Orasure In-Home HIV Test Gets Unanimous Approval Recommendation

May 15, 2012 By Tim Horn

Orasure's oral swab-based rapid in-home HIV test has been recommended for approval by the U.S. Food and Drug Administration's Blood Products Advisory Committee. If the FDA follows its advisory committee's recommendation, the Oraquick In-Home HIV Test will be the first complete home-based screening assay for any infectious disease available for purchase over-the-counter (OTC) from pharmacies and internet retailers.

The advisory committee voted unanimously, 17-0, in favor of the test upon being asked two questions: Do the available clinical trial results provide reasonable assurance that the test is safe and effective? And, importantly, do the benefits of in-home HIV testing outweigh the potential risks, notably false negative and false positive results?

The particulars of the second question were hotly discussed throughout the May 15 meeting in Gaithersburg, Maryland. Of concern to the FDA presenters and advisory committee panelists is the test's reduced sensitivity—its effectiveness at screening for HIV antibodies in those infected with the virus—compared with the professional oral swab OraQuick assay.

However, even with reduced sensitivity, Elliott Cowan, PhD, of the FDA acknowledged, the in-home HIV test is anticipated to have a net public health benefit. "The OraQuick In-Home HIV Test is expected to be associated with a net increase in the number of HIV infections newly identified each year," he said, "with evidence of new infections averted with use of the test."

According to an FDA analysis of available data, nearly 3 million people are expected to use the OTC test if approved and that it may potentially identify 45,000 people living with HIV in the U.S.

Only one OTC HIV testing kit has been approved by the FDA. The Home Access HIV test, approved in 1996, requires blood samples to be collected at home, followed by shipment to a laboratory for analysis—results are provided by a Home Access telephone counselor. The retail price is between $30 and $40.

The OraQuick In-Home HIV Test allows users to collect samples, conduct the test and interpret the results on their own. The test result is read after 20 minutes, but not longer than 40 minutes, after inserting the oral swab device into the vial of developer solution provided with the OTC kit. The price of the test is not yet known, but the company expects it to retail for under $60.

Major talking points at the advisory committee hearing were the test's sensitivity and specificity. An assay's sensitivity reflects its ability to prevent false negatives—an HIV antibody-negative result for someone who is infected with the virus. An assay's specificity reflects its ability to prevent false positives—an HIV antibody-positive results for someone who is not infected with the virus.

The OraQuick In-Home HIV Test has strong specificity (99.98 percent). Whereas the OTC test will yield one false-positive result for every 3,750 true-negative results among people who aren't infected with HIV, the professional oral swab Oraquick test yields one false-positive for every 462 true-negative results.

The OTC's sensitivity, however, averaged only 92.98 percent, compared with the 99 percent sensitivity associated with the professional OraQuick oral swab-based assay. For every 13 "true-positive" results using the In-Home OraQuick test, there may be one false-negative test result—or approximately 3,800 false-negative test results per year—an analysis of the Phase III clinical trial data showed.

Of particular concern to the FDA presenters was the lower end of the estimated sensitivity range in the Phase III clinical trial—the "lower bound of the 95 percent confidence interval" in statistical parlance. Accordingly, the sensitivity may be as low as 86.64 percent, which is significantly lower than the 95 percent that has historically been required by the FDA's Blood Products Advisory Committee.

Looking solely at the "lower bound" analysis, there could be one false negative for every six true-positive results using the OraQuick In-Home HIV Test—approximately 7,000 false-negative test results per year. By comparison, the "lower bound" sensitivity using the professional OraQuick oral-based HIV test would be expected to yield one false-negative for every 62 true-positive results.

"Understanding the public health implications of approving an over-the-counter test that performs at this level of sensitivity and specificity in the hands of lay users is challenging," the FDA notes in their pre-advisory committee meeting briefing document. "There is considerable personal and public health value in informing infected, but otherwise untested, persons of their true positive HIV status. However, this benefit is offset in some measure by HIV-positive individuals who receive an incorrect message that they are not infected (false negatives)."

Public testimony at the hearing was overwhelmingly favorable. Roughly 20 agency representatives—including Phill Wilson of the Black AIDS Institute, Cornelius Baker of the Whitman-Walker Clinic in Washington, DC, Dawn Averitt-Bridge of The Well Project, Larry Bryant of Housing Works, C. Virginia Fields of the National Black Leadership Commission on AIDS and Ernest Hopkins of the San Francisco AIDS Foundation—testified that the Oraquick In-Home HIV Test would be a welcome addition to the HIV testing and awareness tool box, particularly for women and people of color living with, and at risk for, HIV who are not being effectively connected to existing testing programs.

“We are concerned by the data indicating that when administered by consumers the accuracy of the rapid HIV tests drops to 93 percent as compared to 99 percent when conducted by professionals,” testified Kimberly Crump, policy officer at the HIV Medicine Association. Yet, Crump noted, “we still believe the rapid test holds great promise as a self-directed tool for individuals to learn their HIV status. We also urge continued research and education in heavily impacted areas and with the low income and minority populations disproportionately affected by HIV infection to determine how the instructions and accompanying support materials can raise the assurance of the test results closer to the level obtained by professionals.”

A particularly crucial issue is the test’s “window period”—the time between possible exposure to HIV and the assay’s ability to detect antibodies to the virus. Study volunteers who used the OTC test during the test’s window period, coupled with human error, likely contributed to the assay’s reduced sensitivity results.

Orasure says it takes approximately two months post-exposure for the test to produce reliable results. In draft test instructions reviewed by the advisory committee, Orasure indicates users should perform the test at least three months, or 90 days, after engaging in behavior associated with HIV transmission.

Amy Lansky, MPH, PhD, of the U.S. Centers for Disease Control noted that professional fourth-generation tests, designed to look for both antibodies and HIV antigens in blood samples, are the most effective at detecting HIV infection in the first few weeks following potential exposure to the virus. These tests become sensitive and specific within 15 days following high-risk behavior.

The advisory committee panelists noted, on several occasions, the need for strong, clear and concise information in the educational materials that will accompany the test to minimize human error and testing during the window period, spell out the risks of false-negative test results and, importantly, to link those who do test positive to licensed health care providers for follow-up testing and care.

“There has been a lot of talk about the false-negative test results,” said Steven Pipe, MD, of the University of Michigan and a member of the panel. “But I still can’t get over the fact that a quarter of a million people living with HIV haven’t been tested. If the in-home test helps to reduce this number, its benefits ultimately outweigh its risks.”
