whole blood specimen
  - Sterile gauze pads
  - Latex, vinyl or nitrile disposable gloves (optional for oral fluid testing)

**Warnings**

**For in vitro Diagnostic Use**

1. Read the package insert completely before using the product. Follow the instructions carefully. Not doing so may result in inaccurate test results.
2. 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. 8
3. FDA has approved this kit for use with oral fluid, fingerstick whole blood, venipuncture whole blood, and plasma specimens only. Use of this test kit with specimen types other than those specifically approved for use with this device may result in inaccurate test results.
4. This kit should be stored 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.
5. If the test kit is stored at temperatures outside of ambient temperature (15°–27°C, 59°–80°F), or used outside of the operating temperature (15°–37°C, 59°–99°F), use the Kit Controls to ensure performance of the test.
6. Individuals infected with HIV-1 and/or HIV-2 who are receiving highly active antiretroviral therapy (HAART) may produce false negative results.

**Precautions**

**Safety Precautions**

1. Handle blood specimens and materials contacting blood specimens as if capable of transmitting infectious agents.
2. Do not drink, eat, or smoke in areas where specimens are being handled or testing is being performed.
3. Wear disposable gloves while handling blood specimens and performing testing of blood specimens. Change gloves and wash hands thoroughly after performing each test. Dispose of used gloves in a biohazard waste container.
4. Oral fluid is not considered potentially infectious unless it contains blood. Use of gloves for oral fluid testing is optional. Test administrators with breaks in the skin (cuts, abrasions, or dermatitis) should wear gloves when performing oral fluid testing. Wash hands thoroughly after performing each oral fluid test and after contact with oral fluid.
5. Dispose of all test specimens and materials used in the test procedure in a biohazard waste container. Lancets and venipuncture materials should be placed in puncture-resistant container prior to disposal. 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.
6. Wipe all spills thoroughly with a solution of 10% bleach or other appropriate disinfectant. Bleach solutions should be made fresh each day.
7. 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" 8 and "Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis." 8

**Handling Precautions**

1. Use all Specimen Collection Loops, Test Devices, and Developer Solution Vials only once and dispose of properly (see Safety Precautions). Do not reuse any of these test components.
2. Do not use the test beyond the expiration date printed on the Divided Pouch. Always check expiration date prior to testing.
3. Do not interchange Test Devices and Developer Solution Vials from kits with different lot numbers.
4. Avoid microbial contamination and exercise care in handling the kit components.
5. To ensure accurate results, the Test Device must be inserted into the Developer Solution Vial within 60 minutes of collection.
6. When collecting oral fluid specimens the test Device must be inserted into the Developer Solution Vial within 10 minutes of collection.
7. Adequate lighting is required to read a test result.
GENERAL TEST PREPARATION

1. Open the two chambers of the OraQuick® ADVANCE Divided Pouch ("Pouch") by tearing at the notches on the top of each side of the Pouch (see picture a and b). To prevent contamination, leave the Test Device ("Device") in the Pouch until you are ready to use it.

2. 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.

3. 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 c).

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.

SPECIMEN COLLECTION AND TESTING PROCEDURE

The OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test can be used for testing oral fluid, fingerstick whole blood, venipuncture whole blood, and plasma specimens. Refer to the specific testing procedure below.

ORAL FLUID PROCEDURE

STEP 1: COLLECT

1. Have the person being tested remove the Device from its Pouch. DO NOT allow the person to touch the Flat Pad (see picture 1A). Check to make sure that an Absorbent Packet is included with the Device (see picture 24). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.

2. Direct the person to place the Flat Pad above the teeth against the outer gum. Direct the person to gently swab completely around the outer gum, both upper and lower, one time around, using the Flat Pad (see pictures 3A and 44). DO NOT allow the person to swab the roof of the mouth, the inside of the cheek or the tongue. NOTE: Both sides of the Flat Pad may be used during this procedure.

STEP 2: TEST

1. Instruct the person being tested to insert the Flat Pad of the Device all the way into the Vial (see picture 5A). 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 6A).

2. Start timing the test (see picture 7A). DO NOT remove the Device from the Vial while the test is running. Pink fluid will appear and travel up the Result Window. The pink fluid will gradually disappear as the test develops (see picture 8A). Read the results after 20 minutes but not more than 40 minutes in a fully lighted area.

3. Refer to the Test Result and Interpretation of Test Result section in this package insert.

FINGERSTICK WHOLE BLOOD AND VENIPUNCTURE WHOLE BLOOD PROCEDURE

STEP 1: COLLECT

Whole blood specimens may be collected either by fingerstick (see Step 1.A) or by venipuncture (see Step 1.B).

STEP 1.A: 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. Hold the finger downward. Apply gentle pressure beside the point of the puncture. Avoid squeezing the finger to make it bleed (see picture 1B). 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 Specimen Collection Loop ("Loop") by the thick "handle" end (see picture 2B). Put the "rounded" end of the Loop on the drop of blood (see picture 3B). Make sure that the Loop is completely filled with blood (see picture 4B). 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

1. Using standard venous phlebotomy procedures, collect a whole blood sample using a tube containing any of the following anticoagulants: EDTA (lavender top), sodium heparin (green top), sodium citrate (light blue top), or ACD Solution A (yellow top). 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'-18°C (35%-64°F) for up to 30 hours. Prior to testing, mix the blood tube gently by inversion several times to ensure a homogeneous sample.

2. Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (see picture 5B). Put the "rounded" end of the Loop into the tube of blood (see picture 6B). Make sure that the Loop is completely filled with blood (see picture 7B). 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 2: MIX

1. Immediately insert the blood-filled end of the Loop all the way into the Vial (see picture 8B). Use the Loop to stir the blood sample in the Developer Solution ("Solution") (see picture 9B). Remove the used Loop from the Solution. Throw the used Loop away in a biohazard waste container.
2. Check the Solution to make sure that it appears pink. This means that the blood was correctly mixed into the Solution (see picture 16C). If the Solution is not pink, discard all test materials in a biohazard waste container. Start the test over. Use a new Pouch and a new blood sample.

STEP 3: TEST
1. Remove the Device from the Pouch. DO NOT touch the Flat Pad (see picture 16C). Check to make sure that an Absorbent Packet is included with the Device (see picture 12C). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
2. Insert the Flat Pad of the Device all the way into the Vial containing the blood sample (see picture 13C). 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 14B).
3. Start timing the test (see picture 15C). DO NOT remove the Device from the Vial while the test is running. Pink fluid will appear and travel up the Result Window. The pink fluid will gradually disappear as the test develops (see picture 16B). Read the results after 20 minutes but not more than 40 minutes in a fully lighted area.
4. Refer to the Test Result and Interpretation of Test Result section in this package insert.

PLASMA PROCEDURE

NOTE: Testing of plasma samples may only be performed by laboratories certified to perform Moderate Complexity tests.

STEP 1: COLLECT
1. Using standard venous phlebotomy procedures, collect a whole blood sample using a tube containing EDTA (lavender top) 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 or plasma for up to 7 days at 2-27°C (35-80°F), 2°C-8°C (35°F-46°F), 10°C, or 40°C.
2. Centrifuge the tube of blood (1000-1300 x g, for approximately 5 minutes, no refrigeration required) to separate the cells from the plasma. Carefully recap the tube by gently rocking the stopper towards you so that it vents away from you.
3. Pick up an unused Specimen Collection Loop ("Loop") by the thick "handle" end (see picture 1C). Put the "rounded" end of the Loop into the tube of plasma (see picture 2C). Make sure that the Loop is completely filled with plasma (see picture 3C). 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
1. Immediately insert the plasma-filled end of the Loop all the way into the Vial (see picture 4C). Use the Loop to stir the plasma sample in the Developer Solution ("Solution") (see picture 5C). Remove the used Loop from the Solution. Throw the used Loop away in a biohazard waste container.

STEP 3: TEST
1. Remove the Device from the Pouch. DO NOT touch the Flat Pad (see picture 6C). Check to make sure that an Absorbent Packet is included with the Device (see picture 7C). If no Absorbent Packet is present, discard the Device and obtain a new Pouch for testing.
2. Insert the Flat Pad of the Device all the way into the Vial containing the blood sample (see picture 8C). 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 9C).
3. Start timing the test (see picture 10C). DO NOT remove the Device from the Vial while the test is running. Pink fluid will appear and travel up the Result Window. The pink fluid will gradually disappear as the test develops (see picture 11C). Read the results after 20 minutes but not more than 40 minutes in a fully lighted area.
4. Refer to the Test Result and Interpretation of Test Result section in this package insert.

GENERAL TEST CLEAN-UP
1. Dispose of the used test materials in a biohazard waste container.
2. When using gloves, 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

Built-in Control Features
The OraSure ADVANCE Rapid HIV-1/2 Antibody Test has a built-in procedural control that demonstrates assay validity. A reddish-purple line appears next to the triangle labeled "C" in the Control Window indicates that a specimen was added and that the fluid migrated appropriately through the Test Device. The Control line will appear on all valid tests, whether or not the sample is reactive or non-reactive. (Refer to Test Result and Interpretation of Test Result section below.)

External Quality Control
OraSure ADVANCE Rapid HIV-1/2 Antibody Test Kit Controls are available separately for use only with the OraSure ADVANCE Rapid HIV-1/2 Antibody 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 HIV-1 and HIV-2 Positive Controls will produce a reactive test result and have been manufactured to produce a very faint "T" line. The Negative Control produces a non-reactive test result. (Refer to Test Result and Interpretation of Test Result section below.) 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 OraSure ADVANCE Rapid HIV-1/2 Antibody Test.

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 (35-80°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.

Refer to the OraSure ADVANCE Rapid HIV-1/2 Antibody Test Kit Controls package insert for instructions on the use of these reagents. It is the responsibility of each laboratory using the OraSure ADVANCE Rapid HIV-1/2 Antibody Test to establish an adequate quality assurance program to ensure the performance of the device under its specific locations and conditions of use. Contact OraSure Technologies' Customer Service if the Kit Control reagents do not produce the expected results.

TEST RESULT AND INTERPRETATION OF TEST RESULT

Refer to the Result Window on the Test Device.

NON-REACTIVE
The diagram at the right shows an example of a Non-Reactive test result. A test is Non-Reactive if a reddish-purple line appears next to the triangle labeled "C", and NO line appears next to the triangle labeled "T". A Non-Reactive test result means that HIV-1 and HIV-2 antibodies were not detected in the specimen. The test result is interpreted as NEGATIVE for HIV-1 and HIV-2 antibodies. Follow CDC guidelines to inform the test subject of the test result and its interpretation.
REACTIVE

The diagrams at the right show examples of a Reactive test result.

A test is Reactive if:
- A reddish-purple line appears next to the triangle labeled "C" and
- A reddish-purple line appears next to the triangle labeled "T". One of these lines may be darker than the other.

NOTE: The test is Reactive if any reddish-purple line appears next to the "T" triangle and not to the "C" triangle, no matter how faint these lines are.

A Reactive test result means that HIV-1 and/or HIV-2 antibodies have been detected in the specimen. The test result is interpreted as PRELIMINARY POSITIVE for HIV-1 and/or HIV-2 antibodies. Follow CDC guidelines to inform the test subject of the test result and its interpretation.

INVALID

The diagrams at the right show examples of an Invalid test result.

A test is Invalid if any of the following occurs:
- NO reddish-purple line appears next to the triangle labeled "C" (see picture a and b),
- A red background in the Result Window makes it difficult to read the result after 20 minutes (see picture c), or
- If any of the lines are NOT inside the "C" or "T" triangle areas (see picture d) and/or (see picture e).

An Invalid test result means that there was a problem running the test, either related to the specimen or to the Test Device. An Invalid result cannot be interpreted. Repeat the test with a new Divided pouch and a new oral fluid, fingerstick or venipuncture whole blood, or plasma sample. Contact OraSure Technologies' Customer Service if you are unable to get a valid test result upon repeat testing.

LIMITATIONS OF THE TEST

1. The OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test must be used in accordance with the instructions in this package insert to obtain an accurate result.
2. Reading test results earlier than 20 minutes or later than 40 minutes may yield erroneous results.
3. This test is approved by FDA for use with oral fluid, fingerstick or venipuncture whole blood, and plasma specimens only. Use of other types of specimens, testing of venipuncture whole blood specimens collected using a tube containing an anticoagulant other than EDTA, sodium heparin, sodium citrate, or ACD Solution A, or testing of plasma specimens collected using a tube containing an anticoagulant other than EDTA may not yield accurate results.
4. Individuals infected with HIV-1 or HIV-2 who are receiving highly active antiretroviral therapy (HAART) may produce false negative results.
5. Clinical data has not been collected to demonstrate the performance of the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test in persons under 12 years of age.
6. A reactive result using the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test suggests the presence of HIV-1 and/or HIV-2 antibodies in the specimen. The OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test is intended as an aid in the diagnosis of infection with HIV-1 and/or HIV-2. AIDS and AIDS-related conditions are clinical syndromes and their diagnosis can only be established clinically.

7. For a reactive result, the intensity of the test line does not necessarily correlate with the titer of antibody in the specimen.
8. A non-reactive result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to recent exposure may take several months to reach detectable levels.

PERFORMANCE CHARACTERISTICS

SENSITIVITY

DETECTION OF ANTIBODIES TO HIV-1 IN SPECIMENS FROM INDIVIDUALS INFECTED WITH HIV-1

ORAL FLUID

A sensitivity study was performed at eight clinical trial sites using freshly obtained oral fluid specimens collected from 767 individuals reported to be infected with HIV-1. Of the 767 specimens that were identified as seropositive using licensed confirmatory testing, 762 gave a reactive result on the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test. The results of this study are shown in Table 1.

A separate study was performed at four clinical trial sites using freshly obtained oral fluid specimens collected from 3150 previously unprepared individuals from populations at high risk for HIV-1 infection. The results of this study are also shown in Table 1. Of the 73 specimens that were identified as seropositive using licensed confirmatory testing, 72 were reactive using the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test.

TABLE 1

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Total Samples</th>
<th>OraQuick® ADVANCE Reactive</th>
<th>Licensed EIA Repeatedly Reactive</th>
<th>True Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known HIV-1 Positive</td>
<td>767</td>
<td>762</td>
<td>764</td>
<td>767</td>
</tr>
<tr>
<td>High-Risk</td>
<td>3150</td>
<td>72</td>
<td>74</td>
<td>73</td>
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<tr>
<td>TOTAL</td>
<td>3917</td>
<td>834</td>
<td>842</td>
<td>840</td>
</tr>
</tbody>
</table>

1 Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by licensed immunofluorescence assay (IFA).
2 Eight additional specimens were OraQuick® ADVANCE false positive (see table 2).
3 One specimen was EIA false positive, with a negative Western blot.

Combining the number of OraQuick® ADVANCE reactive results obtained from the study of confirmed positives with the number of OraQuick® ADVANCE reactive results obtained from the study of high-risk populations, the sensitivity of the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test in these studies was calculated to be 854/840 = 99.3% (95% C.I. = 98.4% - 99.7%).

PLASMA

A sensitivity study was performed at eleven clinical trial sites using EDTA-plasma specimens collected from 891 individuals reported to be infected with HIV-1. Of the 891 specimens that were identified as seropositive using licensed confirmatory testing, 887 gave a reactive result on the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test. The results of this study are shown in Table 2.

A separate study was performed at six clinical trial sites using EDTA-plasma specimens collected from 533 previously unprepared individuals from populations at high risk for HIV-1 infection. The results of this study are also shown in Table 2. All of the 14 specimens that were identified as seropositive using licensed confirmatory testing, were reactive using the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test.

TABLE 2

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Total Samples</th>
<th>OraQuick® ADVANCE Reactive</th>
<th>Licensed EIA Repeatedly Reactive</th>
<th>True Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known HIV-1 Positive</td>
<td>891</td>
<td>887</td>
<td>891</td>
<td>891</td>
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<tr>
<td>High-Risk</td>
<td>553</td>
<td>14</td>
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<tr>
<td>TOTAL</td>
<td>1424</td>
<td>901</td>
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</tbody>
</table>

1 Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by licensed immunofluorescence assay (IFA) or licensed IFA.
2 Eight additional specimens were OraQuick® ADVANCE false positive (see table 3).

Combining the number of OraQuick® ADVANCE reactive results obtained from the study of confirmed positives with the number of OraQuick® ADVANCE reactive results obtained from the study of high-risk populations, the sensitivity of the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test in these studies was calculated to be 901/905 = 99.6% (95% C.I. = 98.9% - 99.8%).
FINGERSTICK WHOLE BLOOD

A sensitivity study was performed at eight clinical trial sites using freshly obtained fingerstick whole blood samples from 481 individuals known to be infected with HIV-1 and 40 AIDS patients. Of the 521 specimens that were repeatedly reactive using a licensed EIA and positive by Western blot, 519 gave a reactive result on the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test. The results of this study are shown in Table 3.

A separate study was performed at seven clinical trial sites using 625 freshly obtained fingerstick whole blood samples from previously unscreened individuals from populations at high risk for HIV-1 infection. The results of this study are also shown in Table 3. Of the 625 specimens tested, 20 were repeatedly reactive using a licensed EIA, of which 17 were positive by Western blot. These same 17 specimens gave a reactive result using the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test.

TABLE 3
Detection of Antibody to HIV-1 in Fingerstick Whole Blood Samples from Patients with AIDS and from HIV-1 Seropositive Individuals

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Total Samples</th>
<th>OraQuick® ADVANCE Reactive</th>
<th>Licensed EIA Reactively Reactive</th>
<th>True Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Known HIV-1 Positive</td>
<td>481</td>
<td>479</td>
<td>481</td>
<td>481</td>
</tr>
<tr>
<td>High-Risk</td>
<td>625</td>
<td>17</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1146</td>
<td>536</td>
<td>541</td>
<td>538</td>
</tr>
</tbody>
</table>

1 Confirmation performed by licensed HIV-1 Western blot, with confirmation of indeterminate Western blot results by RIPA.

Combining the number of OraQuick® ADVANCE reactive results obtained from the study of confirmed positives with the number of OraQuick® ADVANCE reactive results obtained from the study of high-risk populations, the sensitivity of the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test in these studies was calculated to be 59/538 = 99.6% (95% C.I. = 98.5% - 99.9%).

Reactivity with HIV-1 Specimens From Various Geographic Regions
To assess the sensitivity of the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test for HIV-1 variants from various geographic regions, 215 confirmed HIV-1 antibody-positive serum/plasma specimens were obtained from various parts of the world. Of these 215 specimens, 214 were reactive using the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test. One confirmed HIV-1 antibody-positive specimen from China was non-reactive using the OraQuick® ADVANCE test. An additional 13 specimens representing HIV-1 Subtypes A, C, D, F, and Group O were tested and reactive on OraQuick® ADVANCE.

Reactivity with HIV-1 Seroconversion Panels
Eleven HIV-1 seroconversion panels were tested in comparison with licensed anti-HIV EIA tests. Each panel consisted of sequential serum/plasma specimens obtained from a single individual during seroconversion. The eleven seroconversion panels consisted of 89 specimens. The results of this study are shown in Table 4. In this study, the OraQuick® ADVANCE Rapid HIV-1/2 Antibody Test was demonstrated to be capable of detecting seroconversion similar to currently available FDA licensed EIAs.
ATION OF INFORMATION FROM THE SYSTEM

The primary goal of the Advance Oaks project was to develop an information system that could provide real-time access to critical data and support decision-making processes. The system was designed to integrate various data sources, including sensor data, weather forecasts, and historical records, to enable efficient monitoring and management of the facility's operations.

The system consists of several key components, including a database management system, a data acquisition module, and a user interface. The database management system is responsible for storing and retrieving data, while the data acquisition module captures real-time data from various sensors and systems. The user interface allows authorized personnel to access the data and make informed decisions.

The system was tested extensively to ensure its reliability and effectiveness. The initial testing phase involved simulating various scenarios to evaluate the system's performance under different conditions. The results showed that the system was able to provide accurate and timely information, which was crucial for effective decision-making.

In conclusion, the Advance Oaks project was successful in developing a robust information system that meets the needs of the facility's operations. The system's ability to handle real-time data and provide critical information is expected to enhance the facility's overall performance and efficiency.
Combining the number of OraQuic® ADVANCE reactive results obtained from the study of confirmed positives with the number of OraQuic® ADVANCE non-reactive results obtained from the study of the high-risk populations, the specificity of the OraQuic® ADVANCE Rapid HIV-1/2 Antibody Test in these studies was calculated to be 100% (95% C.I. = 99.8% - 100%).

In addition, 3 HIV-2 infected individuals located in the USA were tested by fingerstick whole blood and oral fluid OraQuic® ADVANCE tests. Fingerstick whole blood and oral fluid samples from all three subjects were reactive on the OraQuic® ADVANCE test.

**SPECIFICITY**

**ORAL FLUID**

A specificity study was performed at four clinical trial sites using freshly obtained oral fluid specimens collected from 605 previously unscreened individuals at low risk for HIV-1 infection. All of the 605 specimens were correctly non-reactive using the OraQuic® ADVANCE Rapid HIV-1/2 Antibody Test. Of the 307 HIV-1 antibody-negative specimens from the four study sites that examined populations at high risk for HIV-1 infection, the OraQuic® ADVANCE test was non-reactive for 306. The results are summarized in Table 7.

**PLASMA**

A specificity study was performed at seven clinical trial sites using EDTA-plasma specimens collected from 1102 previously unscreened individuals at low risk for HIV infection. All of the specimens, except for one, gave non-reactive results using the OraQuic® ADVANCE Rapid HIV-1/2 Antibody Test. In addition, 519 of the 520 HIV antibody-negative specimens from study sites that examined populations at high risk for HIV-1 infection also gave non-reactive results using the OraQuic® ADVANCE test. The results of this study are shown in Table 8.

**FINGERSTICK WHOLE BLOOD**

A specificity study was performed at eight clinical trial sites using freshly obtained fingerstick whole blood samples from 1250 previously unscreened individuals at low risk for HIV-1 infection. In the course of this study, two specimens were confirmed to have antibodies to HIV-1 and were removed from the specificity calculation. All of the remaining specimens gave non-reactive results using the OraQuic® ADVANCE Rapid HIV-1/2 Antibody Test. In addition, all of the 608 HIV-1 antibody-negative specimens from the study sites that examined populations at high risk for HIV-1 infection also gave non-reactive results using the OraQuic® ADVANCE test. The results of this study are shown in Table 9.
temperature (18°C) and tested over a 7-day period. There was no anticoagulant-specific effect observed on assay performance with samples held up to 30 hours at 2°-180C.

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 fixatives, 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.

**REPRODUCIBILITY**

The reproducibility of the OraQuick® ADVANCE 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 blinded-coded panel was tested that consisted of 5 contrived blood specimens (4 antibody-positive and 1 antibody-negative). Test results were recorded at 20-25 minutes and at 55-60 minutes. A total of 405 tests were performed (135/site), with a total of 41 tests per panel member. The overall reproducibility of the OraQuick® ADVANCE 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 20-25 minute read time was reactive at the 55-60 minute read time.

**RESULTS OF UNTRAINED USER STUDY**

An “Untrained User” study was conducted in which participants were given only the test instructions and asked to perform testing of a blinded panel comprised of 6 randomized specimens of different levels (Negative, Low Positive and High Positive OraQuick® ADVANCE test reactivity) consisting of human plasma. The participants were not given any training on the use of the test or the interpretation of the test results, nor were they allowed to observe the performance of the Kit Controls by the Study Coordinator. The study protocol stipulated that professionally trained medical laboratory personnel or persons with prior experience using the OraQuick® ADVANCE device were excluded from participation. A total of 130 participants were enrolled from a total of four sites, representing a diverse demographic (educational, ethnic, age, gender, etc.) population.

The rate of correct results for the overall study was 98.6% (592/600). Refer to the table below for a summary of the performance relative to the specimen type. The eight incorrect results were attributed to six participants. Of these six participants, four obtained 5 of 6 correct results, and two participants obtained 4 of 6 correct results.

<table>
<thead>
<tr>
<th>Untrained Users Rate of Correct Test Results</th>
<th>Negative</th>
<th>Low Positive</th>
<th>High Positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% C.I. (97.1% - 99.7%)</td>
<td>95% C.I. (95.0% - 99.3%)</td>
<td>95% C.I. (97.0% - 99.6%)</td>
<td>95% C.I. (97.4% - 99.4%)</td>
<td></td>
</tr>
</tbody>
</table>

There were 1.1% (10/600) invalid results reported, with 5 of the 10 invalid results attributed to one participant. All tests were successfully repeated, with 6/10 of the repeat test results interpreted correctly. The 2 incorrect repeat results were attributed to one participant. As part of the Untrained User study, a Participant Feedback Questionnaire was completed. All participants rated the test as “easy to use” and felt able to perform the test correctly.

**BIBLIOGRAPHY**
