

Issue Summary
Blood Products Advisory Committee
Gaithersburg, Maryland
November 3, 2005

Topic I: Approach to Validation of Over-the-Counter (OTC) Home-Use HIV Test Kits

Issue

OraSure Technologies, Inc. has made public its imminent plans to seek OTC status for the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test for use with oral fluid specimens. FDA seeks advice regarding the conditions necessary to support approval of a home-use HIV test kit. In particular, we will ask the Committee to consider what studies are needed to validate test accuracy, test interpretation, and medical follow-up based on the provision of informational material in place of a trained test operator and counselor.

Background

Rapid HIV Tests:

- Over the past four years, FDA has approved a number of rapid HIV tests of low complexity, which are simple to use, require no special storage conditions and provide a highly accurate test result within 20 minutes for the detection of antibodies to HIV. Two of these tests were found to be simple enough to perform that they received a CLIA waiver, expanding the availability of testing. FDA has required, as a condition of approval, that the lower 95% confidence bound for estimated test sensitivity and specificity should be 98% or greater.
- Whereas most HIV tests require the use of a blood specimen, FDA also approved the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test in March 2004 to detect antibodies to HIV-1 and HIV-2 in oral fluid specimens. The sensitivity of the test is 99.3% (95% CI = 98.4%-99.7%) and the specificity is 99.8% (95% CI= 99.6%-99.9%), which is within the acceptance performance set by FDA (1). A CLIA waiver for this indication was granted in June 2004.
- Testing using oral fluid involves swabbing the device against the upper and lower gums once, inserting the device into a buffer vial, and reading the test result after 20 minutes. The test result is read visually. A single control line (controls for adequate specimen collection and proper functioning of the device) is a non-reactive result that is interpreted as negative for antibodies to HIV-1 or HIV-2. The presence of both a control line and a test line (consisting of HIV-1 and HIV-2 peptides) is a reactive test result that is interpreted as “preliminary positive” for HIV-1 and/or HIV-2 antibodies and reported to the test subject. Reactive test results should be confirmed using an additional, more specific test, although in practice this may not always occur.

- Since 2002, all rapid HIV tests were approved as restricted devices, with sales and use restrictions in place:
 1. Sale 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.
 2. The test is approved for use only by an agent of a clinical laboratory.
 3. Test subjects must receive a “Subject Information” pamphlet and pre-test counseling prior to specimen collection and appropriate counseling when test results are provided.
 4. The test is not approved for use to screen blood, cell, plasma, or tissue donors.

Purchasers of the test receive a customer letter stating that by purchasing the test they agree to abide by these restrictions.

Home use tests:

- Home-use tests are used at home by untrained persons without the help of a healthcare professional. Most home-use tests, such as tests for blood glucose, cholesterol, and pregnancy, are available OTC without a prescription. There are two types of home-use tests: test kits and collection kits. With a test kit, you take your own sample, test the sample, and read your own result. There are currently no home-use test kits approved for the detection of any infectious agent. With a collection kit, you take your own sample, mail it to a laboratory, and get your result over the phone or in the mail. There is currently one FDA approved home-use collection kit on the market for HIV testing.

History of FDA consideration of OTC for HIV tests:

- FDA has discussed HIV home-use test kits and home-use collection kits over the past 10 years in various forums. This included communications with manufacturers of home collection systems in 1988-89, the BPAC in June 1994, and in Federal Register notices in 1989, 1990, and 1995 (Ref. 2-4).

In the course of these discussions, appropriate regulatory criteria were identified for home-use specimen collection kits for HIV testing, but not for home-use HIV test kits. With improved test kit technology (ease of use, freedom from biohazards, and excellent performance characteristics), we believe it may be feasible to identify regulatory criteria for home-use HIV test kit.

- Throughout all of the discussions, a number of recurring issues emerged:
 - Benefits of HIV home-use test kits include anonymous testing potentially leading to more people knowing their HIV status, empowerment of consumers in

healthcare decisions, earlier diagnosis of HIV infection and therefore earlier intervention.

- Risks of HIV home-use test kits include inappropriate use of the test or test result, including misinterpretation (*e.g.*, relying on the test to provide an accurate result after a very recent exposure); potential adverse outcomes following obtaining a test result without live counseling; inability to reach individuals for follow-up and to perform partner notification (though partners may be informed by the self-tested individual); coercive testing; and use by minors.
- Additional issues include obtaining a test result without a supplemental test, the cost and availability of an HIV home-use test kit for those who need the test the most, and conflict with state and/or federal public health reporting requirements.

Discussion

What test characteristics favor possible approval of an OTC home-use HIV test?

- The risk of an incorrect test result is extremely low in the hands of trained operators.
 - As noted above, data submitted in support of the approval of the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test for use with oral fluid specimens showed a sensitivity of 99.3% (95% CI = 98.4%-99.7%) and specificity of 99.8% (95% CI = 99.6%-99.9%), falling within the acceptable performance set by FDA (1). Additional studies showed that test performance was not affected by conditions that could potentially affect the integrity of an oral fluid specimen, such as eating, drinking, brushing of teeth, mouthwash, smoking, alcohol consumption, and oral cavity infections.
- The test is simple to use compared to other types of HIV tests and earlier versions of rapid HIV tests, suggesting that untrained persons will be able to perform the test properly.
- The test does not require special storage conditions.
- The test provides highly accurate results for the detection of antibody to HIV within 20 minutes.
- The use of a non-infectious oral fluid specimen eliminates concerns about biohazardous conditions (no blood and no sharps).

What information will be discussed at the BPAC meeting?

- FDA will be discussing an approach for HIV home-use test kits at this meeting of the BPAC. The Committee will hear a proposal by OraSure for an OTC claim for the OraQuick ADVANCE Rapid HIV-1/2 Antibody Test for use with oral fluid specimens, including:
 - Proposed studies to validate adequate performance in the hands of intended users

- The ability of informational materials to provide counseling and other information regarding accuracy of testing, correct test interpretation, management of psychological and social issues, and medical referral.
- The BPAC will also hear presentations addressing the role of rapid HIV tests in CDC's Advancing HIV Prevention initiative and CDC's current HIV test counseling recommendations, the role of quality systems in diagnostic testing, psychological and social issues associated with HIV testing, and prior experience with approved home-use test kits.

Questions for the Committee

1. Are FDA's previously established criteria for sensitivity and specificity for rapid HIV tests also appropriate to support OTC use for home-use HIV test kits?
2. Please comment on the design of clinical studies necessary to validate the accuracy of an OTC home-use HIV test kit.
3. Please comment on proposed content of the informational materials and the steps that should be taken to validate the adequacy of the informational materials to communicate or provide pathways to adequately address issues including:
 - a. Accuracy of testing
 - b. Correct test interpretation
 - c. The importance of supplemental testing for confirmation of positive results
 - d. Management of psychological and social issues
 - e. Medical referral

References

1. Blood Products Advisory Committee Sixty-Sixth Meeting, session on Development of Rapid HIV tests, June 15, 2000.
<http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3620t1.pdf>
2. Federal Register, 2/17/89 (54 FR 7279), Blood Collection Kits Labeled for Human Immunodeficiency Virus Type 1 (HIV-1) Antibody Testing; Home Test Kits Designed to Detect HIV-1 Antibody; Open Meeting
3. Federal Register, 7/30/90 (55 FR 30982), Blood Collection Kits Labeled for Human Immunodeficiency Virus (HIV-1) Antibody Testing; Availability of a Letter for Interested Persons
4. Federal Register, 2/23/95 (60 FR 10087), Home Specimen Collection Kit Systems Intended for Human Immunodeficiency Virus (HIV-1 and/or HIV-2) Antibody Testing; Revisions to Previous Guidance