SIEMENS

CE 0197

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

HBc Total (HBcT)

Assay for the Detection of Total Antibodies to Hepatitis B Core Antigen

Current revision and date [a]	Rev. AB, 2021-07	
Product Name	ADVIA Centaur® HBc Total assay	**REF** 07566733
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur HBcT Quality Control Material ADVIA Centaur Wash 1 (2 x 1500 mL) ADVIA Centaur Wash 1 (2 x 2500 mL)	**REF** 07569996 **REF** 01137199 **REF** 03773025
Specimen Types	Serum, EDTA plasma	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

a In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

The ADVIA Centaur® HBc Total (HBcT) assay is an *in vitro* diagnostic test for the qualitative determination of total antibodies to the core antigen of the hepatitis B virus (HBV) in human serum or EDTA plasma using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. This assay can be used as an aid in the diagnosis of individuals with acute or chronic hepatitis B virus (HBV) infection and in the determination of the clinical status of HBV infected individuals in conjunction with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. This assay can also be used as an aid in the differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown.

Summary and Explanation

The ADVIA Centaur HBc Total assay is an antigen bridging microparticle chemiluminometric immunoassay used for the detection of antibodies to hepatitis B core antigen in human serum or plasma.

Hepatitis B virus (HBV) is endemic throughout the world and is the major cause of liver disease. HBV is transmitted through direct contact with blood and body fluids. Common modes of transmission include blood transfusion, needle puncture, direct contact with open wounds, sexual contact, and mother-neonate contact during birth.[1,2]

The average incubation period for HBV infection is 6 to 8 weeks (range 1 to 6 months). Common clinical symptoms include malaise, fever, gastroenteritis, and icterus. HBV infection can result in typical icteric hepatitis, subclinical anicteric hepatitis, fulminant hepatitis, or chronic or persistent hepatitis. In adults, 90 to 95% of patients with HBV infection completely recover from acute illness and clear the virus. Approximately 5 to 10% of patients with HBV become chronic carriers. In HBV infected neonates, approximately 90% develop chronic hepatitis B infection. It is estimated that over 300 million people worldwide are chronic carriers of the virus. HBV infection, particularly in cases of chronic infection, is clearly associated with the development of hepatocellular carcinoma.[1,2,3]

Hepatitis B core antigen (HBcAg), found in liver cells, does not circulate in the bloodstream. However, IgM and IgG antibodies to HBcAg can be detected serologically in HBV infected individuals. Anti-HBc IgM is detectable first and remains detectable for approximately six months. Shortly after the IgM response, anti-HBc IgG appears and can remain detectable indefinitely. The presence of anti-HBc IgM is characteristic of acute infection, while the presence of anti-HBc IgG is characteristic of chronic or recovered stages of HBV infection. Anti-HBc Total assays detect both IgM and IgG anti-HBc responses. Most often levels of anti-HBc will coincide with detectable levels of other HBV markers. Rarely, anti-HBc may be the only detectable HBV marker. This may occur during the brief period when hepatitis B surface antigen (HBsAg) has been cleared from the bloodstream and before antibodies to hepatitis B surface antigen (anti-HBs) become detectable. For this reason, the use of anti-HBc Total assays to detect acute infection is not recommended. Anti-HBc Total assays should be used in conjunction with other marker assays to assess current or past exposure to HBV.[1,2,4,5]

Principles of the Procedure

The ADVIA Centaur HBc Total assay is a two wash antigen sandwich immunoassay in which antigens are bridged by antibody present in the patient sample. The Solid Phase contains a preformed complex of streptavidin coated microparticles and biotinylated recombinant HBc antigen and is used to capture anti-HBc in the patient sample. The Lite Reagent contains recombinant HBc antigen labeled with acridinium ester and is used to detect anti-HBc in the sample. Solid Phase and Chaotrope Reagent are added to the sample, followed by Ancillary Reagent and Lite Reagent. Antibody-antigen complexes will form if anti-HBc antibodies (IgM and IgG) are present in the sample.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur HBcT ReadyPack® primary reagent pack; Lite Reagent	10.0 mL/reagent pack recombinant hepatitis B core antigen (~ 0.2 µg/mL) labeled with acridinium ester in buffer with surfactant and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur HBcT ReadyPack primary reagent pack; Solid Phase Reagent	25.0 mL/reagent pack streptavidin coated paramagnetic microparticles preformed with biotinylated recombinant HBcAg (~ 0.2 µg/mL) in buffer with potassium thiocyanate (5.0%), bovine serum albumin, surfactant, and sodium azide (< 0.1%)	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur HBcT ReadyPack primary reagent pack; Chaotrope Reagent[a]	6.0 mL/reagent pack buffer with potassium thiocyanate (40%) and surfactant	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur HBcT ReadyPack ancillary reagent pack; Ancillary Reagent ANC	25.0 mL/reagent pack buffer with potassium thiocyanate (5.0%) and surfactant	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 28 days
ADVIA Centaur HBcT calibrator	2.0 mL/vial processed human plasma positive for HBc antibodies, bovine serum albumin, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 8 hours
ADVIA Centaur HBcT quality control material[b]	7.0 mL/vial processed human plasma negative and positive for anti-HBc with preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 8 hours
ADVIA Centaur Wash 1[b] WASH 1	1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month
ADVIA Centaur Wash 1[b] WASH 1	2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month

a The Chaotrope Reagent is colorless to pinkish in color.

b See *Materials Required but Not Provided*.

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

CAUTION POTENTIAL BIOHAZARD

Some components of this product contain human source material. No known test method can offer complete assurance that products derived from human blood will not transmit infectious agents. All products manufactured using human source material should be handled as potentially infectious. Handle this product according to established good laboratory practices and universal precautions.[6–8]
The negative control has been assayed by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2. The positive control and calibrators contain human plasma that may be reactive for HBsAg. The units were treated with a BPL-UV inactivation procedure, however, all products manufactured using human source material should be handled as potentially infectious.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

H412	Harmful to aquatic life with long lasting effects.
P273, P501	Avoid release to the environment. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** Potassium Thiocyanate; ADVIA Centaur HBcT ReadyPack, ADVIA Centaur HBcT Ancillary Reagent

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the system operating instructions.

Note The Ancillary Reagent provided in this kit is matched to the Solid Phase and Lite Reagent. Do not mix Ancillary Reagent lots with different lots of Solid Phase and Lite Reagent.

Note

- Discard reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

Specimen Collection and Handling

Serum or EDTA plasma are the recommended sample types for this assay. Do not use specimens with obvious microbial contamination. The performance of the ADVIA Centaur HBc Total assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma such as saliva, urine, amniotic, or pleural fluids.

The following general recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI),[9] and augmented with additional sample handling studies using the ADVIA Centaur HBc Total assay:

- Handle all samples as if capable of transmitting disease.
- Samples are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post draw. When testing 10 samples where the centrifugation step was varied up to 24 hours post draw, no clinically significant differences were observed.
- Test samples as soon as possible after collecting. Store samples at 2–8°C if not tested immediately.
- Store samples in secondary tubes, stoppered and upright at all times at 2–8°C up to 7 days.
- Store primary tube samples at 2–8°C up to 7 days. Keep samples stoppered and upright at all times. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel barrier blood collection tubes. When 10 samples in these primary tubes were tested up to 7 days, no clinically significant differences were observed.
- Freeze samples, devoid of red blood cells, at or below -20°C for longer storage. Do not store in a frost-free freezer. When 10 samples were subject to 2 freeze/thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge before using.
- Package and label samples for shipment in compliance with applicable federal and international regulations covering the transport of clinical samples and etiological agents. Samples maintained at room temperature up to 12 hours or refrigerated up to 7 days demonstrated no qualitative differences. Store samples stoppered and upright at 2–8°C upon arrival. If shipment is expected to exceed 7 days, ship specimens frozen.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
07566733	1 ReadyPack primary reagent pack containing ADVIA Centaur HBcT Lite Reagent, Solid Phase, and Chaotrope Reagent	200
	1 Ancillary pack containing ADVIA Centaur HBcT Ancillary Reagent ANC	
	ADVIA Centaur and ADVIA Centaur CP HBcT Master Curve card	
	1 vial ADVIA Centaur HBcT low calibrator CAL L	
	1 vial ADVIA Centaur HBcT high calibrator CAL H	
	ADVIA Centaur and ADVIA Centaur CP HBcT Calibrator Assigned Value card	

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description	
REF 07569996	ADVIA Centaur HBcT quality control material	2 x 7.0 mL negative control CONTROL – 2 x 7.0 mL positive control CONTROL + Expected Value card
REF 01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF 03773025	ADVIA Centaur Wash 1[a] WASH 1	2 x 2500 mL/pack

a For use with systems with 2500 mL capacity.

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

- Dispenses 50 µL of sample into a cuvette and incubates for 6 minutes at 37°C.
- Dispenses 125 µL of Solid Phase and incubates for 18 minutes at 37°C.
- Dispenses 30 µL of Chaotrope Reagent.

  Note The Chaotrope Reagent is colorless to pinkish in color.
- Washes the cuvette with Wash 1.
- Dispenses 100 µL of Ancillary Reagent, incubates the mixture for 5.75 minutes at 37°C.
- Dispenses 50 µL of Lite Reagent, incubates the mixture for 18 minutes at 37°C.
- Separates the Solid Phase from the mixture and aspirates the unbound reagent.
- Washes the cuvette with Wash 1.
- Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
- Reports results according to the selected option, as described in the system operating instructions .

A direct relationship exists between the level of anti-HBc antibodies found in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of positive or negative is determined according to the Index level established with the calibrators. Refer to *Interpretation of Results* for a description of the Cutoff Value calculation.

Preparing the System

Ensure that the system has sufficient primary and ancillary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack primary reagent packs in the primary reagent compartment using the arrows on the packs as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. Load the ReadyPack ancillary reagent packs in the ancillary reagent entry. For detailed information about loading reagents, refer to the system operating instructions.

Preparing the Samples

This assay requires 50 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, refer to the system operating instructions.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter. Remove particulates by centrifugation.
- Samples are free of bubbles or foam.

On-System Stability

The ADVIA Centaur HBcT assay reagents are stable unopened until the expiration date on the carton or onboard the system for 28 days.

Performing Calibration

For calibration of the ADVIA Centaur HBc Total assay, use ADVIA Centaur HBc Total Calibrators provided with each kit. The calibrators provided in this kit are matched to the ReadyPack primary reagent pack.

Note The Low and High Calibrators provided in this kit are matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagent packs.

Each lot of calibrators contains a Calibrator Assigned Value card to facilitate entering the calibration values on the system. Enter the values using the barcode scanner or the keyboard. For detailed information about entering calibrator values, refer to the system operating instructions.

Note This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate.

1. Schedule the calibrators to the worklist.
2. Label two sample cups with calibrator barcode labels: one for the low and another for the high.
3. Gently mix the Low and High Calibrators and dispense at least 4 to 5 drops into the appropriate sample cups.

   Note Each drop from the calibrator vial is approximately 50 µL.
4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Note Dispose of any calibrator remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

Calibration Frequency

Calibrate the assay at the end of the 14-day calibration interval.

Additionally, the ADVIA Centaur HBc Total assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Using Barcode Labels

Note Calibrator barcode labels are lot-number specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

Use the ADVIA Centaur HBc Total Calibrator barcode labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur HBc Total assay. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Performing Master Curve Calibration

The ADVIA Centaur HBc Total assay requires a Master Curve calibration when using a new lot number of Lite Reagent, Solid Phase, and Chaotrope Reagent. For each new lot number of Lite Reagent, Solid Phase, and Chaotrope Reagent use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

For quality control of the ADVIA Centaur HBc Total assay, use ADVIA Centaur HBc Total quality control materials. Refer to the Expected Value card for the suggested expected values specific for the lot number of the positive and negative controls.

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, quality control samples should be assayed on each workshift that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Note This procedure uses control volumes sufficient to measure each control in duplicate.

1. Schedule the quality control samples to the worklist.
2. Label two sample cups with quality control barcode labels: one for the positive, and another for the negative.
3. Gently mix the quality control materials and dispense at least 5 to 6 drops into the appropriate sample cups.

   Note Each drop from the control vial is approximately 50 µL.
4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Note Dispose of any quality control materials remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh quality control materials.

Using Barcode Labels

Note Control barcode labels are lot-number specific. Do not use barcode labels from one lot of controls with any other lot of controls.

Use the ADVIA Centaur HBc Total quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur HBc Total assay. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Taking Corrective Action

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports anti-HBc Total results in Index Values and as reactive or nonreactive.

Interpretation of Results

- Samples with a calculated value of less than 0.50 Index Value are considered nonreactive for total antibodies to hepatitis B core antigen.
- Samples with a calculated value greater than or equal to 0.50 Index Value are considered reactive for total antibodies to hepatitis B core antigen.
- The cutoff for the ADVIA Centaur HBc Total assay was verified based on results of Receiver-Operator characteristics (ROC) Curve[10] and clinical agreement generated from clinical studies.
- Sample results are invalid and must be repeated if the controls are out of range.

Limitations

The following information pertains to limitations of the assay:

- The ADVIA Centaur HBc Total assay is limited to the detection of total antibodies to hepatitis B core antigen in human serum or EDTA plasma. Assays for the detection of anti-HBc may not identify all patient samples that contain hepatitis B virus or potentially infectious units of blood and may generate false reactive results.
- Assay performance characteristics have not been established when the ADVIA Centaur HBc Total assay is used in conjunction with other manufacturers' assay for specific HBV serological markers.
- Assay performance characteristics have not been established for the use of the ADVIA Centaur HBc Total assay as an aid in determining susceptibility to HBV infection prior to or following vaccination in infants, children, or adolescents.
- The performance of the ADVIA Centaur HBc Total assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic, or pleural fluids.
- The performance of the assay has not been established for populations of immunocompromised or immunosuppressed patients.
- Do not use specimens with obvious microbial contamination.
- Results from patients taking biotin supplements or receiving high-dose biotin therapy should be interpreted with caution due to possible interference with this test.

Expected Values

In a population of 4945 blood donor samples, the number of samples found reactive (≥ 0.50 Index Value) for anti-HBc using the ADVIA Centaur HBc Total assay was 21 (0.42%).

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[11]

Performance Characteristics

The performance of the ADVIA Centaur HBc Total assay was determined by testing a total of 5564 samples at 2 sites. The ADVIA Centaur HBc Total results were compared to test results using a commercially available automated anti-HBc Total assay. The samples included the following populations: HBV positive samples, normal blood donors, and hospitalized patients. Further evaluation was performed with the discordant samples using another commercially available assay for anti-HBc Total.

Sensitivity

To examine the analytical sensitivity of the ADVIA Centaur HBc Total assay, the Paul Ehrlich Institute (PEI) anti-HBc Total reference sample was used to prepare a dilution series which was assayed using two ADVIA Centaur HBc Total reagent lots. Linear regression was used to determine the concentration of PEI reference sample which corresponds to the ADVIA Centaur HBc Total cutoff (Index Value = 0.50). The PEI International Unit (IU) concentration at the assay cutoff was determined to be 0.22 PEI IU/mL.

Clinical Sensitivity and Specificity

Clinical Specificity

A population of 4945 random blood donors and 217 hospitalized patients was tested using the ADVIA Centaur HBc Total assay and a commercially available automated anti-HBc Total assay. The performance of the ADVIA Centaur HBc Total assay is shown in the following table:

Patient Group	Number	Nonreactive (%)	Reactive (%)	Confirmed Reactive	Specificity
Random Blood Donors	4945	4924 (99.57%)	21 (0.42%)	12	99.82%
Hospitalized patients	217	206 (94.93%)	11 (5.1%)	7	98.09%
Total	**5162**	**5130 (99.38%)**	**32 (0.62%)**	**19**	**99.75%**

The resolved specificity of the ADVIA Centaur HBc Total assay was 99.75% (5130/5143) with a 95% confidence interval (CI) of 99.57 to 99.87%.

Clinical Sensitivity

A population of 402 HBV patient samples previously determined to be positive for HBsAg was tested using the ADVIA Centaur HBc Total assay and a commercially available anti-HBc Total assay. 402 of these HBV patient samples were found to be positive for anti-HBc Total using the comparative assay with the same intended use and 402 were positive using the ADVIA Centaur HBc Total assay. The initial relative sensitivity was 100% (402/402).

	Comparative Anti-HBc Total Assay		
ADVIA Centaur HBc Total Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	402	0	402
Nonreactive	0	0	0
Total	**402**	**0**	**402**

The resolved sensitivity of the ADVIA Centaur HBc Total assay was 100% (402/402) with a 95% confidence interval (CI) of 99.09 to 100%.

Seroconversion Panels

Commercially available HBV patient seroconversion panels were tested using the ADVIA Centaur HBc Total assay to determine the seroconversion sensitivity of the assay. The performance of the ADVIA Centaur HBc Total assay on the seroconversion panels closely matched the performance of the comparative assay. The following results were obtained:

	Anti-HBc Total Positive Result From Initial Draw Date		
Panel ID	**Comparative Assay (Days)**	**ADVIA Centaur Assay (Days)**	**Comparative Assay vs ADVIA Centaur Assay Difference in Bleed Numbers[a]**
RP-009	36	36	0
RP-0016	60	57	+1
RP-0017	71	71	0
BCP-62433	41	41	0
Nabi-SB0413	69	69	0
Nabi-SB0411	35	35	0
Serologicals 2263-D	78	63	+3

a The difference in bleed numbers is relative to the comparative assay. For example, a +1 means that the comparative assay required 1 additional bleed before reactivity was determined as compared to the time-point when ADVIA Centaur assay confirmed positive.

Precision

Precision was evaluated according to the Clinical and Laboratory Standards Institute protocol EP5-A2.[12] A 6 member panel and controls were assayed in 2 replicates, 2 times a day, for 20 days. The following results were obtained using 1 reagent lot and a stored calibration curve.

Sample	Mean Index	Within-run		Run-to-run		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)
Serum 1	0.06	0.02	NA[a]	0.01	NA	0.02	NA
Serum 2	1.13	0.06	5.1	0.05	4.5	0.09	8.4
Serum 3	1.22	0.04	3.6	0.05	4.2	0.08	6.8
Serum 4	1.35	0.08	5.8	0.05	3.8	0.10	7.1
Serum 5	2.40	0.12	4.9	0.08	3.4	0.19	7.7
Serum 6	4.54	0.20	4.4	0.21	4.7	0.29	6.5

a NA = Not Applicable.

Interferences

Serum specimens that are or that contain . . .	Demonstrate a ≤ 10% change in results or have an insignificant effect on the assay up to . . .
hemolyzed	500 mg/dL of hemoglobin
lipemic	1000 mg/dL of intralipids
icteric	60 mg/dL of conjugated bilirubin
icteric	40 mg/dL of unconjugated bilirubin
hyperproteinemic	12.0 g/dL of protein
hypoproteinemic	3.5 g/dL of protein
hyper IgG	60 mg/mL of immunoglobulin G
biotin	150 ng/mL of biotin

	Biotin Test Level (ng/mL)						
	0	150	330	650	1300	2600	3500
Negative Sample							
Index Value	0.3	0.27	0.23	0.23	0.22	0.21	0.23
Interpretation	NR[a]	NR	NR	NR	NR	NR	NR
% Bias	—	-11	-24	-25	-26	-29	-25
Positive Sample							
Index Value	2.74	2.38	2.13	2.12	2.1	2.1	2.02
Interpretation	R[b]	R	R	R	R	R	R
% Bias	—	-11	-24	-25	-26	-29	-25

a NR = Nonreactive
b R = Reactive

Specimens that contain biotin at concentrations less than 150 ng/mL demonstrate ≤ 10% change in results or have an insignificant effect on the assay. Biotin concentrations greater than this lead to higher negative bias and can lead to falsely depressed results.

The recommended adult daily dietary intake for biotin is 30 µg/day. Over the counter dietary supplements promoted for use in hair, skin and nail health may contain 5–100 mg of biotin, with recommendations to take multiple pills per day. Some pharmacokinetic studies in a small number of apparently healthy adults have shown that ingesting 5 mg, 10 mg, and 20 mg of biotin serum concentrations of biotin can reach up to 73 ng/mL, 141 ng/mL, and 355 ng/mL, respectively.[13] However, some patients may be taking supplements with biotin at levels greater than 20 mg per day. Subjects who take up to 300 mg of biotin per day may have plasma biotin levels as high as 1160 ng/mL.[14] Clearance of biotin could be different in patients that are not apparently healthy, for example patients with impaired renal function may have higher concentrations of biotin in serum.

Interference testing was determined according to CLSI Document EP7-A2.[15]

Cross-Reactivity

The ADVIA Centaur HBc Total assay was evaluated for potential cross-reactivity with other viral antibodies and disease state specimens. The anti-HBc Total status of each specimen was verified using another commercially available anti-HBc Total assay. The following results were obtained using the ADVIA Centaur HBc Total assay.

		Number of Positive Anti-HBc Total Results	
Clinical Category	**Number Tested**	**ADVIA Centaur Assay**	**Reference Assay**
Hepatitis A Infection (HAV)	9	3	3
Hepatitis C Infection (HCV)	11	5	5
Non-viral Liver Disease	9	0	0
Epstein-Barr Virus (EBV) IgG	10	2	2
Epstein-Barr Virus (EBV) IgM	10	3	3
Herpes Simplex Virus (HSV) IgG	10	3	3
Herpes Simplex Virus (HSV) IgM	10	4	4
CMV IgG	10	7	7
CMV IgM	3	1	1
Toxoplasma IgG	10	2	2
Toxoplasma IgM	10	0	0
Syphilis IgG	10	1	1
Human Immunodeficiency Virus (HIV 1/2)	10	2	2
VZV IgG	10	4	4
Multiparity	10	1	1
Rubeola IgG	10	5	4[a]
Alcoholic Hepatitis	2	0	0
Rheumatoid Arthritis	10	0	0
Anti-Nuclear Antibody (ANA)	10	1	1
Systemic Lupus Erythematosus (SLE)	10	1	1

Clinical Category	Number Tested	Number of Positive Anti-HBc Total Results	
		ADVIA Centaur Assay	Reference Assay
HAMA	10	0	0
Flu vaccine Recipient	10	3	3
Total Samples Tested	**204**	**48**	**47**

a The non-confirmed ADVIA Centaur HBc Total positive result was ADVIA Centaur anti-HBs positive.

Standardization

The ADVIA Centaur HBc Total assay traceability is based upon the relative clinical agreement with commercially available anti-HBc Total assays. Refer *to Performance Characteristics*. Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

siemens.com/healthcare

References

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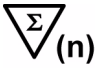
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat		Up
	Use by		Contains sufficient for (n) tests
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details		Green dot
	Recycle		Printed with soy ink

Trademarks

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