OTC HIV Rapid Tests: Issue Summary

Below is contextual information regarding the design of proposed studies to support marketing approval of Over-the-Counter (OTC) home-use HIV test kits which includes an historical overview of rapid HIV test kit approval in the United States, and key issues for consideration by the FDA Blood Products Advisory Committee. Once posted, transcripts of the March 10, 2006 advisory committee meeting will be available on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cber06.html#BloodProducts

Issue

FDA seeks the advice of the Committee on proposed studies that would be needed to validate a home-use HIV test kit with regard to 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 labeled 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. [Note that reports of reduced specificity of the test (to a level as low as 99.1%) in some locations are under investigation at this time.]

- 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. However, this requires an independent action that may not always occur. Those with confirmed positive test results should be counseled appropriately and be referred for medical follow-up.

- 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.

Key Issues:

- There are a number of potential benefits to home-use HIV test kits:
  - Of the approximately one million HIV-infected individuals in the US, approximately 25% are not aware of their HIV status. Anonymous testing could potentially lead to more of these people knowing their HIV status.
  - Home-use test kits empower consumers in their healthcare decisions.
  - Home-use HIV test kits may lead to earlier diagnosis of HIV infection and therefore earlier intervention, translating into better clinical outcomes with currently available therapies.

- There are a number of potential risks associated with home-use HIV test kits:
  - 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), may lead to a false sense of security. Continued high risk behavior may result in additional HIV infections.
  - Home-use tests kits rely on informational material for pre-test and post-test counseling. Without live counseling there is a potential for adverse outcomes following obtaining a positive test result.
  - Individuals may not be able to be reached for follow-up and for partner notification (though partners may be informed by the self-tested individual).

- Additional issues include:
  - Obtaining a test result without a supplemental test
  - The cost and availability of an home-use HIV test kit for those who need the test the most
  - Potential conflict with state and/or federal public health reporting requirements

Consideration of a home-use test kit by FDA will require the test kit manufacturer to demonstrate that the test is safe and effective.

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, 1995, and, most recently, in 2005 (Ref. 2-5).

  In the course of discussions held prior to 2005, 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.

- On November 3, 2005, FDA brought the issue of approaches to the validation of over-the-counter (OTC) home-use HIV test kits to BPAC for discussion in response to renewed interest in home-use HIV test kits.

At that meeting, the Committee heard presentations from OraSure Technologies for a home-use test kit based on its currently approved OraQuick ADVANCE Rapid HIV-1/2 Antibody Test when used with oral fluid specimens; from CDC on changes in HIV testing practices and counseling recommendations, including the role of rapid HIV tests in the HHS *Advancing HIV Prevention* initiative and the results of post-marketing surveillance for rapid HIV tests and home sample collection HIV tests; from CDC on quality system considerations for home-use HIV test kits; from an expert on psychological and social issues associated with HIV testing, including the finding that, although death from suicide is common among people with advanced HIV infection, notification of a positive HIV test does not appear to lead to a sudden and substantial rise in suicide death; and from CDRH on its review practice for OTC IVDs.

Eighteen individuals spoke at the Open Public Hearing, including those who spoke in favor of home-use HIV test kits, those against home-use HIV test kits, and those who recommended a cautious approach.

Committee discussions addressed acceptable levels of test performance, approaches to clinical trials to evaluate test performance in the hands of potential users, and the content of test kit informational materials that would be needed to allow the test to be performed in the absence of live counseling. By virtue of this discussion, the Committee acknowledged that criteria could be established to permit FDA approval of a home-use HIV test kit.

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. This would be supported by a demonstration of analytical and clinical sensitivity and specificity, as well as demonstration that the test is not affected by conditions of operational stress.
- 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).
- Informational materials supplied with the test are sufficient to provide adequate information to potential users on performing the test and to substitute for live counseling.

What information will be discussed at the BPAC meeting?

- After considering comments from the BPAC at the November 3, 2005 meeting, FDA has drafted a set of proposed studies to support the approval of home-use HIV test kits, addressing the following:
  - Identification of potential users of home-use HIV test kits through qualitative research
  - Acceptable minimal levels of test performance (analytical and clinical sensitivity and specificity)
  - Determination of analytical sensitivity and specificity
  - Validation of test performance under conditions of operational stress, including collection of an adequate specimen
  - Validation of test performance in the hands of potential users who are monitored and tested in parallel by a professional healthcare worker
  - Validation of test performance in the hands of potential users, unmonitored in sites of intended use
  - Validation of comprehensibility of informational materials in the hands of potential users
  - Validation of informational materials to provide adequate pre-test and post-test counseling, including:
    - ✓ Information on the accuracy of testing
    - ✓ Correct test interpretation
    - ✓ Limitations of the test kit
    - ✓ Prevention of adverse psychological effects
    - ✓ Medical referral for follow-up testing and treatment
- At this meeting, FDA will be presenting to the BPAC, for its comments and recommendations, details of the proposed studies needed to support approval of home-use HIV test kits.

Questions for the Committee

1. Does the Committee concur with FDA's proposed criteria for test performance (analytical and clinical sensitivity and specificity) for home-use HIV test kits?
2. Does the Committee concur with FDA's proposal for clinical studies that would be needed to validate the accuracy of a home-use HIV test kit?
3. Does the Committee concur with FDA's proposed content needed for informational materials provided with home-use HIV test kits and the steps that should be taken to validate the adequacy of those 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
4. If the Committee does not concur with any of the proposals in Questions 1-3, what additional information/modification would be needed to support approval of a home-use HIV test kit?

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.
5. Blood Products Advisory Committee Sixty-Sixth Meeting, session on Approach to Validation of Over-the-Counter (OTC) Home-Use HIV Tests, November 3, 2005. http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4190t1.htm

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