Evaluation of the Abbott PRISM HIV Ag/Ab Combo Assay

Introduction

The Abbott PRISM HIV Ag/Ab Combo assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the simultaneous qualitative detection of HIV p24 antigen and/or antibodies to HIV-1 and/or HIV-2 in human serum or plasma. The assay is intended to be used for screening donated blood and plasma and as an aid in the diagnosis of HIV-1/HIV-2 infection.

Methods

All testing for this evaluation was performed at the Australian Red Cross Blood Service, Adelaide, South Australia using panels provided by NRL.

Specificity

Specimens from a single blood donor population as well as a single diagnostic population were tested on the Abbott PRISM HIV Ag/Ab Combo assay. All samples initially reactive were retested in duplicate. Repeatedly reactive specimens were tested in the NRL HIV-1/2 confirmatory algorithm to determine their true status. Specimens that were confirmed as HIV-positive were excluded from calculation of specificity and negative delta value.

Sensitivity

A total of 427 confirmed anti-HIV positive specimens were tested on the Abbott PRISM HIV Ag/Ab Combo assay: 384 specimens were anti-HIV-1 positive and 43 specimens were anti-HIV-2 positive. Sensitivity and positive delta values were calculated for the overall results for the anti-HIV positive samples; positive delta values were also calculated separately for the anti-HIV-1 and anti-HIV-2 positive samples.

A total of 75 specimens, collected as series of sequential samples from seven individuals undergoing HIV seroconversion were also tested. The results of testing these seven seroconversion panels on the Abbott PRISM HIV Ag/Ab Combo assay were compared with the results of testing the same panels on the benchmark assay (BMA). The mean difference in detecting a reactive sample was determined.

False Reactivity

Sixty-two specimens that had given falsely reactive results on previously evaluated anti-HIV assays were tested on the Abbott PRISM HIV Ag/Ab Combo assay. Data from testing these samples were used to determine the

degree of common false reactivity between the Abbott PRISM HIV Ag/Ab Combo assay and other currently registered anti HIV assays.

Reproducibility

A QC sample of appropriate antibody reactivity and a QC sample of appropriate p24 antigen reactivity for the Abbott PRISM HIV Ag/Ab Combo assay were selected and tested at prescribed intervals. A total of 152 replicates of the antibody QC sample and 154 replicates of the p24 antigen QC sample were tested. Reproducibility was assessed for antibody and antigen detection by determining mean, standard deviation (SD) and coefficient of variation (CV). Outlying results were identified using Grubbs' test.

Results and Discussion

Specificity

Samples presumed HIV negative from a blood donor population

Table 1: Results of testing antibody negative blood donor samples on the Abbott PRISM HIV Ag/Ab Combo assay

Samples Tested	Initial Reactors	Repeat Reactors	
		True Positives	False Positives
5000	2	0	2

Two specimens from a single blood donor population repeatedly gave reactive results on the Abbott PRISM HIV Ag/Ab Combo assay. Neither of these specimens was confirmed positive in the NRL testing algorithm. This gave a specificity of 99.96% (95% CI: 99.84% - 99.99%) and a negative delta value of 4.38.

Samples presumed HIV antigen / antibody negative from a diagnostic population

Table 2: Results of testing presumed HIV antibody and antigen negative diagnostic samples on the Abbott PRISM HIV Ag/Ab Combo assay

Samples Tested	Valid Results	Initial Reactors	Repeat Reactors	
			True Positives	False Positives
445	431	0	0	0

A total of 14 specimens failed to yield valid results on the Abbott PRISM HIV Ag/Ab Combo assay. These samples 'voided', despite repeat testing, as a result of either poor sample quality or instrument malfunction. The remaining HIV negative diagnostic samples were all non-reactive on the Abbott PRISM

HIV Ag/Ab Combo assay, resulting in a specificity of 100% (95% CI: 98.9% - 100%) and a negative delta value of 4.9.

Sensitivity

Confirmed anti-HIV positive samples

Table 3: Results of testing anti HIV-1 and anti HIV-2 positive samples on the Abbott PRISM HIV Ag/Ab Combo assay

Type of Sample	Samples Tested	Valid Results	Reactive Samples	δ Value
HIV-1 Positive	384	320	320	7.63
HIV-2 Positive	43	26	26	3.46
TOTAL	**427**	**346**	**346**	**-**

A 'void' result was obtained for 64 HIV-1 positive specimens and 17 HIV-2 positive specimens despite repeat testing and failed to yield valid results. Of the 346 specimens for which valid results were obtained, all 320 confirmed anti HIV-1 positive and all 26 confirmed anti HIV-2 positive samples were reactive on the Abbott PRISM HIV Ag/Ab Combo assay. This gave an estimated sensitivity of 100% (95% CI: 98.6%-100%) and positive delta values of 7.6 for anti HIV-1, 3.5 for anti HIV-2 and an overall positive delta value of 5.35.

Seroconversion panels

Seroconversion sensitivity was determined by comparing the sequential sample number in a panel in which the BMA detected reactivity, with the sequential sample number in which the Abbott PRISM HIV Ag/Ab Combo assay detected reactivity in the same panel.

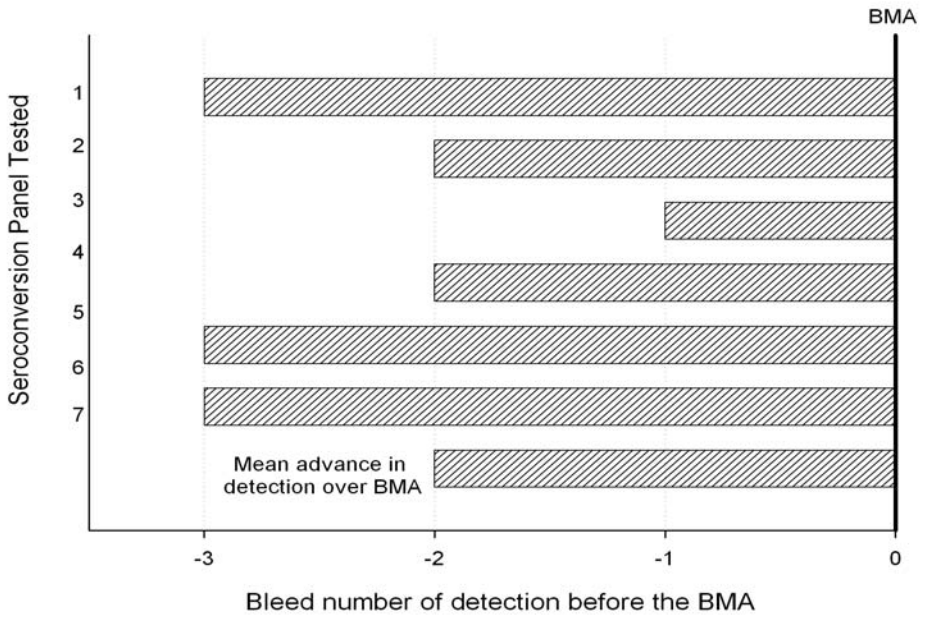

Figure 1: Performance of the Abbott PRISM HIV Ag/Ab Combo assay relative to the performance of the Serodia PA assay (BMA) in seven seroconversion panels.

In the seven seroconversion panels tested the Abbott PRISM HIV Ag/Ab Combo assay detected HIV earlier than the benchmark assay by between one and three bleeds (average sensitivity -2.29 bleeds).

False Reactivity

Table 4: Results of testing falsely reactive samples on the Abbott PRISM HIV Ag/Ab Combo assay

Assay Producing False Reactivity	Abbott PRISM HIV Ag/Ab Combo		Samples Showing Common False Reactivity
	Samples Tested	Samples Non-reactive	
Bio-Rad Genscreen HIV-1/2 EIA	3	3	0
Bio-Rad Genscreen Ultra Ag/Ab EIA	4	4	0
Abbott PRISM HIV-1/2 ChLIA	23	22	1
Abbott Murex HIV Ag/Ab Combination EIA	6	5	1
Abbott Murex HIV 1/2/O	2	2	0
Abbott ARCHITECT HIV Ag/Ab Combo Assay	3	3	0
ADVIA Centaur 1/O/2	5	4	1
Roche Elecsys HIV Combi	6	5	1
TOTAL	**52**	**48**	**4**

A panel of 62 specimens found to be falsely reactive in other assays was tested in the Abbott PRISM HIV Ag/Ab Combo assay. Results could not be obtained for a total of ten specimens in this panel because of sample 'voiding'. Of the remaining 52 specimens, 48 were found to be non-reactive in the Abbott PRISM HIV Ag/Ab Combo assay. Each of the four reactive specimens was also previously reactive in either the Abbott PRISM HIV-1/2 ChLIA, Abbott Murex HIV Ag/Ab Combination EIA, Siemens Advia Centaur 1/O/2 assay or the Roche Elecsys HIV Combi assay, respectively.

Reproducibility

Table 5: Results of testing replicate antigen QC samples

QC Sample	Test Runs	Observations	Mean (S/Co)	SD	% CV
Antigen	9	154	2.59	0.35	13.35*
Antibody	9	152	1.78	0.17	9.67

* A single value identified as an outlier using Grubbs' test was excluded from calculation.

Results for replicate QC samples demonstrated an acceptable reproducibility (CV < 20%). One antigen QC result, with a value of S/Co = 4.01 was identified as an outlier using Grubbs' test. This value was removed from the data for calculation of the CV.

The assay has since been included on the Australian Register of Therapeutic Goods.