

Introduction

Rapid, point of care (POC) testing has been increasingly deployed as an aid in the diagnosis of human immunodeficiency virus (HIV) infection, due to its ability to deliver rapid, actionable results while the healthcare provider still has access to the patient being tested. Specifically, the OraQuick® ADVANCE™ HIV 1/2 Antibody Test has been widely used to identify HIV infection outside of traditional laboratory settings, due to its simplicity, ease of use and the ability to utilize oral fluid as an alternative specimen to blood. The OraQuick® ADVANCE™ HIV 1/2 Rapid Test has been widely used in STD clinics,¹ and community outreach centers;² hospital emergency departments;³ as well as to identifying HIV infection among pregnant women;^{4,5} and to manage occupational exposure to infection.⁶

The OraQuick® ADVANCE™ HIV 1/2 Antibody Test is FDA approved for HIV-1 and HIV-2 testing of whole blood either by venipuncture or fingerstick phlebotomy, plasma and oral fluid. The oral fluid application was approved and launched in 2004. In addition, the OraQuick® POC test is CLIA-waived for oral fluid and whole blood specimens and is thus widely used outside of traditional laboratory settings. We have studied the sensitivity of the POC test compared to 3rd generation HIV EIAs used in traditional laboratory settings. In addition, we analyzed the post-launch performance of the product using oral fluid, at 89 public-health testing centers in 2005 throughout the United States.

Methods

The OraQuick® HIV test is a visually read, qualitative, lateral flow immunoassay for the detection of antibodies to HIV-1 and HIV-2. HIV-1 and HIV-2 antigens are immobilized on a single test line on a nitrocellulose strip and antibodies reactive with these antigens are visualized by colloidal gold labeled with protein-A. Oral fluid samples are collected directly on a swab protruding from the device, or alternatively, whole blood (from fingerstick) or plasma is collected on a specimen loop and mixed in a vial of pre-measured developer solution before inserting the device in the vial. Reactive results generate a reddish-purple line at the test zone. A second control line which detects human IgG ensures that patient sample has been collected and has migrated beyond the test zone. Devices are interpreted after 20 minutes (Figure 1). Sensitivity for HIV antibodies was compared to a 3rd generation

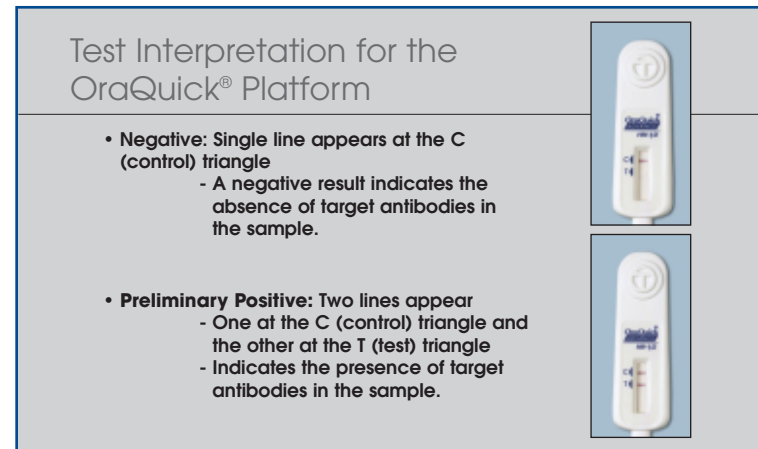


Figure 1

EIA (Ortho Clinical Diagnostics) by testing 401 HIV positive plasma specimens that were supplied by the vendor (BBI/SeraCare Diagnostics) as positive by western blot and viral load testing. In addition, serial specimens from 30 HIV seroconversion panels were tested by OraQuick® and 3rd gen HIV EIA (Ortho or Dade-Behring). The specificity of the OraQuick® test device in blood, was measured by testing 287 low risk individuals using finger-stick whole blood. In addition, field performance data was analyzed from 89 public health testing centers in the U.S., which screened at-risk individuals using oral fluid during 2005.

Results

All 401 HIV positive plasma specimens were detected by both EIA and the OraQuick® test, for a sensitivity of 100% (Figure 2). Among the 30 seroconversion panels tested (average time between bleeds = 5.5 days), 3rd generation EIA was slightly more sensitive than OraQuick® for the detection of HIV seroconversion, although the differential was small, with an average differential in time to detection of -2.5 days (95% CIs: -1.2 to -3.8 days) (Figures 3 and 4). All 287 low risk individuals tested with finger-stick whole blood were negative by OraQuick®, for a specificity of 100%. A total of 51,353 oral fluid screening results from 89 U.S. testing sites were analyzed (Figure 5). Calculated specificity after resolution by western blot was 99.86% (99.83-99.89%).

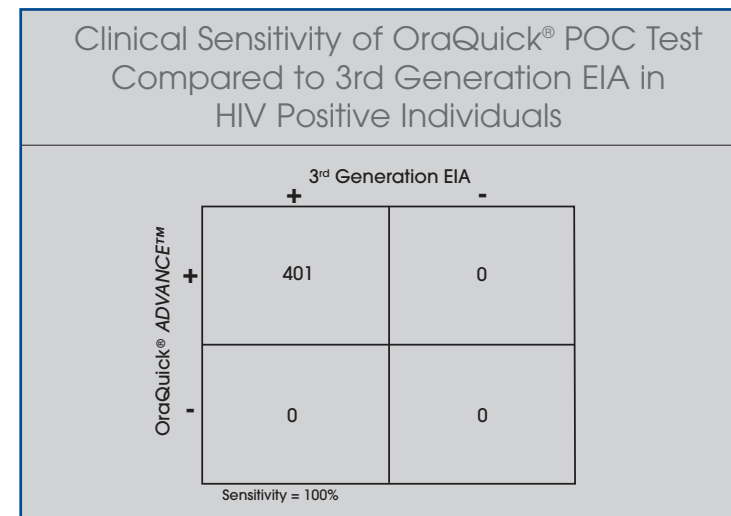
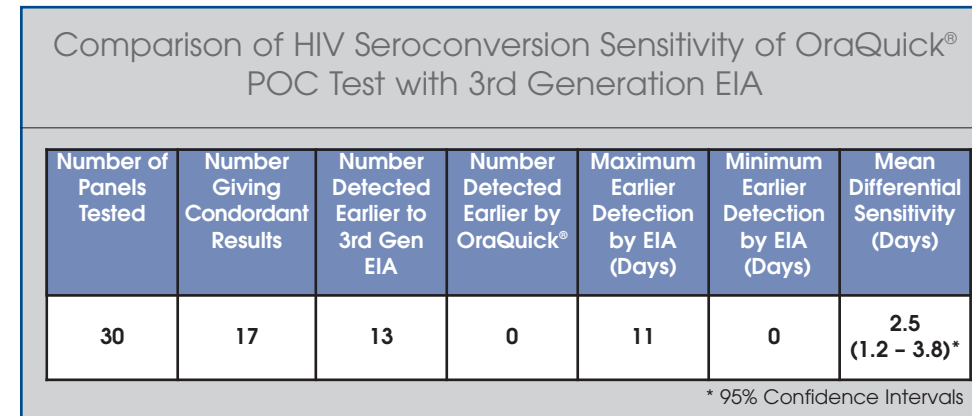


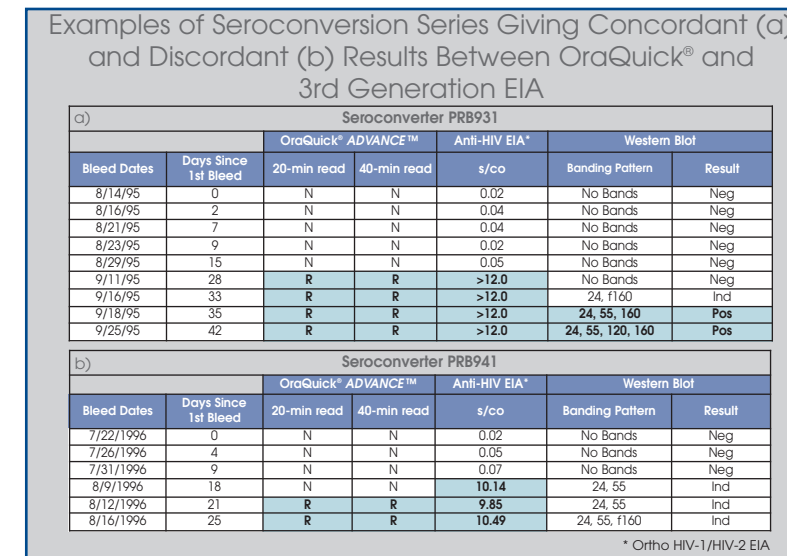
Figure 2



Number of Panels Tested	Number Giving Concordant Results	Number Detected Earlier to 3rd Gen EIA	Number Detected Earlier by OraQuick®	Maximum Earlier Detection by EIA (Days)	Minimum Earlier Detection by EIA (Days)	Mean Differential Sensitivity (Days)
30	17	13	0	11	0	2.5 (1.2 - 3.8)*

* 95% Confidence Intervals

Figure 3



a) Seroconverter PRB931

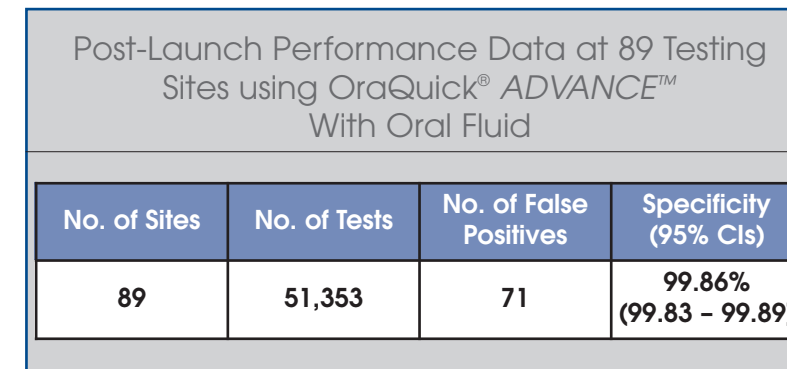
Bleed Dates	Days Since 1st Bleed	OraQuick® ADVANCE™		Anti-HIV EIA*	Western Blot	
		20-min read	40-min read	s/co	Banding Pattern	Result
8/14/95	0	N	N	0.02	No Bands	Neg
8/16/95	2	N	N	0.04	No Bands	Neg
8/21/95	7	N	N	0.04	No Bands	Neg
8/23/95	9	N	N	0.02	No Bands	Neg
8/29/95	15	N	N	0.05	No Bands	Neg
9/11/95	28	R	R	>12.0	No Bands	Neg
9/16/95	33	R	R	>12.0	24, 1160	Ind
9/18/95	35	R	R	>12.0	24, 55, 160	Pos
9/25/95	42	R	R	>12.0	24, 55, 120, 160	Pos

b) Seroconverter PRB941

Bleed Dates	Days Since 1st Bleed	OraQuick® ADVANCE™		Anti-HIV EIA*	Western Blot	
		20-min read	40-min read	s/co	Banding Pattern	Result
7/22/1996	0	N	N	0.02	No Bands	Neg
7/26/1996	4	N	N	0.05	No Bands	Neg
7/31/1996	9	N	N	0.07	No Bands	Neg
8/9/1996	18	N	N	10.14	24, 55	Ind
8/12/1996	21	R	R	9.85	24, 55	Ind
8/16/1996	25	R	R	10.49	24, 55, 1160	Ind

* Ortho HIV-1/HIV-2 EIA

Figure 4



No. of Sites	No. of Tests	No. of False Positives	Specificity (95% CIs)
89	51,353	71	99.86% (99.83 - 99.89)

Figure 5

Conclusions

1. Clinical performance of the OraQuick® ADVANCE™ HIV test for detection of HIV antibodies, was comparable to current, state of the art, laboratory-based tests.
2. Analysis of seroconversion sensitivity among series with closely spaced bleed intervals, indicated that the differential in seroconversion sensitivity between highly sensitive 3rd generation EIA and the OraQuick® POC test was very small (average of -2.5 days).
3. The specificity obtained in oral fluid testing of individuals by clinics in the U.S., subsequent to launch of the oral fluid application, was very high (99.8%) and consistent with the published performance claims of the product.
4. Performance in blood, plasma and oral fluid, support the use of rapid tests as a preferred alternative to conventional laboratory testing in many settings
5. The availability of highly sensitive and specific POC tests represent an important additional tool in interdiction in the HIV epidemic, through increased availability of testing in risk settings and consequent identification of HIV infected persons.

References

1. Rapid HIV Testing of Clients of a Mobile STD/HIV Clinic. Liang, TS et al. AIDS Patient Care and STDs 2005; 19: 253-257.
2. Choosing HIV Counseling and Testing Strategies for Outreach Settings- A Randomized Trial. Spielberg, F et al. J. Acquir. Immune Defic. Syndr. 2005; 38: 348-355.
3. The Role of Rapid vs Conventional Human Immunodeficiency Virus Testing for Inpatients. Lubelchek, R et al. Arch Intern Med. 2005; 165: 1956-1960.
4. Rapid Point-of-Care Testing for HIV-1 During Labor and Delivery-Chicago, Illinois, 2002. MMWR 2003; 52 (36):866-868.
5. Rapid HIV-1 testing During Labor- A Multi-Center Study. Bulterys M et. al. JAMA 2004; 292: 219-223.
6. Usefulness of a Rapid Human Immunodeficiency Virus-1 Antibody Test for the Management of Occupational Exposure to Blood and Body Fluid. Landrum, ML et al. Infect. Control. Hosp. Epidemiol. 2005; 26: 768-774.