

White Paper

# Siemens ADVIA Centaur XP CHIV, HBsAgII, and HCV assays are highly specific in a Norwegian blood-donor population.

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# Siemens ADVIA Centaur XP CHIV, HBsAgII, and HCV assays are highly specific in a Norwegian blood-donor population.

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## Background

In vitro diagnostic tests that are CE marked and can be used for screening of blood donations are becoming increasingly available. The CHIV,<sup>2</sup> HBsAgII,<sup>2</sup> and HCV<sup>2</sup> immunoassays offered by Siemens Healthcare Diagnostics on its ADVIA Centaur<sup>®</sup> Immunoassay Systems can be used for this purpose. The ADVIA Centaur XP Immunoassay System was used in this study.

To verify assay performance in a study population of Norwegian blood donors, testing was performed to determine the serological profile that could be expected in such a population. It was also desirable to document the separation between the cutoff/gray zone and the values that can be obtained in a population that displays seronegativity for these parameters.

This paper describes results from testing nearly 1,000 blood donors who gave blood in the period from September to October 2012 at Bærum Hospital and Drammen Hospital, both of Vestre Viken Health Trust in Norway.

## Materials and Methods

In this study, 961 CHIV,<sup>3</sup> 962 HBsAgII,<sup>4</sup> and 948 HCV<sup>5</sup> assays were performed. The Siemens HBsAgII assay is a single-pass magnetic particle chemiluminometric immunoassay, and the Siemens HCV and CHIV assays are two-wash antigen/antibody sandwich immunoassays. Analytical times for the single- and two-wash assays are 29 and 58 minutes, respectively.

The study was conducted on established blood donors and thus was focused on verifying assay specificities relative to the predicate system (Abbott ARCHITECT). Donors had previously been screened with an Abbott ARCHITECT i2000SR system and corresponding assays.

The study was not designed to assess method sensitivity but rather to correlate ADVIA Centaur assay results with samples preselected by the Abbott ARCHITECT assays. Sensitivity is documented in the respective Siemens instructions for use, which report assay performance using seroconversion panels in which a variety of subtypes/mutants are represented.

An assay's degree of separation between true negative and gray zone/positive samples is an important consideration in a laboratory's daily routine. In this study, we plotted for each method the distribution of index values in this seronegative population. The gray zone used for the ADVIA Centaur XP system was 0.8–1.0 index value. Note that the instructions for use do not have a gray zone for the ADVIA Centaur HBsAgII or CHIV assays; however, for the purposes of this study, the investigators incorporated a gray zone across all the assays tested. The gray zones used for the ARCHITECT system appear in Table 1.

**Table 1.** Ranges of index values constituting the gray zones used for this study at Drammen Hospital and Bærum Hospital for the ARCHITECT HIV, HBV, and HCV assays.

	Drammen	Bærum
HIV	0.85–1.15	0.80–1.20
HBV	0.90–1.10	0.90–1.10
HCV	0.85–1.15	0.90–1.10

The nominal cutoff for both systems was 1.0. Vestre Viken performs semiannual revision of gray zones on the basis of observed precision for an independent kit control.

## Siemens HIV testing

Specimens with an index value greater than the gray zone's upper limit were considered positive for HIV-1 and/or HIV-2 and/or p24 antigen. Specimens with an index value less than the gray zone's lower limit<sup>6</sup> were considered nonreactive for antibodies to HIV-1 and HIV-2 and p24 antigen. Specimens with an index value within the gray zone were considered initially reactive and were retested in duplicate. If both of the duplicates retested with an index value less than the gray zone's lower limit, the specimen was considered negative for HIV-1/HIV-2 antibodies and/or p24 antigen. If one or both of the duplicates were reactive, the specimen was repeatedly reactive. Repeatedly reactive specimens were investigated using supplemental tests for HIV-1 and/or HIV-2 and/or p24 antigen. In specimens giving indeterminate supplemental test results, testing of a subsequent sample drawn at a later date (such as 1–6 months) was recommended.

## Siemens HBV testing

Samples with a calculated index value less than the gray zone's lower limit<sup>7</sup> were considered nonreactive (negative) for HBsAg. Those with an index value greater than or equal to the gray zone's lower limit but less than or equal to 50 were considered reactive (positive) for HBsAg, and the test was repeated in duplicate. If two of the three results were nonreactive (negative), the sample was considered negative for HBsAg. If at least two of the three results were reactive (positive), the sample was repeatedly reactive (positive) and the presence of HBsAg was confirmed with the ADVIA Centaur HBsAg Confirmatory assay, additional HBV marker assays, or another approved confirmatory method. If the sample was greater than 50 or flagged as "> Index Range," the specimen was reactive (positive) for HBsAg, and no further testing was required.

### Siemens HCV testing

Samples with a calculated value of less than 0.80 index value were considered nonreactive (negative) for IgG antibodies to HCV; those with a value greater than or equal to 0.80 index value and less than 1.00 index value were considered equivocal; and those with a value greater than or equal to 1.00 index value were considered reactive.<sup>8</sup> Equivocal samples were repeated in duplicate. If two of the three sample results were less than 0.80 index value, the sample was considered nonreactive. If two of the three sample results were greater than or equal to 1.00 index value, the sample was considered reactive, and supplemental testing of the sample was performed. If two of the three sample results were greater than or equal to 0.80 index value and less than 1.00 index value, supplemental testing of the sample was recommended. Supplemental testing was also performed in the case of an initially reactive sample.

Sample collection and analysis were performed in parallel in routine runs at the two hospital sites from September to October 2012. Siemens Healthcare Diagnostics employees performed the analyses using the ADVIA Centaur XP system. Informed consent was obtained from all blood donors in the study. Samples reactive by any assay were confirmed by a reference laboratory, and blood donations were quarantined until final results were available. Findings from this study protocol were not surprising.

### Results

Specificities observed in this study were as follows:

aHCV (n = 948): 99.79%

HBsAgII (n = 962): 99.90%

CHIV (n = 961): 99.79%

Six samples were repeatedly reactive upon reanalysis: one for ARCHITECT (HBsAg) and five for ADVIA Centaur (HCV, 2; HIV, 2; and HBsAg, 1). The HBsAg sample that was repeatedly reactive by the ARCHITECT system was not the same sample as either of those that were repeatedly reactive by the ADVIA Centaur system. All of the results repeatedly reactive by both systems were determined to be false positive according to the negative results obtained by confirmatory testing at the National Public Health Institute and Drammen Hospital.

Figures 1, 2, and 3 show the distribution of index values for the three Siemens assays.

### Conclusion and Discussion

All three analyses showed good specificity, indicating the Siemens assays' suitability for use in routine screening of blood donors. This conclusion is underscored by the fact that the population had already been prescreened with the Abbott assay: donors who incorrectly appeared to be seropositive (that is, any false positives) by the Abbott assay would be screened out, since these individuals would be excluded as donors. While this prohibits an accurate assessment relative to false-positive results between the two assays, it does support the excellent correlation between the reactives previously identified by the ARCHITECT assay.

The three ADVIA Centaur XP assays demonstrated very good separation between seronegative samples and the cutoff/gray zone, with over 80 percent of the results with an index value less than 0.2 for each assay. This is an important consideration in the daily operation of the laboratory, where one can expect a few samples to fall within the gray zone, and consequently contributes to minimizing the need for reanalysis. We conclude that the ADVIA Centaur XP assays are suitable for blood-screening applications and allow confident interpretation, given the robust separation demonstrated between seronegative and seropositive samples.

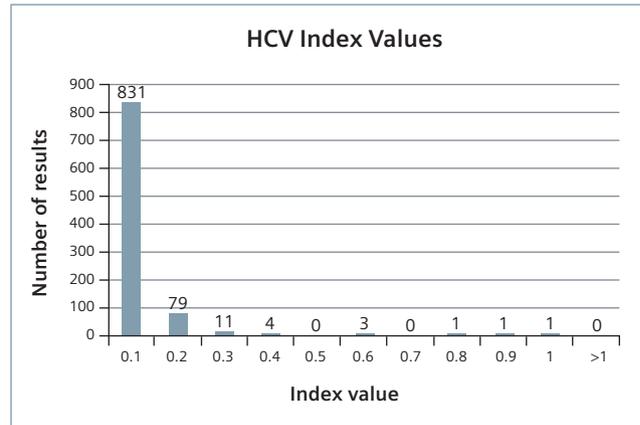


Figure 1. Distribution of index values for HCV.

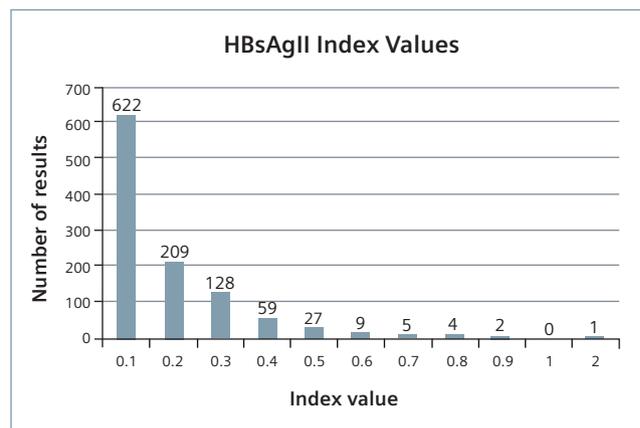


Figure 2. Distribution of index values for HBsAgII.

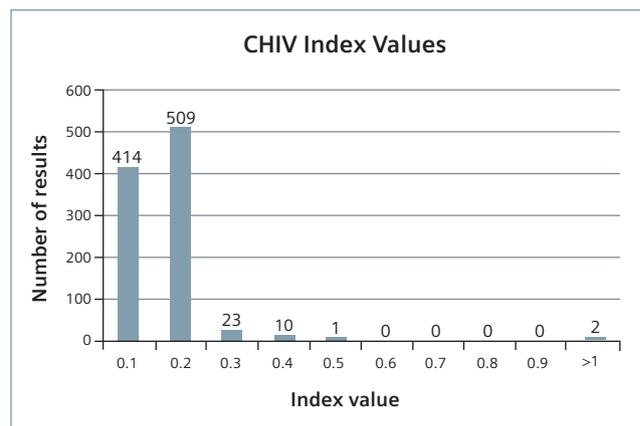


Figure 3. Distribution of index values for CHIV.

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The ADVIA Centaur HCV and HIV assays are developed, manufactured, and sold by Siemens Healthcare Diagnostics for Ortho-Clinical Diagnostics, Inc. and Novartis Vaccines and Diagnostics, Inc.

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#### Notes

1. Product availability may vary from country to country and is subject to varying regulatory requirements.
2. This assay has not been FDA approved for the screening of blood or plasma donors.
3. The ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay is an in vitro diagnostic immunoassay for the simultaneous qualitative detection of human immunodeficiency virus p24 antigen and antibodies to human immunodeficiency viruses type 1 (including group O) and type 2 in serum and plasma (potassium-EDTA) using the ADVIA Centaur and ADVIA Centaur XP systems to aid in the diagnosis of HIV infection.
4. The ADVIA Centaur HBsAgII (HBsII) assay is an in vitro immunoassay for the qualitative detection of hepatitis B surface antigen (HBsAg) in human serum and plasma (EDTA, lithium-heparin, sodium-heparin, or sodium-citrate) using the ADVIA Centaur and ADVIA Centaur XP systems. The assay may be used in conjunction with other serological and clinical information to diagnose individuals with acute or chronic hepatitis B infection. The assay may also be used to screen for hepatitis B infection in pregnant women to identify neonates who are at risk of acquiring hepatitis B during the perinatal period.
5. The ADVIA Centaur HCV (aHCV) assay is an in vitro diagnostic immunoassay for the qualitative determination of immunoglobulin G (IgG) antibodies to hepatitis C virus (HCV) in human serum or plasma (EDTA, lithium, or sodium heparinized) using the ADVIA Centaur and ADVIA Centaur XP systems. The assay may be used in conjunction with other serological and clinical information to aid in the diagnosis of individuals with symptoms of hepatitis and in individuals at risk for hepatitis C infection.
6. The Siemens CHIV assay's instructions for use specify an index value of 1.0 for the cutoff and no gray zone.
7. The Siemens HBsAgII assay's instructions for use specify an index value of 1.0 for the cutoff and no gray zone.
8. Siemens HCV testing was performed according to the assay's instructions for use, which specify the same equivocal range as that used in this study.

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