US CLINICAL STUDY RESULTS

Results from a Multi-Centre US Clinical Study of the INSTI™ HIV-1 Antibody Test for Use in Point-of-Care, Clinical and Laboratory Settings

SENSITIVITY

A sensitivity study was performed in 14 clinical trial sites using freshly obtained matching fingerstick whole blood, EDTA whole blood, and EDTA plasma specimens collected from 1076 individuals known to be infected with HIV-1. Additionally, matching fingerstick whole blood, EDTA whole blood, and EDTA plasma specimens were collected from 782 previously unscreened individuals from populations at high risk for HIV-1 from which 22 were confirmed seropositive by an FDA approved test. For the 1098 total HIV-1 positives, results for fingerstick whole blood, venipuncture whole blood and plasma are shown in **Tables 1, 2 and 3.**

Table 1: Detection of Antibody to HIV-1 in Fingerstick Whole Blood Specimens from Seropositive Individuals and Individuals at High Risk of HIV Infection

Test Group	Total Specimens	INSTI™ Reactive	INSTI™ Non-Reactive	INSTI™ Invalid[1]	Approved Test Repeatedly Reactive	Approved Test Non-Reactive	True Positive[2]
Known HIV-1 Positive	1075	1074	1	0	1075	0	1075
High Risk	782	22[3]	756[4]	4	22	760	22
Total	1857	1096	757	4	1097	760	1097

1 Invalid results were not included in the calculations of sensitivity
2 Confirmed by approved HIV-1 Western Blot
3 Of the 22 INSTI™ Reactive specimens, one was Non-Reactive by the approved test
4 Of the 756 INSTI™ Non-Reactive specimens, one was repeatedly Reactive by the approved test

Of the 1076 known HIV-1 positive individuals, one did not provide a fingerstick specimen. Of the 1075 fingerstick specimens collected from the known HIV-1 positive patients that were repeatedly Reactive by an FDA approved test, 1074 gave a Reactive result with INSTI™. Within the high risk group, 22 specimens were confirmed seropositive by an FDA approved test and of those, 21 were Reactive with INSTI. One additional fingerstick specimen from the high risk population was INSTI falsely Reactive. The overall sensitivity of the INSTI™ HIV-1 Antibody Test in **fingerstick whole blood** specimens for the confirmed HIV-1 positives from the combined high risk and known HIV-1 positive populations was calculated to be 1095/1097=99.8% (95% CI=99.3%-99.9%)

Table 2: Detection of Antibody to HIV-1 in Venipuncture Whole Blood Specimens from Seropositive Individuals and Individuals at High Risk of HIV Infection

Test Group	Total Specimens	INSTI™ Reactive	INSTI™ Non-Reactive	INSTI™ Invalid	Approved Test Repeatedly Reactive	Approved Test Non-Reactive	True Positive[1]
Known HIV-1 Positive	1076	1075	1	0	1076	0	1076
High Risk	782	22	760	0	22	760	22
Total	1858	1097	761	0	1098	760	1098

1 Confirmed by approved HIV-1 Western Blot

Of the 1076 known HIV-1 positive EDTA whole blood specimens, 1075 gave Reactive results with INSTI™. Within the high risk group, 22 EDTA whole blood specimens were confirmed seropositive by an FDA approved test and these same 22 were Reactive with INSTI™. The overall sensitivity of the INSTI™ HIV-1 Antibody Test in **venipuncture whole blood** specimens for the confirmed HIV-1 positives from the combined high risk and known HIV-1 positive populations was calculated to be 1097/1098=99.9% (95% CI=99.5%-100%)

Table 3: Detection of Antibody to HIV-1 in Plasma Specimens from Seropositive Individuals and Individuals at High Risk of HIV Infection

Test Group	Total Specimens	INSTI Reactive	INSTI Non-Reactive	INSTI Invalid	Approved Test Repeatedly Reactive	Approved Test Non-Reactive	True Positive[1]
Known HIV-1 Positive	1076	1075	1	0	1076	0	1076
High Risk	782	22	760	0	22	760	22
Total	1858	1097	761	0	1098	760	1098

1 Confirmed by approved HIV-1 Western Blot

Of the 1076 known HIV-1 positive EDTA plasma specimens, 1075 gave Reactive results with INSTI™. Within the high risk group, 22 plasma specimens were confirmed seropositive by an FDA approved test and these same 22 were Reactive with INSTI™. The overall sensitivity of the INSTI™ HIV-1 Antibody Test in **plasma** specimens for the confirmed HIV-1 positives from the combined high risk and known HIV-1 positive populations was calculated to be 1097/1098=99.9% (95% CI=99.5%-100%).

SPECIFICITY

A specificity study was performed in the same 14 clinical trial sites using freshly obtained matching fingerstick whole blood, EDTA whole blood, and EDTA plasma specimens collected from 1410 low or unknown risk and high risk individuals. Of the 1388 individuals identified as HIV negative using an approved comparator assay, 2 did not provide a fingerstick specimen. Of the remaining 1386 fingerstick specimens, 1376 gave a Non-Reactive result with INSTI™, and 4 were invalid. Within the high risk group, 22 specimens were confirmed seropositive by Western Blot and of those, 21 were Reactive with INSTI™; an additional 1/782 high risk specimens was INSTI™ false Reactive. Of the 1388 matching EDTA whole blood and plasma specimens, 1388 gave Non-Reactive results with INSTI™. Results are shown in **Tables 4, 5, and 6.**

Table 4: Performance of the INSTI™ HIV-1 Antibody Test on Fingerstick Whole Blood Specimens from Individuals Presumed to be HIV Negative and Individuals at High Risk of HIV Infection

Test Group	Total Specimens	INSTI™ Non-Reactive	INSTI™ Reactive	INSTI™ Invalid[1]	Approved Test Non-Reactive	Approved Test Reactive	True Negative[2]
Low or Unknown Risk	626	620	6	0	626	0	626
High Risk	782	756	22[3]	4	760	22	760
Total	1408	1376	28	4	1386	22	1386

1 Invalid results were not included in the calculations of specificity
2 Reactives were confirmed by approved HIV-1 Western Blot and excluded from the calculation of specificity
3 Of the 22 INSTI™ Reactive specimens, one was Non-Reactive by the approved test, ie. INSTI™ falsely reactive

A total of 7 INSTI™ false Reactive results (1 from the high risk group, 6 from the low or unknown risk group) were obtained from the 1382 specimens from HIV-negative individuals that produced valid INSTI™ results. The overall specificity of the INSTI™ HIV-1 Antibody Test in **fingerstick whole blood** specimens from the combined HIV negative high risk and low or unknown risk populations, minus the invalid results, was calculated to be 1375/1382 = 99.5% (95% CI=99.0%-99.8%).

Table 5: Performance of the INSTI™ HIV-1 Antibody Test on Venipuncture Whole Blood Specimens from Individuals Presumed to be HIV negative and Individuals at High Risk of HIV Infection

Test Group	Total Specimens	INSTI™ Non-Reactive	INSTI™ Reactive	INSTI™ Invalid	Approved Test Non-Reactive	Approved Test Reactive	True Negative[1]
Low or Unknown Risk	628	628	0	0	628	0	628
High Risk	782	760	22	0	760	22	760

Total	1410	1388	22	0	1388	22	1388

1 Reactives were confirmed by approved HIV-1 Western Blot and excluded from the calculation of specificity

The overall specificity of the INSTI™ HIV-1 Antibody Test in **venipuncture whole blood** specimens from the combined HIV negative high risk and low or unknown risk populations, was calculated to be 1388/1388 = 100% (95% CI=99.7%-100%).

Table 6: Performance of the INSTI™ HIV-1 Antibody Test on Plasma Specimens from Individuals Presumed to be HIV Negative and Individuals at High Risk of HIV Infection

Test Group	Total Specimens	INSTI™ Non-Reactive	INSTI™ Reactive	INSTI™ Invalid	Approved Test Non-Reactive	Approved Test Reactive	True Negative[1]
Low or Unknown Risk	628	628	0	0	628	0	628
High Risk	782	760	22	0	760	22	760
Total	1410	1388	22	0	1388	22	1388

1 Reactives were confirmed by approved HIV-1 Western Blot and excluded from the calculation of specificity

The overall specificity of the INSTI™ HIV-1 Antibody Test in **plasma** specimens from the combined HIV negative high-risk and low or unknown risk populations, was calculated to be 1388/1388=100% (95% CI=99.7%-100%).

CONCLUSIONS DRAWN FROM STUDIES

Risk/Benefit Analysis

Rapid tests for identification of antibodies to HIV, particularly if conducted in point-of-care settings, provide significant advantages for the testing population. The risk of false Reactive or false Non-Reactive results with the INSTI test is small, as demonstrated by clinical studies. This very low risk of false results must be weighed against the benefits of being tested to the patient and to public health surveillance and prevention initiatives.

Safety

No significant adverse events were observed in any of the clinical studies conducted. All operators conducted testing in accordance with instructions for use of the INSTI™ device and training provided.

Effectiveness

The accuracy of the INSTI™ HIV-1 Antibody test for all specimen types studied (fingerstick whole blood, venipuncture whole blood, plasma) is greater than or equal to 99.5% with the lower boundary of the 95% confidence interval (CI) greater than or equal to 99.0% for all sample types. This meets the FDA established requirements for approval of a rapid HIV test device.