The OraQuick ADVANCE Rapid HIV Test

- The OraQuick ADVANCE device is a rapid test designed to detect HIV-1 and HIV-2 antibodies in 20 minutes.
- Rapid HIV tests allow people to learn test results on the day they are tested. Use of rapid HIV tests substantially increases the number of people who learn of their HIV status. HIV-negative results do not require confirmation; preliminary positive results do require confirmation.
- The test is operated by collecting an oral fluid sample on the porous flat pad of the test kit, or by inserting a drop of whole blood into a vial containing a reagent, and then inserting the test kit into the vial. The specimen and solution flow through the device and results are ready in 20 to 40 minutes.

TESTING YOUR PROFICIENCY WITH THE RAPID TEST

- Anyone collecting a sample, running the test, reading results or supervising someone doing any of these activities must take a proficiency exam during Day One of the Basic I training.
- The exam involves running 5 OraQuick ADVANCE tests in a row using a written checklist. You must correctly follow the steps outlined on the checklist and correctly interpret results of the 5 tests as well as correctly interpret 10 additional pictures of results printed on a handout.
- To prepare you for the proficiency exam, your trainers will first use a test kit to demonstrate the proper use and interpretation of the test. They will then guide you step-by-step in the use of the checklist to practice a rapid test on your own. You will then pair with another participant to practice and observe again. By the time you take the proficiency exam, you will have seen the test administered twice, practiced it twice yourself and been able to ask plenty of questions about the test kit operation and interpretation.
- To pass the proficiency exam, you must score 100 percent. The best way to prepare yourself is to read this section thoroughly and to listen attentively during the training.

BACKGROUND ON THE ORAQUICK ADVANCE RAPID HIV ANTIBODY TEST

- The OraQuick ADVANCE test is a CLIA* waived point-of-care test. This means it can be administered outside of a clinical laboratory. CLIA requires anyone performing a laboratory test classified as waived to follow the manufacturer's instructions contained in the package insert.
- California has additional requirements for quality assurance standards and procedures, some of which will be covered here and others in the Basic I training. Further requirements specific to OraQuick ADVANCE are contained in an addendum detailed in the *California Office of AIDS OraQuick Rapid HIV Testing Guidelines*.

* Clinical Laboratory Improvement Amendments, a federal law establishing quality standards for all laboratory testing.

- The current package insert (including instructions for operation) for the OraQuick ADVANCE test is available on the OraSure Technologies, Inc. website (www.orasure.com).
- The *California Quality Assurance Guidelines* are available on the Office of AIDS website (www.dhs.ca.gov/aids).
- More information about the OraQuick ADVANCE Rapid HIV test is available on the CDC website (www.cdc.gov/HIV/rapid_testing).

COMPARING RAPID AND CONVENTIONAL HIV TESTING

- The OraQuick ADVANCE Rapid Test is very similar to the initial EIA used in conventional testing. Just as in conventional testing, a screening test that develops a negative result does not require confirmation but one that develops a preliminary positive result does.
- Recall from Section 8 that in conventional HIV antibody testing, laboratories use a screening test called the EIA (also known as an ELISA) to look for antibodies to HIV. If no antibodies are found using the EIA, the result is reported as HIV-negative to the client, who may then retest at a later date if the current test falls within the window period. If antibodies are found using the conventional EIA test, the sample is often tested again with another EIA but is always confirmed using a confirmatory test, the Western Blot or IFA, before being designated an HIV-positive result.
- Running the OraQuick ADVANCE is much like running a conventional EIA, except that the OraQuick ADVANCE is even more accurate. The additional accuracy of the OraQuick ADVANCE means we can confidently deliver results from this screening test directly to clients, though preliminary positive results still need to be confirmed using a Western Blot or IFA just as in conventional testing.

ACCURACY OF THE ORAQUICK ADVANCE RAPID TEST

- Accuracy involves two qualities of a test: sensitivity and specificity.

Sensitivity of OraQuick ADVANCE*

- Sensitivity refers to a test's ability to detect a true positive. That is, a test that is extremely sensitive is very unlikely to "miss" a true positive.
- Screening tests like the conventional EIA and OraQuick ADVANCE are selected and designed to be extremely sensitive, so they will not "miss" positives. If there is something there to find, these tests are very good at finding it. (That's why we do NOT need to confirm HIV-negative results.)

The data below from the CDC show that the OraQuick ADVANCE is at least as sensitive as the conventional EIA screening test. Out of 340 samples that were known to be HIV-positive, all of

* These data from the CDC are based on blood samples. Manufacturer data based on oral fluid reflect similar sensitivity (see package insert at www.orasure.com).

them tested positive on the EIA (see the line beginning with "EIA 1"), even when tested a second time (see "EIA RR").

Test	True Positive	Tested Positive	False Negative	Sensitivity
EIA 1	340	340	0	100%
EIA RR*	340	340	0	100%

- The sensitivity of the EIA was 100 percent. This means that a negative result on the EIA can be confidently reported as HIV-negative to the client. If there had been antibodies present in the client's sample, the EIA would have found them.
- As you can see from the data below, the sensitivity of the OraQuick ADVANCE test is the same as the EIA. If a client tests negative on the OraQuick ADVANCE, an HIV-negative result is delivered to the client, just as with the conventional EIA.

Test	True Positive	Tested Positive	False Negative	Sensitivity
OraQuick 1	340	340	0	100%
OraQuick RR	340	340	0	100%

- These data reveal two important aspects of accuracy to remember when delivering HIV-negative results:
- There is no need to confirm an HIV-negative result on the OraQuick ADVANCE. If there were antibodies there to find, this test would have found them.
- The OraQuick ADVANCE is reliable—when the test was "re-run" it gave the same answer—so we do not need to repeat the test.
- In addition, the window period is the same for EIA and OraQuick ADVANCE, so clients who receive an HIV-negative result who are still in the window period should be advised to re-test at the appropriate time. (See *Section 9: The Window Period*.)

Specificity of OraQuick ADVANCE**

- Specificity refers to the ability of a test to detect true negatives. A test that is very specific will rarely have false positives. This means that the higher the specificity of a test, the more accurately a preliminary positive result is truly HIV-positive.
- The data below from the CDC demonstrate that the OraQuick ADVANCE is extremely specific to HIV antibodies—its specificity is greater than that of the conventional EIA.

* RR: "repeated reactive."

** These data from the CDC are based on blood samples. Manufacturer data based on oral fluid reflect similar sensitivity (see package insert at www.orasure.com).

- In the first set of data shown below, the EIA resulted in 25 false positives when 467 known negative samples were tested (see "EIA 1"). When repeated with the same samples, the number of false positives fell to 4 out of 467 known negative samples (see "EIA RR"). This is why even in conventional testing, all positive results on the EIA must be confirmed with a Western Blot or IFA before being reported to the client as HIV-positive.

Test	True Negative	Tested Negative	False Positive	Specificity
EIA 1	467	442	25	94.7%
EIA RR*	467	463	4	99.1%

- In comparison, the data below show that OraQuick testing resulted in only 1 false positive when 464 known negative samples were tested. These results were consistent when the samples were tested again.

Test	True Negative	Tested Negative	False Positive	Specificity
OraQuick 1	464	463	1	99.8%
OraQuick RR	464	463	1	99.8%

- These data reveal two important aspects of accuracy to remember when delivering preliminary positive results:
- The OraQuick ADVANCE is more specific than the conventional EIA; it is much more acceptable to deliver a preliminary positive OraQuick ADVANCE result because we know it will almost always be confirmed.
- The OraQuick ADVANCE is reliable—when the test was "re-run" it gave the same answer—so we do not need to repeat the test, even for preliminary positive results.
- These CDC data show that the OraQuick ADVANCE test is very specific to HIV antibodies, and rarely results in false positives. However, it is the standard of care in the United States to confirm preliminary positive results from screening tests to rule out false positives and to ensure that clients receive the correct result. Recall that confirmatory testing is done on positive EIA samples, too—it just happens at the lab before the result returns to the test site.
- Either blood or oral fluid may be used for confirmatory testing, but blood is preferred whenever possible.
- The counseling aspects of delivering preliminary positive results will be dealt with in your Basic I training. Know that delivering preliminary positive results is already in practice, and clients are responding fine to the need for confirmatory testing.
- Any screening test, including OraQuick ADVANCE, will sometimes have a false positive result. The package insert lists some of the co-factors that were present when OraQuick ADVANCE resulted in a false positive. This happens so rarely that there is not enough data to conclude which combination of factors may cause this effect.

* RR: "repeated reactive."

Additional Data on the Accuracy of OraQuick ADVANCE

- Additional data testing people of unknown status reveals similar sensitivity and specificity to previous data. When testing 780 people of unknown status, OraQuick ADVANCE correctly identified all participants who were truly HIV-negative (100% sensitivity). Of the participants who tested preliminary positive, only one result was a false positive (99.9% specificity).

CDC Clinical Trial: Test performed on 780 persons of unknown serostatus; 35 proved to be HIV-positive.	
Sensitivity	100%
Specificity	99.9%

- Data from the manufacturer, Orasure Technologies, Inc. reflects similar overall accuracy, though the sensitivity and specificity were slightly different. These differences are reasonable to expect in any test, and nonetheless reflect the very high level of accuracy when using OraQuick ADVANCE.

Manufacturer Data		
Sensitivity	536/538	99.6%
Specificity	1856/1856	100%
Overall Accuracy	2392/2394	99.9%

- When discussing OraQuick ADVANCE with clients, emphasize that the test is "extremely accurate" or "highly accurate" and de-emphasize statistics and percentages. Clients who would like additional information about the accuracy of the test may refer to the Subject Information Flyer designed to answer questions about the OraQuick ADVANCE.

QUALITY ASSURANCE

- Inaccuracies in test results are exceedingly rare. When they do happen, they often involve human error in the operation or interpretation of the test kit. For this reason, the Office of AIDS requires very strict adherence to quality assurance guidelines.
- Quality assurance refers to planned processes that provide confidence in a product's suitability for its intended purpose. The following are the key points to remember about quality assurance requirements for OraQuick ADVANCE. They are compiled from the manufacturer's information.
- Remember that small mistakes can lead to major errors, such as a client receiving an inaccurate test result. With conventional testing, California's public health labs conduct these and more quality assurance procedures. During rapid testing, it is up to test sites to follow quality assurance guidelines and ensure that ALL clients receive accurate test results.

BRIEF QUALITY ASSURANCE OVERVIEW

- All sites conducting rapid HIV testing are required to meet specific quality assurance requirements designed to ensure that every client receives an accurate test result. In addition to training requirements for personnel operating the test, sites must have:

Adequate Lighting

- Full or bright light to read test device lines. In some cases, a stationary task light will be necessary.

Temperature Control

- Perform test: 59 to 99 degrees Fahrenheit (or as indicated in current package insert)
- Store test: 35 to 80 degrees Fahrenheit (or as indicated in current package insert)

Space for Undisturbed Testing Process

- Space separate from the counseling area where tests may sit undisturbed for at least 20 minutes. There must be no smoking, eating, drinking, applying of make-up (including lip balm), etc., in the testing area.

External Controls

- Sites must also ensure that the test kits are working properly by running external controls under specific circumstances. An external quality control unit consists of three vials of clear fluid made from human plasma. One vial contains fluid that will test negative; a second vial contains fluid that will test HIV-1 positive; a third vial contains fluid that will test HIV-2 positive. Although the two positive results will not look any different in the test kit window, two separate positive control vials are needed to determine that the test kits are able to detect both HIV-1 and HIV-2.
- The external quality control process consists of running three OraQuick ADVANCE tests and using a drop of fluid from each of the control vials, to ensure that the tests are obtaining the proper result.

When to Run External Controls

- By each new operator prior to performing testing on patient specimens;
- In each new setting or whenever conditions in a setting have changed significantly;
- When opening a new test kit lot or when a new shipment of test kits is received;
- If the temperature of the test storage area falls outside of acceptable 35 to 80 degrees Fahrenheit range;
- If the temperature of the testing area falls outside of acceptable 59 to 99 degrees Fahrenheit range;

- At periodic intervals as dictated by the user facility;
- Whenever two invalid results in a row are obtained.
- More details about quality assurance requirements and procedures are available in the Office of AIDS OraQuick Rapid HIV Testing Guidelines at www.dhs.ca.gov/aids.

IMPORTANT NOTES ON QUALITY ASSURANCE

- There should be at least two separate spaces in which to provide rapid testing: one room or location for counseling and another for the test to develop.
- External controls allow us to determine if the OraQuick ADVANCE is working properly. For example, if the operation temperature falls out of range (below 59 or above 99 degrees Fahrenheit), then external controls are used to make sure the test kits are still working properly. Do your best to memorize when to run external controls.
- The "new operator" requirement comes from the manufacturer. By the end of the Basic I, you will have run tests using the HIV-negative and the HIV-1 external controls. Back at your test site, you will need to run the HIV-2 external control prior to conducting OraQuick ADVANCE testing with clients.
- If you will be administering the test using finger stick blood samples, you will have to go through separate training to become certified to perform finger sticks. Further information will be available from your supervisor.