

Evaluation of the ADVIA Centaur HCV Assay

Introduction

The Bayer ADVIA Centaur HCV assay (Centaur HCV) is an *in vitro* diagnostic immunoassay for the qualitative determination of immunoglobulin G (IgG) antibodies to hepatitis C virus (HCV) in human serum and plasma (EDTA or heparinized) using the ADVIA Centaur System. The Centaur HCV assay was evaluated by the NRL in collaboration with Gribbles Pathology (Vic) Pty Ltd and Mayne Health-Dorevitch Pathology.

Methods

Specificity

5029 specimens from a single blood donor population and 2008 specimens from two presumed antibody status HCV negative populations presenting at separate diagnostic laboratories, were tested on the ADVIA Centaur HCV assay. All samples initially reactive were retested in duplicate. Samples repeatedly reactive were tested in the NRL HCV confirmatory algorithm to determine their true status. Results of specimens that were indeterminate or confirmed as positive were excluded from the specificity and negative delta calculations.

Sensitivity

A total of 188 confirmed anti-HCV positive specimens were tested on the ADVIA Centaur HCV assay. Sensitivity and positive delta values were calculated.

A total of 91 specimens, collected as series of bleeds from nine individuals undergoing HCV seroconversion were also tested. The results of testing these nine seroconversion panels on the ADVIA Centaur HCV assay were compared with the results of testing the same panels on the benchmark assay (BMA) the assay that detected reactivity in the earliest sample in each panel. The mean difference in detecting reactivity was determined.

False Reactivity

Forty-two specimens that had given falsely reactive results on previously evaluated anti-HCV assays were tested on the ADVIA Centaur HCV assay. Data from testing these samples were used to determine the degree of common false reactivity between the ADVIA Centaur HCV assay and other currently registered anti-HCV assays.

Reproducibility

A quality control (QC) sample of appropriate reactivity for the ADVIA Centaur HCV assay was selected and tested at prescribed intervals, at two collaborating laboratories. Inter and intra laboratory reproducibility was assessed by determining mean, standard deviation (S.D.) and coefficient of variation (C.V.) for each laboratory's results and for the overall results. Outlying results were identified using Grubbs' test and removed prior to analysis.

Results

Specificity

Blood Donor Samples

Ten specimens of 5029 from a single blood donor population were repeatedly reactive on the ADVIA Centaur HCV assay. This gave a specificity of 99.8% and a negative delta value of -8.6.

Table 1: Results of testing antibody negative blood donor samples on the ADVIA Centaur HCV assay (with corresponding estimated specificity and delta values).

Laboratory ID	Samples Tested (n)	Initial Reactors (n)	Repeat Reactors (n)
A	5029	10	10
Estimated Specificity	99.8% (95% CI 99.6% - 99.9%)		
δ value	- 8.6		

Anti-HCV Negative Diagnostic Samples

Of the total of 2008 negative diagnostic samples tested on the ADVIA Centaur HCV assay 16 were initially reactive; 12 of the 16 samples were confirmed as truly positive and excluded from the calculations. Of the 1996 negative diagnostic samples two were repeatedly reactive. This gave an estimated specificity of 99.9% and a negative delta value of -3.1.

Table 2: Results of testing antibody negative diagnostic samples on the ADVIA Centaur HCV assay (with corresponding estimated specificity and delta values).

Laboratory ID	Samples Tested (n)	Initial Reactors (n)	Repeat Reactors (n)	
			True Positive	False Positive
B	1021	6	4	2
C	987	10	8	0
TOTAL	2008	16	12	2
Estimated Specificity	99.9% (95%CI 99.6 – 100.0)			
δ value	- 3.1			

Sensitivity

Confirmed Anti-HCV Positive Samples

All 188 known anti-HCV positive samples were reactive on the ADVIA Centaur HCV assay. This gave an estimated sensitivity of 100% (CI 97.5-100%) and a positive delta value of +5.8.

Table 3: Results of testing anti-HCV positive samples on the ADVIA Centaur HCV assay (with corresponding estimated sensitivity and delta values).

Laboratory ID	Number of anti-HCV Positive Samples Tested	Number Correct
A	188	188
Estimated Specificity	100% (95% CI 97.5 – 100.0%)	
δ value	+ 5.8	

Seroconversion Samples

In one of the nine seroconversion panels (panel 5) the ADVIA Centaur HCV assay detected reactivity one sample before the BMA; in one panel (panel 6) the ADVIA Centaur HCV assay detected reactivity one after the BMA. For the other seven seroconversion panels the ADVIA Centaur HCV assay detected reactivity in the same sample as the BMA. The mean difference in detection between the ADVIA Centaur HCV assay and the BMA was zero.

False Reactivity

Forty-two falsely reactive samples were tested on the ADVIA Centaur HCV assay. Thirty-seven samples were non-reactive. Three of the five reactive samples were also falsely reactive in the Abbott PRISM HCV ChLIA; one was falsely reactive in the Roche Cobas Core Anti-HCV EIA II; and one was falsely reactive in the Innogenetics Innostest HCV Ab IV.

Table 4: Results of testing falsely reactive samples on the ADVIA Centaur HCV assay.

Assay Producing False Reactivity	ADVIA Centaur HCV		Samples Showing Common False Reactivity (n)
	Samples Tested (n)	Samples Non-reactive (n)	
Roche Cobas Core Anti-HCV EIA II	3	2	1
Innogenetics Innotest HCV Ab IV	5	4	1
BioRad Monolisa Anti-HCV Plus	8	8	0
Murex Anti-HCV Version 4.0	1	1	0
Abbott PRISM HCV ChLIA	25	22	3
TOTAL	42	37	5

Reproducibility

A total of 165 observations from 31 test runs were obtained for QC sample MULTI:SER:09. Grubbs' test identified two outlying results (one from each laboratory). The CV of the results was <20% in each laboratory.

Table 5: Results of testing the QC sample MULTI:SER:09 on the ADVIA Centaur HCV assay.

Laboratory ID	Test Runs (n)	Observations (n)	Mean (Index)	S.D.	C.V. (%)
A	20	142	6.13	0.30	4.85
C	11	23	6.22	0.69	11.08
Total	31	165	6.14	0.37	6.11

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

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