Evaluation of the Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay

Introduction

The ADVIA Centaur HIV Ag/Ab Combo assay is an in vitro diagnostic immunoassay for the simultaneous qualitative detection of HIV p24 antigen and/or antibodies to HIV-1/2 in human serum and plasma (potassium EDTA). The assay is intended to be used to aid in the diagnosis of HIV infection, using the ADVIA Centaur and ADVIA Centaur XP systems.

Methods

All testing was performed by NRL staff using an ADVIA Centaur XP analyser in routine use at the Peter MacCallum Cancer Centre (PMCC), Melbourne, Victoria.

Specificity

Specimens from a single blood donor population as well as specimens from a diagnostic population were tested on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay. Any repeatedly reactive specimens were tested in the NRL HIV-1/2 confirmatory algorithm to determine their true status. Specimens that were confirmed as positive were excluded from the specificity and negative delta calculations.

Sensitivity

A total of 422 confirmed HIV antibody positive specimens were tested on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay: 381 specimens were anti-HIV-1 positive and 41 were anti-HIV-2 positive. Sensitivity and an overall positive delta value were calculated for the combined anti-HIV positive samples; positive delta values were also calculated separately for the HIV-1 and HIV-2 positive panels.

A total of 74 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 Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV) 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

Fifty-one specimens that had given falsely reactive results on previously evaluated HIV assays were tested on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) Assay. Data from testing these samples were used to determine the

degree of common false reactivity between the ADVIA Centaur HIV Ag/Ab Combo (CHIV) Assay and other currently registered HIV assays.

Reproducibility

A QC sample of appropriate antibody reactivity and a QC sample of appropriate antigen reactivity for the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay were tested at prescribed intervals. A total of 49 replicates of the antibody QC sample and 45 replicates of the 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 antigen / antibody negative from a blood donor population

Table 1: Results of testing antibody negative blood donor samples on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay

Initial Reactors	Repeat Reactors	
	True Positives	False Positives
2	0	1

Two samples from the panel of 2025 blood donor specimens initially produced a reactive result. Although subsequent testing on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay identified one of the specimens as repeatedly reactive it was not confirmed positive in the NRL testing algorithm. Hence the specificity of the assay in this blood donor population was determined to be 99.95% (95% CI: 99.68% - 100%) with a negative delta value of 7.01.

Samples presumed HIV antigen / antibody negative from a diagnostic population

Table 2: Results of testing presumed HIV negative diagnostic samples on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay

Initial Reactors	Repeat Reactors	
	True Positives	False Positives
3	0	3

Three samples from a panel of 785 low-risk diagnostic specimens were repeatedly reactive on ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay. These specimens were not confirmed positive, resulting in a specificity of 99.62% (95% CI: 98.79% - 99.90%) and a negative delta value of 6.93 in the diagnostic sample population tested.

Sensitivity

Confirmed anti-HIV positive samples

Table 3: Results of testing HIV-1 and HIV-2 antibody positive samples on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay

Type of Sample	Samples Tested	Samples with Valid Results	Reactive Samples	δ value
HIV-1 Positive	381	380*	380	17.74
HIV-2 Positive	41	41	41	2.83
TOTAL	**422**	**421**	**421**	**-**

*A single specimen failed to yield results, despite repeat testing, because of sample integrity errors.

The sensitivity of the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay was determined to be 100% (95% CI: 98.9% - 100%) in this population of HIV positive specimens with a combined delta value of 7.81.

Seroconversion samples

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 ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay detected reactivity, in the same panel.

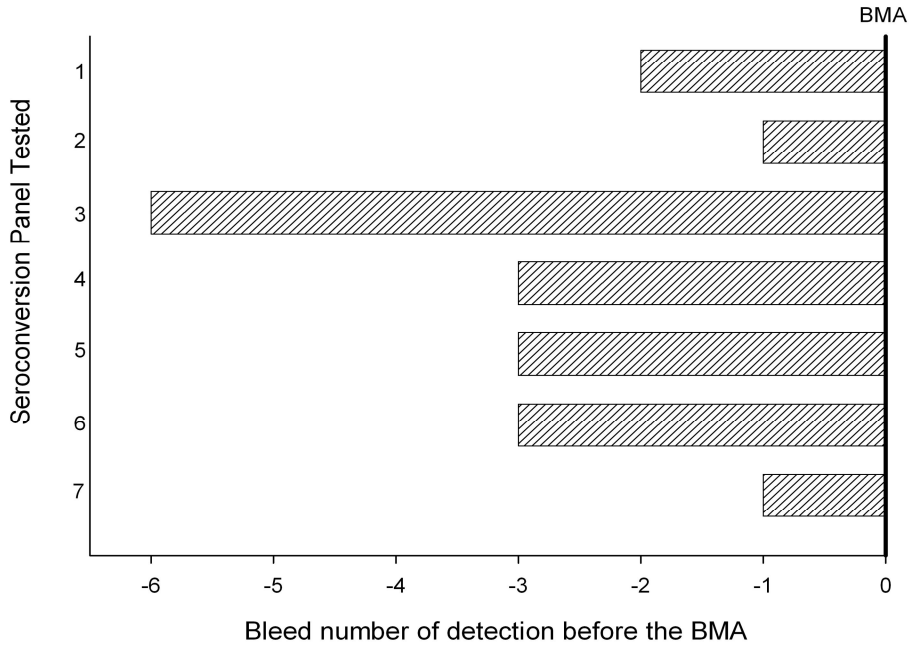

Figure 1: Performance of the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay relative to the performance of the Serodia PA assay (BMA) in seven seroconversion panels.

In the seven seroconversion panels tested the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay detected HIV earlier than the benchmark assay by between one and six bleeds (average advance in detection 2.7 bleeds).

False Reactivity

Table 4: Results of testing falsely reactive samples on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay

Assay Producing False Reactivity	Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV)		Samples Showing Common False Reactivity
	Samples Tested	Samples Non-reactive	
Bio-Rad Genscreen HIV-1/2 EIA	5	5	0
Bio-Rad Genscreen Ultra Ag/Ab EIA	1	1	0
Abbott PRISM HIV-1/2 ChLIA	26	25	1
Abbott Murex HIV Ag/Ab Combination EIA	7	7	0
Abbott Murex HIV 1/O/2	4	4	0
ADVIA Centaur 1/O/2	2	0	2
Roche Elecsys HIV Combi	6	6	0
TOTAL	**51**	**48**	**3**

A total of 51 samples found to be falsely reactive in other HIV Assays were tested with the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay. All samples tested produced a valid result. Forty-eight of the samples in this panel tested non-reactive in the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay. Two specimens that had previously been observed to be reactive on the ADVIA Centaur 1/O/2 assay were both also reactive on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay. The other sample that produced a reactive result was previously found to be reactive on the Abbott PRISM HIV-1/2 ChLIA assay.

Reproducibility

Table 5: Results of testing an antibody QC sample and an antigen QC sample on the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay

QC Sample	Test Runs	Observations	Mean (S/Co)	SD	% CV
Antibody	7	48*	3.97	0.21	5.30
Antigen	7	45	2.37	0.37	15.67

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

Results for replicate QC samples were generated across seven separate assay runs using a total of 45 replicates of the p24 antigen QC sample and 48 replicates of the antibody QC sample. One antibody QC result was identified as an outlier using Grubbs' test (S/Co = 3.13), this value was excluded from the data set prior to calculation of mean, SD and CV. Both QC samples demonstrated an acceptable level of variation (CV < 20%) in the ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay.

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