Evaluation of the Roche Elecsys HIV Combi

Introduction

The Roche Elecsys HIV combi is an electrochemiluminesce immunoassay for the qualitative determination of HIV-1 p24 antigen and antibodies to HIV-1, (including group O), and HIV-2 in human serum and plasma. It is intended for use on the Elecsys 2010, Modular Analytics E170, cobas e 411 and cobas e 601 analysers.

Methods

Specificity

5011 samples from a single blood donor population and 556 samples from a single diagnostic population were tested on the Elecsys HIV combi assay. All samples initially reactive were retested in duplicate. Samples repeatedly reactive were tested in the NRL HIV confirmatory algorithm to determine the true status. Samples that were confirmed as positive were excluded from the specificity and negative delta calculations.

A total of 1000 donor samples and all 556 diagnostic negative samples were tested on the cobas e 411 analyser; the remaining 4011 donor samples were tested on the Modular Analytics E170 analyser.

Sensitivity

A total of 327 confirmed anti-HIV positive samples were tested on the Elecsys HIV combi assay: 272 samples were anti HIV-1 positive, and 55 samples were anti-HIV-2 positive. Sensitivity was calculated for the overall results for the anti-HIV positive samples; positive delta values were calculated separately for the anti-HIV-1 and anti-HIV-2 positive samples.

A total of 74 specimens, collected as a series of sequential samples from seven individuals undergoing HIV seroconversion were also tested. The results of testing these seven seroconversion panels on the Elecsys HIV combi 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.

All sensitivity tests were performed on the cobas e 411 analyser.

False Reactivity

Fifty-four samples that had given falsely reactive results on previously evaluated and registered anti-HIV or HIV Ag/Ab assays were tested on the Elecsys HIV combi assay. Data from testing these “problem” samples were used to determine the degree of common false reactivity between the Elecsys HIV combi assay and these other currently registered anti HIV or HIV Ag/Ab assays.

All 55 problem samples were tested on the cobas e 411 analyser.

Reproducibility

A QC sample of appropriate antibody reactivity and a QC sample of appropriate p24 antigen reactivity for the Elecsys HIV combi assay were selected and tested at prescribed intervals on the cobas e 411 and Modular Analytics E170 analysers. A total of 80 replicates of the antibody QC sample and a total of 81 replicates of the p24 antigen QC sample were tested. Reproducibility was separately assessed for antigen and antibody by analyser, by determining mean, standard deviation (SD) and coefficient of variation (CV). Outlying results were identified using Grubbs’ test.

Results

Specificity

Blood Donor Samples

Nine of 5011 samples from a single blood donor population were repeatedly reactive on the Elecsys HIV combi assay. This gave a specificity of 99.82% and negative delta values of 10 for samples tested on the cobas e 411 analyser and 7.6 for samples tested on the Modular.Analytics E170 analyser.

Table 1: Results of testing antibody negative blood donor samples on the Elecsys HIV combi assay (with corresponding specificity and delta values).

Analyser	Samples Tested (n)	Initial Reactors (n)	Repeat Reactors (n)	
			True Positives	False Positives
Cobas e 411	1000	0	0	0
Modular Analytics E170	4011	9	0	9
Total	**5011**	**9**	**0**	**9**

Specificity	**99.82% (95%CI 99.65% – 99.91%)**
δ value (cobas e 411)	**- 9.99**
δ value (E170)	**- 7.55**

Anti-HIV Negative Diagnostic Samples

One of 556 samples from a single low risk diagnostic population was repeatedly reactive on the Elecsys HIV combi assay. The single repeat reactor was not confirmed positive. This gave a specificity of 99.8% and a negative delta value of 6.

Table 2: Results of testing presumed anti-HIV negative diagnostic samples on the Elecsys HIV combi assay (with corresponding specificity and delta values).

Samples Tested (n)	Initial Reactors (n)	Repeat Reactors (n)	
		True Positives	False Positives
556	1	0	1

Specificity	**99.8% (95%CI 98.8% - 100%)**
δ value	**- 5.97**

Sensitivity

Confirmed anti HIV Positive Samples

All 272 confirmed anti HIV-1 positive and all 55 confirmed anti HIV-2 positive samples were reactive on the Elecsys HIV combi assay. This gave an estimated sensitivity of 100% and positive delta values of 10.4 for anti-HIV-1, and 5.9 for anti-HIV-2.

Table 3: Results of testing anti-HIV-1 and anti-HIV-2 positive samples on the Elecsys HIV combi assay (with corresponding sensitivity and delta values).

Type of sample	Number of Positive Samples Tested	Number Correct	δ Value
Anti HIV-1 Positive	272	272	10.35
Anti HIV-2 Positive	55	55	5.85
Total	**327**	**327**	

Sensitivity	**100% (95%CI 98.55% - 100%)**

Seroconversion Samples

In five of the seven seroconversion panels the Elecsys HIV combi assay detected reactivity before the BMA; in one panel the Elecsys HIV combi assay detected seroconversion in the same sample as the BMA. The mean difference in seroconversion sensitivity for these six panels was -2 samples (range 0 to -3 samples).

In one panel weak reactivity was detected in sample 9 and strong reactivity in sample 11; but no reactivity in samples 1 – 8 or sample 10 on the Elecsys HIV combi assay, compared with no reactivity in any sample on the BMA, i.e. there was a net increase of two samples where reactivity was detected on the Elecsys HIV combi assay compared to the BMA. The weak reactivity shown in sample 9 is probably due to the presence of low levels of HIV antigen. However it is very important to note that the index value dropped below the cut-off value in sample 10 before becoming strongly positive in sample 11 presumably this time due to the presence of HIV antibody. The transitory peak in reactivity seen in sample 9 is mirrored by the HIV-1 RNA levels for this seroconversion panel.

False Reactivity

Fifty of 55 samples falsely reactive on other assays were non-reactive on the Elecsys HIV combi assay. Four of 26 samples falsely reactive on the Abbott PRISM HIV-1/2 ChLIA and one of seven samples falsely reactive on the Abbott Murex HIV Ag/Ab Combination EIA were also falsely reactive on the Elecsys HIV combi assay.

Table 4: Results of testing falsely reactive samples on the Elecsys HIV combi assay.

Assay Producing False Reactivity	Roche Elecsys HIV combo		Samples Showing Common False Reactivity (n)
	Samples Tested (n)	Samples Non-reactive (n)	
Bio-Rad Genscreen HIV-1/2 EIA	5	5	0
Bio-Rad Genscreen Plus Ag/Ab EIA	1	1	0
Abbott PRISM HIV-1/2 ChLIA	26	22	4
Abbott Murex HIV Ag/Ab Combination EIA	7	6	1
Abbott ARCHITECT HIV Ag/Ab Combo	4	4	0
Abbott Murex HIV 1/2/O EIA	1	1	0
Siemens ADVIA Centaur HIV 1/O/2 Enhanced (HIV)	5	5	0
Bio-Rad Genscreen HIV Ag-Ab ULTRA	6	6	0
TOTAL	**55**	**50**	**5**

Reproducibility (1)

Although some variation between the two analysers was noted, the CV of replicate results obtained from testing the QC sample Pelispy Type 38 on the cobas e 411 and Modular Analytics E170 analysers demonstrated acceptability reproducibility (CV < 20%). Grubbs' test did not detect any outliers.

Table 5: Results of testing the QC sample Pelispy Type 38 on the Elecsys HIV combi assay.

Analyser	Test Runs (n)	Observations (n)	Mean (S/Co)	S.D.	C.V. (%)
cobas e 411	19	29	2.71	0.11	3.92
Modular Analytics E170	12	51	3.10	0.21	6.72

Reproducibility (2)

The CV of replicate results obtained from testing the QC sample p24:AA:03 on the cobas e 411 and Modular Analytics E170 analysers demonstrated acceptable inter and intra analyser reproducibility (CV < 20%). Grubbs' test did not detect any outliers.

Table 8: Results of testing the QC sample p24:AA:03 on the Roche Elecsys HIV combi assay.

Analyser	Test Runs (n)	Observations (n)	Mean (S/Co)	S.D.	C.V. (%)
cobas e 411	20	30	2.268	0.096	4.21
Modular Analytics E170	12	51	2.269	0.100	4.42

This assay has since been registered on the Australian Register of Therapeutic Goods.

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