

Anti-HBs2 (aHBs2)

Assay for the Detection of Antibodies to Hepatitis B Surface Antigen

Assay Summary

Sample Type	Serum, plasma (EDTA, lithium-heparinized, or sodium-heparinized)
Sample Volume	100 µL
Calibrator	aHBs2
Assay Range	3.1–1000 mIU/mL

Contents

REF	Contents	Number of Tests
04670661	1 ReadyPack® primary reagent pack containing ADVIA Centaur® Anti-HBs2 Lite Reagent, Solid Phase, and Ancillary Reagent ADVIA Centaur Anti-HBs2 Master Curve card 1 vial Anti-HBs2 Low Calibrator CAL L 1 vial Anti-HBs2 High Calibrator CAL H ADVIA Centaur Anti-HBs2 Calibrator Assigned Value cards	200

Intended Use

The ADVIA Centaur anti-HBs2 assay is an *in vitro* diagnostic immunoassay for the qualitative and quantitative determination of total antibodies to hepatitis B surface antigen in human adult, adolescent, and pediatric serum or plasma (EDTA, lithium-heparinized, or sodium-heparinized) and neonatal samples using the ADVIA Centaur and ADVIA Centaur XP systems. The assay results may be used as an aid in the determination of susceptibility to hepatitis B virus (HBV) infection in individuals prior to or following HBV vaccination or where vaccination status is unknown. Assay results may be used with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. A reactive assay result will allow a differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown.

This assay has not been FDA-cleared or approved for the screening of blood or plasma donors.

Materials Required but Not Provided

REF	Description	Contents
	ADVIA Centaur or ADVIA Centaur XP System	
01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
	or	
03773025	ADVIA Centaur Wash 1 WASH 1 *	2 x 2500 mL/pack

*for use with systems with 2500 mL capacity

Optional Reagents

REF	Description	Contents
06521435	ADVIA Centaur aHBs2 quality control material	2 x 10.0 mL Negative Control CONTROL - 2 x 10.0 mL Positive Control CONTROL + Expected Value card
05699280 (117228)	ADVIA Centaur Multi-Diluent 11 M-DIL 11	2 ReadyPack ancillary reagent packs containing 5 mL/pack
03479704 (111088)	Multi-Diluent 11 M-DIL 11	10 mL/vial

Summary and Explanation of the Test

The ADVIA Centaur Anti-HBs2 assay is an antibody-capture microparticle direct chemiluminometric immunoassay used to measure the amount of antibody to hepatitis B surface antigen in human serum and 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. HBV is transmitted sexually and through direct contact with blood and body fluids.

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}

The presence of antibody to hepatitis B surface antigen (anti-HBs) is used to determine immune status to HBV or disease progression in individuals infected with HBV. An increase in anti-HBs levels, together with a loss of detectable circulating hepatitis B surface antigen (HBsAg), denotes convalescence in hepatitis B infections. Furthermore, anti-HBs levels can be measured to determine if vaccination is needed or, following a vaccination regimen, to determine if protective immunity has been achieved.^{4,5}

Assay Principle

The ADVIA Centaur Anti-HBs2 assay is a sandwich immunoassay using direct, chemiluminometric technology. HBsAg (ad and ay) is coupled to magnetic latex particles in the Solid Phase. In the Lite Reagent, the HBsAg (ad and ay) is labeled with acridinium ester. Nonmagnetic latex particles are added from the ancillary well.

The sample is incubated simultaneously with Lite Reagent, Solid Phase, and Ancillary Reagent. Antibody-antigen complexes will form if anti-HBs is present in the sample.

The ADVIA Centaur/Centaur XP system automatically performs the following actions:

- Dispenses 100 µL of sample into a cuvette.

- Dispenses 50 μL of Lite Reagent and 20 μL of Ancillary reagent and incubates for 2.75 minutes at 37°C.
- Dispenses 125 μL of Solid Phase and incubates the mixture for 5.5 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 or in the online help system.

A direct relationship exists between the amount of anti-HBs activity present in the patient sample and the amount of relative light units (RLUs) detected by the system. Refer to *Interpretation of Results* for a description of the Cutoff Value calculation.

Specimen Collection and Handling

Serum and plasma (EDTA, lithium-heparinized, or sodium-heparinized) are the recommended sample types for this assay. Do not use specimens with obvious microbial contamination. The performance of the ADVIA Centaur anti-HBs2 assay has not been established with cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma such as saliva, urine, amniotic, or pleural fluids.

CAUTION: Thoroughly mix and centrifuge thawed specimens before using. Centrifuge thawed specimens (10,000 x g for 2 minutes) and collect the supernatant into a clean vial.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS),⁶ and augmented with additional sample handling studies using the ADVIA Centaur Anti-HBs2 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.
- Test samples as soon as possible after collecting.
- Store samples stoppered at all times at 2° to 8°C up to 7 days.
- Store primary tube samples at 2° to 8°C up to 7 days. Keep samples stoppered 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.
- Freeze samples, devoid of red blood cells, at or below -20°C for longer storage. Do not store in a frost-free freezer. When samples were subjected to 4 freeze/thaw cycles, no clinically significant differences were observed.⁷ 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 refrigerated up to 7 days demonstrated no qualitative differences. Serum and EDTA plasma samples maintained at room temperature up to 7 days and heparinized plasma samples maintained at room temperature up to 3 days demonstrated no qualitative differences. Store samples stoppered at 2° to 8°C upon arrival. If during shipment, samples may be subjected to temperatures above 25°C, then ship samples frozen.

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. (example: 1500 x g for 10 minutes; follow tube manufacturer's recommendations⁶)
- Samples are free of bubbles or foam. Remove any visual lipid layer.

Reagents



Store the reagents upright at 2–8°C.

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 operator's guide.



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

Reagent Pack	Reagent	Volume	Ingredients	Storage	Stability
ADVIA Centaur Anti-HBs2 ReadyPack primary reagent pack	Lite Reagent	11.0 mL/ reagent pack	inactivated human hepatitis B surface antigen (ad and ay) (~1 µg/mL) labeled with acridinium ester in protein buffer with bovine serum, albumin, surfactant, and preservatives	2–8°C	Until the expiration date on the pack label. For onboard stability, refer to Onboard Stability and Calibration Interval.
	Solid Phase	26.0 mL/ reagent pack	recombinant hepatitis B surface antigen (ad and ay) (~3 µg/mL) coupled to magnetic latex particles in protein buffer with bovine serum albumin, surfactant, and preservatives	2–8°C	Until the expiration date on the pack label. For onboard stability, refer to Onboard Stability and Calibration Interval.
	Ancillary Reagent	5.0 mL/ reagent pack	non-magnetic latex particles in tris buffer with surfactant and preservatives	2–8°C	Until the expiration date on the pack label. For onboard stability, refer to Onboard Stability and Calibration Interval.
Anti-HBs2 Calibrator vials	Calibrators	2.0 mL/ vial	processed human plasma positive for antibodies to HBsAg with preservatives	2–8°C	Until the expiration date on the vial or onboard—8 hours.
Anti-HBs2 quality control material vials**	Controls	10.0 mL/ vial	processed human plasma negative and positive for antibodies to HBsAg with preservatives	2–8°C	Until the expiration date on the vial or onboard—8 hours.
ADVIA Centaur  *	Wash 1	1500 mL/ pack	phosphate buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	Until the expiration date on the vial or onboard—1 month.
ADVIA Centaur  *	Wash 1	2500 mL/ pack	phosphate buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	Until the expiration date on the vial or onboard—1 month.

Reagent Pack	Reagent	Volume	Ingredients	Storage	Stability
ADVIA Centaur  ReadyPack ancillary reagent pack**	Multi-Diluent 11	5.0 mL/ reagent pack	tris buffer with goat serum with protein stabilizers and preservatives	2–8°C	Until the expiration date on the pack label or 28 consecutive days after accessing the ancillary reagent pack.

* See Materials Required but Not Provided.

** See Optional Reagents.

Precautions and Warnings

Safety data sheets (MSDS/SDS) are available on www.siemens.com/diagnostics.

 Some components of this product contain human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.8-10

The controls and calibrators have 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 human derived HBsAg used in the manufacture of this product was obtained from units tested by FDA-approved methods and found nonreactive for antibody to HCV and HIV-1/2. The units were inactivated and the HBsAg was purified; 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.

NOTE: Some components of this product contain 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 the buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

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.

Loading Reagents

Ensure that the system has sufficient primary reagent. For detailed information about preparing the system, refer to the system operating instructions or to the online help system.

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 operator's guide.

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. For detailed information about loading reagents, refer to the system operating instructions or to the online help system.

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.

Onboard Stability and Calibration Interval

Onboard Stability	Calibration Interval
90 days	42 days

Additionally, the ADVIA Centaur Anti-HBs2 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

NOTE:

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

Master Curve Calibration

The ADVIA Centaur Anti-HBs2 assay requires a Master Curve calibration when using a new lot number of Lite Reagent, Solid Phase, and Ancillary Reagent. For each new lot number of Lite Reagent, Solid Phase, and Ancillary 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 or to the online help system.

Calibration

For calibration of the ADVIA Centaur Anti-HBs2 assay, use ADVIA Centaur Anti-HBs2 Calibrators provided with each kit. The calibrators provided in this kit are matched to the ReadyPack primary reagent pack.

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 Anti-HBs2 Calibrator barcode labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur Anti-HBs2 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 a Calibration

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 or to the online help system.

Perform the calibration procedure using the following steps:

NOTE: This procedure uses calibrator volumes sufficient to measure each calibrator in triplicate.

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.

NOTE: Each drop from the calibrator vial is approximately 35 to 40 μ L.

3. Gently mix the Low and High Calibrators and dispense at least 12 to 14 drops into the appropriate sample cups.

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.

Quality Control

Follow government regulations or accreditation requirements for quality control frequency. For quality control of the ADVIA Centaur Anti-HBs2 assay, use of ADVIA Centaur Anti-HBs2 quality control material is recommended. Refer to the Expected Value card for the suggested expected values specific for the lot number of the positive and negative controls. Additional controls may be tested according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations.

NOTE: The recommended quality control material is intended to monitor substantial reagent failure. If additional controls are desired, it is recommended to run a negative control and positive control close to the clinically relevant decision point (10 mIU/mL). Further, the recommended quality control is in a serum matrix. It may not adequately control the assay for plasma specimens. The user should provide alternate control material for plasma.

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 Anti-HBs2 quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur Anti-HBs2 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 Quality Control

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

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

Perform the quality control procedure using the following steps:

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.

NOTE: Each drop from the control vial is approximately 35 to 40 μ L.

3. Gently mix the quality control materials and dispense at least 8 to 10 drops into the appropriate sample cups.
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.

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:

1. Investigate and determine the cause of the unacceptable control results:
 - 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.
2. When the condition is corrected, retest the controls, and confirm that results are within acceptable limits.
3. Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Sample Volume

This assay requires 100 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 *Sample Volume Requirements* in the *ADVIA Centaur Reference Manual*.

NOTE: The sample volume required to perform onboard dilution may differ from the sample volume required to perform a single determination. Refer to the following information for the sample volume required to perform onboard dilutions:

Dilution	Sample Volume (µL)
1:2	100
1:5	40
1:10	20

Assay Procedure

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

Procedural Notes

Dilutions

The following information pertains to dilutions:

- Samples with anti-HBs levels greater than 1000 mIU/mL may be diluted and retested.
- Patient samples can be automatically diluted by the system or prepared manually.

- For automatic dilutions, ensure that ADVIA Centaur Multi-Diluent 11 is loaded and set the system parameters as follows:

Dilution point: ≤ 1000 mIU/mL

Dilution factor: 2, 5, 10

For detailed information about automatic dilutions, refer to the system operating instructions or to the online help system.

- Manually dilute the patient samples when patient results exceed the linearity of the assay using automatic dilution, or when laboratory protocol requires manual dilution.
- Use Multi-Diluent 11 to manually dilute patient samples, and then load the diluted sample in the sample rack, replacing the undiluted sample.

Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of Results

Results should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

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

The ADVIA Centaur Anti-HBs2 assay is traceable to the World Health Organization (WHO) Hepatitis B Immunoglobulin 1st International Reference Preparation (1977). Samples with a calculated value of 10 mIU/mL or greater are considered reactive (protective) in accordance with the CDC guidelines.⁵ The accepted criteria for immunity to HBV is anti-HBs activity ≥ 10 mIU/mL, as defined by the WHO International Reference Preparation.

The system reports anti-HBs antibody results in mIU/mL, and as reactive (positive), nonreactive (negative), or needing retest.

- Nonreactive: Samples with an initial value < 8 mIU/mL. Anti-HBs is below 10 mIU/mL and the patient is considered not to have protective immunity to HBV infection.
- Reactive: Samples with an initial value ≥ 12 mIU/mL. Anti-HBs is detected at ≥ 10 mIU/mL and the patient is considered to have protective immunity to HBV infection.
- Retest Zone: Samples with an initial value ≥ 8 and < 12 mIU/mL. If results are within the retest zone after initial testing, samples must be retested in duplicate. After retesting, if 3 results are available and 2 results are ≥ 10 , then the sample is considered to be reactive. If 3 results are available and 2 results are < 10 , then the sample is considered to be nonreactive.

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:

- United States federal law restricts this device to sale by or on the order of a physician.
- The ADVIA Centaur Anti-HBs2 assay is limited to the detection of antibodies to HBsAg in human serum and plasma (EDTA, sodium-heparinized, or lithium-heparinized).
- Assay performance characteristics have not been established when the ADVIA Centaur Anti-HBs2 assay is used in conjunction with other manufacturers' assays for specific HBV

serological marker, and therefore, users are responsible for establishing their own performance characteristics.

- Assay performance characteristics have not been established in pregnant women, or in populations of immunocompromised or immunosuppressed patients, and therefore, users are responsible for establishing their own performance characteristics in these populations.
- This assay does not differentiate between a vaccine-induced immune response and an immune response induced by infection with HBV. To determine if the anti-HBs response is due to vaccine or HBV infection, a total anti-HBc assay may be performed.
- This assay is not intended for use in screening blood or plasma donors.
- The performance of the ADVIA Centaur Anti-HBs2 assay has not been established with cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic, or pleural fluids.
- Do not use specimens with obvious microbial contamination.
- Results obtained with ADVIA Centaur Anti-HBs2 assay may not be used interchangeably with values obtained with different manufacturer assay methods.
- Individuals that have received blood component therapies, for example, whole blood, plasma, immunoglobulin administered during the previous 3–6 months may have a false reactive anti-HBs result due to passive transfer of anti-HBs.
- The prevalence of the analyte in the population tested will affect the assay's predictive value.
- A positive anti-HBs result does not exclude co-infection by another hepatitis virus.
- High-Dose Hook Effect: In the ADVIA Centaur Anti-HBs2 assay, patient samples with levels of antibodies to HBsAg as high as 200,000 mIU/mL do not demonstrate a decrease in the RLUs (high-dose hook effect). Specimens having anti-HBs activity greater than 200,000 mIU/mL are extremely rare.

Expected Results

The prospective study population for the ADVIA Centaur Anti-HBs2 assay consisted of 2030 patients. Of these 2030 patients, 1098 patients (54.09%) were from the high risk population, 828 patients (40.79%) were from the signs and symptoms population, 83 patients (4.09%) were from the dialysis population, and 21 patients (1.03%) were transplant recipients. The prospective study population was 60.15% Black, 19.80% Caucasian, 17.04% Hispanic, 1.77% Asian, 0.39% American Indian or Alaskan Native, and 0.84% from unknown or other ethnicity. The majority of patients were male (64.43% male and 35.57% female). The mean age was 46.0 years (range of 13 to 91 years). Patients in the prospective study population were from the following geographic regions: Florida (55.67%), District of Columbia (23.94%), Texas (11.18%), California (5.32%), Maryland (3.15%) and other states (0.74%).

The ADVIA Centaur Anti-HBs2 results for the prospective population for all sites combined by age group and gender are summarized in the following table:

Distribution of High Risk, Signs and Symptoms, Dialysis, and Transplant Recipient Population by Age Group and Gender (All Testing Sites)

Age (Years)	Gender	Reactive (N)	Nonreactive (N)	Total (N)
0-9	Male	0	0	0
	Female	0	0	0
10-19	Male	8	4	12
	Female	8	3	11
20-29	Male	74	48	122
	Female	43	31	74
30-39	Male	61	105	166
	Female	35	59	94
40-49	Male	216	235	451
	Female	125	131	256
50-59	Male	216	232	448
	Female	88	130	218
60-69	Male	32	58	90
	Female	24	28	52
≥ 70	Male	4	15	19
	Female	4	13	17
All	Male	611	697	1308
	Female	327	395	722
Total		938	1092	2030

Performance Characteristics

Limit of Blank and Limit of Detection

A study was conducted based on guidance from CLSI EP17-A producing a Limit of Blank (LoB) of 1.7 mIU/mL and a Limit of Detection (LoD) of 3.1 mIU/mL.¹¹

Prospective Study

The HBV disease classification for each patient in the high risk, signs and symptoms, dialysis, and transplant populations (2030 patients total) was determined by serological assessment using resultant hepatitis marker profiles obtained from results of commercially available, FDA-approved reference assays. The serological assessment included the following 4 HBV markers: HBsAg, total antibody to hepatitis B virus core antigen (Anti-HBc Total), IgM antibody to hepatitis B virus core antigen (Anti-HBc IgM), and total antibody to hepatitis B virus surface antigen (anti-HBs) (quantitative). Testing of these specimens occurred at diagnostic laboratories located in Miami, FL (34.3%), Dallas, TX (36.2%), and Tarrytown, NY (29.5%). The individual ADVIA Centaur HBV assay result was compared to the reference HBV assay result and to the patient classification. No patients were excluded from the complete study set due to incomplete reference HBV serological results.

Each patient's HBV infection was classified based on the reactive (+)/nonreactive (-) patterns of the 4 reference HBV serological markers. Disease classification for each patient was based only on the HBV serological marker results, and was not affected by additional laboratory or clinical information. There were 14 unique reference marker patterns. These patterns are presented in the following table:

Classification by HBV Reference Markers (All Testing Sites)

HBV Classification	HBV Reference Markers			
	HBsAg	IgM Anti-HBc	Total Anti-HBc	Anti-HBs
Early Acute	+	-	-	-
Acute	+	+	+	-
Late Acute	+	+	+	+
Chronic	+	-	+	+
Chronic	+	-	+	-
Chronic	+	-	-	+
Early Recovery	-	+	+	+
Early Recovery	-	Equivocal	+	+
Early Recovery	-	+	+	-
Early Recovery	-	+	-	+
Immune due to hepatitis vaccination	-	-	-	+
Immune natural infection	-	-	+	+
Recovered	-	-	+	-
Not Previously Infected	-	-	-	-

+ = Reactive

- = Nonreactive

Comparison of Results

Following the assignment of specimen classification, the HBV results obtained using the ADVIA Centaur Anti-HBs2 assay were compared with results obtained using the reference anti-HBs assay for each result category (reactive and nonreactive). Specimens with an anti-HBs2 value and/or an anti-HBs value within the retest zone were retested and interpreted as described under *Interpretation of Results*.

The method comparison for all testing sites combined is presented in the following table:

Comparison of Results in High Risk, Signs and Symptoms, Dialysis, and Transplant Recipient Populations by HBV Classification
 ADVIA Centaur Anti-HBs2 Assay versus Reference Anti-HBs Assay (All Testing Sites)¹

HBV Classification	Reference Anti-HBs Assay Nonreactive		Reference Anti-HBs Assay Reactive		Total (N)
	ADVIA Centaur Anti-HBs2 Assay		ADVIA Centaur Anti-HBs2 Assay		
	Reactive (N)	Nonreactive (N)	Reactive (N)	Nonreactive (N)	
Early Acute	0	8	0	0	8
Acute	0	10	0	0	10
Late Acute	0	0	0	2	2
Chronic	0	112	6	1	119
Early Recovery	0	2	20	0	22
Immune due to hepatitis vaccination	1	2	362	6	371
Immune due to natural infection	0	8	522	9	539
Recovered	13	207	3	2	225
Not Previously Infected	11	723	0	0	734
Total	25	1072	913	20	2030

¹ In this study, 73 of 2030 specimens (3.6%) fell within the aHBs2 retest zone. Thirty-four of these specimens (46.6%) were determined to be reactive after retesting.

The percent agreement between the ADVIA Centaur Anti-HBs2 assay (including the upper and lower 95% confidence intervals) and the reference anti-HBs assay for each specimen classification was performed. The positive, negative, and overall percent agreements were calculated as follows:

Positive percent agreement =

$$\frac{\text{Number of ADVIA Centaur Anti-HBs2 reactive results in agreement with reference anti-HBs}}{\text{Total number of reference anti-HBs reactive results}} \times 100$$

Negative percent agreement =

$$\frac{\text{Number of ADVIA Centaur Anti-HBs2 nonreactive results in agreement with reference anti-HBs}}{\text{Total number of reference anti-HBs nonreactive results}} \times 100$$

Overall percent agreement =

$$\frac{\text{Number of ADVIA Centaur Anti-HBs2 results in agreement with reference anti-HBs}}{\text{Total number of reference anti-HBs reactive and nonreactive results}} \times 100$$

The percent agreement between the ADVIA Centaur Anti-HBs2 assay and the reference anti-HBs assay for the high risk, signs and symptoms, and dialysis populations across all testing sites is summarized in the following table:

**Percent Agreement and Confidence Intervals by HBV Classification in High Risk, Signs and Symptoms, Dialysis, and Transplant Recipient Populations
ADVIA Centaur Anti-HBs2 Assay versus Reference Anti-HBs Assay (All Testing Sites)**

HBV Classification	Positive Percent Agreement % (x/n)	95% Exact Confidence Interval	Negative Percent Agreement % (x/n)	95% Exact Confidence Interval
Early Acute			100 (8/8)	68.8–100
Acute			100 (10/10)	74.1–100
Late Acute	0 (0/2)	0–77.6		
Chronic	85.7 (6/7)	42.1–99.6	100 (112/112)	97.4–100
Early Recovery	100 (20/20)	86.1–100	100 (2/2)	22.4–100
Immune due to Hepatitis B vaccination	98.4 (362/368)	96.5–99.4	66.7 (2/3)	9.4–99.2
Immune due to natural infection	98.3 (522/531)	96.8–99.2	100 (8/8)	68.8–100
Recovered	60 (3/5)	14.7–94.7	94.1 (207/220)	90.1–96.8
Not Previously Infected			98.5 (723/734)	97.3–99.3
Total	97.9 (913/933)	96.7–98.7	97.7 (1072/1097)	96.7–98.5

Pediatric / Adolescent Comparison

One hundred and ten (110) pediatric / adolescent retrospective serum samples (age range from 1 to 17 years) were evaluated using the ADVIA Centaur anti-HBs2 assay and another commercially available assay. Interpretive results for reactive or nonreactive samples were compared between the two assays. The following results were obtained:

Pediatric Population (age range from 1 to 11 years)

		Reference anti-HBs Assay		
		Reactive	Nonreactive	Total
ADVIA Centaur anti-HBs2 Assay	Reactive	29	0	29
	Nonreactive	1	28	29
	Total	30	28	58

% Overall Agreement = 98.28% (57/58)

95% Confidence Interval: 90.76–99.96%

Adolescent Population (age range from 12 to 17 years)

		Reference anti-HBs Assay		
		Reactive	Nonreactive	Total
ADVIA Centaur anti-HBs2 Assay	Reactive	30	2	32
	Nonreactive	2	18	20
	Total	32	20	52

% Overall Agreement = 92.31% (48/52)

95% Confidence Interval: 81.46–97.86%

Neonate Comparison

Twenty (20) retrospectively collected neonate samples were evaluated using the ADVIA Centaur aHBs2 assay and another commercially available assay. Interpretive results for reactive or nonreactive samples were compared between the two assays. The following results were obtained.

		Reference anti-HBs Assay		
		Reactive	Nonreactive	Total
ADVIA Centaur anti-HBs2 Assay	Reactive	9	0	9
	Nonreactive	0	11	11
	Total	9	11	20

% Overall Agreement = 100.00% (20/20)
 95% Confidence Interval: 86.10–100.00%

HBV Vaccinee Panel Study

A study was conducted using 52 well-characterized, commercially available serum samples from 26 individuals before and after vaccination. Testing of these specimens occurred at diagnostic laboratories located in Miami, FL (34.6%), Dallas, TX (34.6%), and Tarrytown, NY (30.8%). Samples were tested using the ADVIA Centaur Anti-HBs2 assay and the reference anti-HBs assay, and the results were compared. The percent agreement between the ADVIA Centaur Anti-HBs2 assay and the reference anti-HBs assay for the vaccination panel population is summarized in the following table:

Comparison of ADVIA Centaur Anti-HBs2 and Reference Anti-HBs Results in Pre- and Post-Vaccinated Populations¹

ADVIA Centaur Anti-HBs2 Results	Reference Anti-HBs Results		
	Nonreactive (N)	Reactive (N)	Total (N)
Pre-vaccination			
Nonreactive, N (%)	26 (100%)	0	26 (100%)
Reactive, N (%)	0	0	0
Percent agreement: 100%			
95% confidence interval: 89.1–100			
Post-vaccination			
Nonreactive, N (%)	0	0	0
Reactive, N (%)	0	26 (100%)	26 (100%)
Percent agreement: 100%			
95% confidence interval: 89.1–100			

¹ For the vaccinee panel (samples from 26 patients), the percent agreement between ADVIA Centaur Anti-HBs2 results and reference results was determined for pre-vaccination and for post-vaccination.

Precision and Reproducibility Studies

Precision Estimates for All Testing Sites and Reagent Lots

The ADVIA Centaur Anti-HBs2 precision and reproducibility study was performed at 3 external sites using 2 reagent lots per site. An 8-member serum panel was assayed in replicates of 4 in 2 runs per day over at least 5 days for each lot. The study was completed with a single calibration of the assay (one calibration interval).

The data from all 3 sites and from all 3 reagent lots were combined to obtain SD and percent CV for within run, between run, between testing site, between lot, and total. The precision estimates were derived from variance component analysis.

The reproducibility results are presented in the following table:

Precision Estimates for All Testing Sites and Reagent Lots

Panel Member	Mean Concentration (mIU/mL) ¹	Within Run ²		Between Run ³		Between Testing Site ⁴		Between Lot ⁵		Total ⁶		Number of Observations
		SD ⁷	CV (%)	SD ⁷	CV (%)	SD ⁷	CV (%)	SD ⁷	CV (%)	SD ⁷	CV (%)	
1	3.1	0.22	7.0	0.11	3.4	0.37	12.0	0.20	6.6	0.49	16.1	248
2	6.3	0.27	4.4	0.17	2.7	0.49	7.8	0.25	4.0	0.64	10.2	248
3	13.1	0.39	2.9	0.31	2.4	0.73	5.6	0.37	2.8	0.96	7.3	248
4	20.7	0.56	2.7	0.43	2.1	1.05	5.1	0.58	2.8	1.39	6.7	248
5	133.7	2.86	2.1	2.60	1.9	5.45	4.1	4.23	3.2	7.91	5.9	248
6	401.8	8.14	2.0	7.51	1.9	14.16	3.5	13.77	3.4	22.65	5.6	248
7	638.7	15.01	2.4	15.86	2.5	23.34	3.7	24.46	3.8	40.33	6.3	248
8	906.8	17.65	1.9	16.10	1.8	31.56	3.5	23.04	2.5	45.80	5.1	234
Positive Control	115.9	2.72	2.4	3.29	2.8	6.03	5.2	1.45	1.2	7.53	6.5	164

- 1 Arithmetic mean of all results (all testing sites and reagent lots)
- 2 Variability of the assay performance within day (all testing sites and reagent lots)
- 3 Variability of the assay performance between days (all testing sites and reagent lots)
- 4 Variability of the assay performance between testing sites (from testing site to testing site)
- 5 Variability of the assay performance between reagent lots (from reagent lot to reagent lot, across all testing sites)
- 6 Variability of the assay performance incorporating all testing sites, all reagent lots, and all days
- 7 SD of mean concentration (mIU/mL)

NOTE: 4 replicates per panel in 2 runs per day for at least 5 days

Precision Estimates in Serum, EDTA, Lithium Heparin and Sodium Heparin Matrices

The ADVIA Centaur Anti-HBs2 precision and reproducibility in various sample matrices was examined in a 20-day precision protocol¹² (CLSI EP5-A2) using two (2) lots of reagent. Thirty-two specimens in four matrices were prepared to measure the precision of the assay at different dose levels. In addition to serum matrix, the anticoagulants tested were potassium EDTA, sodium heparin, and lithium heparin. The specimens were assayed in duplicate twice per day for 20 time points. A single instrument was used in this study over the course of 30 days with one recalibration.

The matrix reproducibility results from a representative lot of reagent are presented in the following table. The precision estimates were derived from variance component analysis. Calculations for within run, between day, and total precision were performed as recommended by the guidance protocol.¹²

Member	Matrix	Mean Concentration (mIU/mL) ¹	Within Run ²		Between Days ³		Total ⁴		Number of Observations
			SD ⁵	CV (%)	SD ⁵	CV (%)	SD ⁵	CV (%)	
E-2	EDTA plasma	3.9	0.24	6.1	0.15	3.9	0.32	8.1	80
E-3		9.2	0.27	2.9	0.12	1.4	0.46	5.0	80
E-4		14.2	0.40	2.8	0.00	0.0	0.71	4.9	80
E-5		96.4	1.95	2.0	1.44	1.5	4.14	4.3	80
E-6		242.2	4.89	2.0	0.96	0.4	9.76	4.0	80
E-7		498.9	9.51	1.9	4.52	0.9	18.16	3.6	80
E-8		585.7	12.39	2.1	13.78	2.4	24.59	4.2	80
E-9		790.8	16.88	2.1	21.20	2.7	32.45	4.1	80
Li-2		Lithium	4.8	0.22	4.7	0.20	4.1	0.36	7.5
Li-3	Heparin	10.6	0.29	2.7	0.43	4.1	0.60	5.7	80
Li-4		17.4	0.35	2.0	0.48	2.7	0.78	4.5	80
Li-5		176.5	3.78	2.1	5.64	3.2	7.56	4.3	80
Li-6		309.2	5.86	1.9	9.39	3.0	12.70	4.1	80
Li-7		513.0	10.59	2.1	15.08	2.9	20.19	3.9	80
Li-8		599.4	13.67	2.3	18.47	3.1	34.79	5.8	80
Li-9		850.4	15.61	1.8	25.40	3.0	36.36	4.3	80
Na-2	Sodium	3.9	0.21	5.4	0.20	5.2	0.33	8.6	80
Na-3	Heparin	8.8	0.24	2.7	0.28	3.2	1.01	11.5	80
Na-4		15.1	0.31	2.0	0.24	1.6	0.69	4.6	80
Na-5		55.8	1.33	2.4	0.68	1.2	2.56	4.6	80
Na-6		206.5	3.82	1.9	3.27	1.6	8.21	4.0	80
Na-7		362.3	8.01	2.2	2.03	0.6	13.67	3.8	80
Na-8		617.5	13.19	2.1	9.61	1.6	23.06	3.7	80
Na-9		863.7	16.88	2.0	8.82	1.0	29.21	3.4	80
S-2	Serum	3.1	0.16	5.1	0.18	5.8	0.28	9.2	80
S-3		6.2	0.23	3.7	0.26	4.2	0.43	6.9	80
S-4		12.7	0.30	2.3	0.49	3.8	0.66	5.2	80
S-5		20.0	0.54	2.7	0.49	2.5	1.00	5.0	80
S-6		128.3	3.16	2.5	3.80	3.0	6.21	4.8	80
S-7		382.7	7.07	1.8	8.14	2.1	14.79	3.9	80
S-8		606.6	14.86	2.4	13.76	2.3	23.68	3.9	80
S-9		870.1	17.37	2.0	16.27	1.9	34.38	4.0	80

- 1 Arithmetic mean of all results
- 2 Variability of the assay performance within run
- 3 Variability of the assay performance between days
- 4 Variability of the assay performance incorporating all days and runs.
- 5 SD of mean concentration (mIU/mL)

Cross-Reactivity

The ADVIA Centaur Anti-HBs2 assay was evaluated for potential cross-reactivity with viral antibodies and disease state specimens. The nonreactive anti-HBs status of each specimen was verified using a commercially available reference anti-HBs assay. The following results were obtained on the ADVIA Centaur Anti-HBs2 assay:

Clinical Category	Number Tested	ADVIA Centaur Anti-HBs2 Results	
		Nonreactive	Reactive
Hepatitis A Infection (HAV)	17	17	0
Hepatitis B Infection (HBsAg+)	12	12	0
Hepatitis C Infection (HCV)	24	24	0
Non-Viral Liver Disease	8	8	0
Rheumatoid Arthritis	8	8	0
Autoimmune Disease (Systemic Lupus & ANA)	15	15	0
Influenza Vaccination	6	6	0
Syphilis Infection	9	9	0
Cytomegalovirus (CMV)	13	13	0
Herpes Simplex Virus I/II (HSV)	22	22	0
<i>Toxoplasma gondii</i> Infection	12	12	0
Human Immunodeficiency Virus (HIV)	9	9	0
Rubella IgG	34	34	0
Varicella-Zoster Virus (VZV)	31	31	0
Epstein-Barr Virus (EBV)	54	54	0
Total Samples Tested	274	274	0

Interference

Serum specimens that are ...	Demonstrate \leq 15% change in results up to ...
hemolyzed	500 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	40 mg/dL of conjugated bilirubin
icteric	40 mg/dL of unconjugated bilirubin
proteinemic (high)	12 g/dL of total protein
proteinemic (low)	3 g/dL of total protein*
hyper IgG	6 g/dL of immunoglobulin G
biotin	500 ng/mL of biotin

* Demonstrates \leq 15% change in results with protein as low as 3 g/dL.

Interference testing was determined according to CLSI Document EP7-A2.¹³

Alternative Sample Types

The ADVIA Centaur Anti-HBs2 assay can use plasma specimens collected using sodium-heparin, lithium-heparin, or EDTA anticoagulants. In a matched matrix study of specimens around the cutoff value (10.0 mIU/mL), drawn in four tube types including serum, EDTA, sodium-heparin and lithium-heparin vacutainer tubes, the recovery of the heparinized samples was comparable to that of the serum control.

Matrix Bias Study of Samples Near the Cutoff

N = 11 samples: (3 samples > 10.0 mIU/mL, 8 samples < 10.0 mIU/mL)

Range: approximately 2.5 to 24 mIU/mL

Statistic	Serum (mIU/mL)	EDTA (mIU/mL)	Lithium Heparin (mIU/mL)	Sodium Heparin (mIU/mL)
Mean	10.11	11.13	8.68	9.11
SD	7.51	8.32	7.54	7.50
Bias to Serum (mIU/mL)	NA	1.02	-1.42	-1.00
SD of Bias	NA	1.25	0.92	1.05
Bias to Serum (% recovery)	NA	10.09	-14.10	-9.87

Matched specimens from 70 individuals, drawn in serum and plasma (EDTA, lithium-heparinized, and sodium-heparinized) vacutainer tubes were analyzed by linear regression analysis. The anti-HBs activity of these specimens spanned a range of approximately 2 to 1000 mIU/mL. Slope and intercept estimates by linear regression analysis (see following regression equations):

(EDTA) = 1.083 (Serum) - 0.20, R² = 1.00; N = 70

(Lithium heparin) = 0.939 (Serum) - 0.78, R² = 1.00; N = 70

(Sodium heparin) = 0.943 (Serum) - 0.33, R² = 1.00; N = 70

Standardization

The ADVIA Centaur Anti-HBs2 assay is standardized against the World Health Organization (WHO) 1st International Reference Preparation (1977).

Technical Assistance

For customer support, contact your local technical support provider or distributor.
www.siemens.com/diagnostics

References

1. Gitlin N. Hepatitis B: diagnosis, prevention, and treatment. *Clinical Chemistry* 1997;43:8(B):1500-1506.
2. Mahoney, FJ. Update on Diagnosis, Management, and Prevention of Hepatitis B Virus Infection. *Clinical Microbiology Reviews* 1999;12(2):351-366.
3. Juszczyk, J. Clinical course and consequences of hepatitis B infection. *Vaccine* 2000;18:S23-S25.
4. Vivek R. Treatment of hepatitis B. *Clin Cornerstone* 2001;3(6):24-36.
5. Centers for Disease Control. Protection Against Viral Hepatitis Recommendations of the Immunization Practices Advisory Committee. *MMWR* 1990;39(RR-2):1-26.
6. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline - Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2004. CLSI Document H18-A3.
7. Data on file at Siemens Healthcare Diagnostics, Diagnostics Division.
8. Centers for Disease Control. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR* 1988;37:377-82, 387-8.
9. Clinical and Laboratory Standards Institute (formerly NCCLS). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline - Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document M29-A3.
10. Federal Occupational Safety and Health Administration, Bloodborne Pathogens Standard, 29 CFR 1910.1030
11. Clinical and Laboratory Standards Institute (formerly NCCLS). *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline*. Wayne, PA: Clinical and Laboratory Standards Institute; 2004. CLSI Document EP17A.

12. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2004. CLSI Document EP5-A2.

13. Clinical and Laboratory Standards Institute (formerly NCCLS). *Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP7-A2.

ADVIA Centaur and ReadyPack are trademarks of Siemens Healthcare Diagnostics.
© 2010 Siemens Healthcare Diagnostics. All rights reserved.
US Pats 5,609,822; 5,788,928

Origin: US



Siemens Healthcare Diagnostics Inc.
Tarrytown, NY 10591-5097 USA



Siemens Healthcare Diagnostics Ltd.
Sir William Siemens Sq.
Frimley, Camberley, UK GU16 8QD

Siemens Healthcare
Diagnostics Pty Ltd
885 Mountain Highway
Bayswater Victoria 3153
Australia

シーメンスヘルスケア
ダイアグノスティクス株式会社
東京都品川区東五反田 3-20-14
Siemens Healthcare Diagnostics




SIEMENS



Anti-HBs2 (aHBs2)

Contents

REF	Contents
06521435	2 vials of Negative Control
	2 vials of Positive Control
	Expected Values Card and barcode labels

06521443 Rev. C, 2009-04

Intended Use

For *in vitro* diagnostic use in monitoring the performance of the Anti-HBs2 assay on the ADVIA Centaur® Systems. The performance of the Anti-HBs2 quality control material has not been established with any other anti-HBs assays.

Control Description

Volume	Ingredients	Storage	Stability
10.0 mL/vial	Processed human plasma negative and positive for antibodies to HBsAg with preservatives	2–8°C	Until the expiration date on the vial label or onboard—8 hours



CAUTION! POTENTIAL BIOHAZARD: The controls 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.¹⁻³ Use eye protection and gloves when handling this product; wash hands after handling.

The controls have 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.

For *in vitro* diagnostic use.

Preparing the Quality Control Material

Gently swirl and invert the vials to ensure homogeneity.

Using the 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 Anti-HBs2 quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur Anti-HBs2 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 Quality Control

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

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.

- Schedule the quality control samples to the worklist.
- Label two sample cups with quality control barcode labels: one for the positive, and another for the negative.

NOTE: Each drop from the control vial is approximately 35 to 40 µL.

- Gently mix the quality control materials and dispense at least 8 to 10 drops into the appropriate sample cups.
- Load the sample cups in a rack.
- Place the rack in the sample entry queue.
- Ensure that the assay reagents are loaded.
- 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.

Reviewing, Editing, and Printing Results

For detailed information about reviewing, editing, and printing quality control results, refer to the system operating instructions or to the online help system.

Expected Results

Refer to the *Expected Values* card for the assigned values specific for the lot number of the Anti-HBs2 quality control material. The expected values are traceable to the standardization of the Anti-HBs2 assay. For additional information, refer to the reagent instructions for use.

The expected values should be used only as a guide in evaluating performance. Because performance is subject to the design and condition of each instrument or reagent system, it is recommended that each laboratory establish its own expected values and acceptable limits. The mean values established should fall within the range specified in *Expected Values*. Individual results may fall outside the range.

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.

Limitations

The results obtained using the Anti-HBs2 quality control material depend on several factors. Erroneous results can occur from improper storage, inadequate mixing, or sample handling errors associated with system or assay procedures.

- Do not return any quality control materials back into the vials after testing because evaporation and contamination can occur, which may affect results.
- Dispose of any quality control material 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.

Disposal

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 all federal, state, and local requirements.

Technical Assistance

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

www.siemens.com/diagnostics

References

- Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline - Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2004. NCCLS Document H18-A3.
- Centers for Disease Control. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR* 1988;37:377-82, 387-8.
- Clinical and Laboratory Standards Institute (formerly NCCLS). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline - Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document M29-A3.

ADVIA Centaur is a trademark of Siemens Healthcare Diagnostics.

© 2008 Siemens Healthcare Diagnostics Inc. All rights reserved.

The following symbols may appear on the product labeling: / Les symboles suivants peuvent apparaître sur les étiquettes des produits: / Die folgenden Symbole können auf dem Produktetikett verwendet werden: / Sulle etichette del prodotto possono essere presenti i seguenti simboli: / Los siguientes símbolos pueden aparecer en la etiqueta del producto: / Os seguintes símbolos podem aparecer no rótulo dos produtos: / Følgende symboler kan forekomme på produktmærkningen: / Føljande symboler kan förekomma på produktetiketten: / Τα ακόλουθα σύμβολα ενδέχεται να εμφανίζονται στην επισήμανση του προϊόντος: / Følgende symboler kan stå på produktmerkingen: / 製品のラベルには次の記号が使用される場合があります:

Symbol	Definition	Symbol	Definition	Symbol	Definition
	En: In vitro diagnostic medical device Fr: Dispositif médical de diagnostic in vitro De: Medizinisches Gerät zur In-vitro Diagnose It: Dispositivo medico per diagnostica in vitro Es: Dispositivo médico para diagnóstico in vitro Pt: Dispositivo médico para diagnóstico in vitro Da: Medicinsk in vitro-diagnostiseringsenhed Sv: Medicinsk utrustning för in vitro-diagnostik El: in vitro διαγνωστική ιατρική συσκευή No: Medicinsk utstyr til in vitro diagnostisk Ja: 体外診断用医薬品		En: Caution! Potential Biohazard Fr: Avertissement! Risque biologique potentiel De: Vorsicht! Biologisches Risikomaterial It: Attenzione! Potenziale Pericolo Biologico Es: ¡Precaución! Peligro Biológico Potencial Pt: Precaução! Potenciais Riscos Biológicos Da: Advarsel! Potentielt biologisk smittefare Sv: Viktigt! Potentiellt biologisk smittofara El: Προσοχή! Διυνητικός βιολογικός κίνδυνος No: Forsiktig! Potensielt biologisk smittefare Ja: 注意! バイオハザードの可能性がります		En: Contains sufficient for (n) tests Fr: Suffisant pour (n) tests De: Es reicht für (n) tests It: Contiene materiale sufficiente per (n) test Es: Contiene material para (n) pruebas Pt: Contém o suficiente para (n) testes Da: Indhold tilstrækkeligt til (n) tests Sv: Räcker till (n) antal tester El: Περιεχόμενο επαρκές για (n) εξετάσεις No: inneholder nok til (n) analyser Ja: nテスト回数分の十分な量が入っています
REF	En: Catalog Number Fr: Numéro de référence catalogue De: Katalog-Nummer It: Numero catalogo Es: Número de referencia Pt: Número de catálogo Da: Katalognummer Sv: Katalognummer El: Αριθμός καταλόγου No: Katalognummer Ja: カタログ番号		En: Temperature limitation (2-8°C) Fr: Limites de température (2-8°C) De: Temperaturgrenze (2-8°C) It: Limiti di temperatura (2-8°C) Es: Limitación de la temperatura (2-8°C) Pt: Limites de temperatura (2-8°C) Da: Temperaturbegrensning (2-8°C) Sv: Förvaringstemperatur (2-8°C) El: Περιορισμός θερμοκρασίας (2-8°C) No: Temperaturgrense (2-8°C) Ja: 限界温度 (2-8°C)		En: Green dot Fr: Point vert De: Grüner Punkt It: Punto verde Es: Punto verde Pt: Ponto Verde Da: Der Grüne Punkt Sv: Gröna punkten El: Πρόσβηη κουκκίδη No: Grønt punkt Ja: グリーンドット
	En: Manufacturer Fr: Fabricant De: Hersteller It: Produttore Es: Fabricante Pt: Fabricante Da: Producent Sv: Tillverkare El: Κοσσκευαστής No: Produsent Ja: 製造元		En: Upper limit of temperature ($\le -20^{\circ}\text{C}$) Fr: Limite supérieure de température ($\le -20^{\circ}\text{C}$) De: Obere Temperaturgrenze ($\le -20^{\circ}\text{C}$) It: Limite superiore di temperatura ($\le -20^{\circ}\text{C}$) Es: Limitación superior de la temperatura ($\le -20^{\circ}\text{C}$) Pt: Limite máximo de temperatura ($\le -20^{\circ}\text{C}$) Da: Øvre temperaturbegrensning ($\le -20^{\circ}\text{C}$) Sv: Högsta temperatur ($\le -20^{\circ}\text{C}$) El: Ανώτερο όριο θερμοκρασίας ($\le -20^{\circ}\text{C}$) No: Øvre temperaturgrense ($\le -20^{\circ}\text{C}$) Ja: 最高保存温度 ($\le -20^{\circ}\text{C}$)		En: Store upright Fr: Conserver en position verticale De: Aufrecht lagern It: Conservare in posizione verticale Es: Conservar en posición vertical Pt: Armazenar em posição vertical Da: Opbevares oprejst Sv: Förvaras stående El: Φυλάσσετε σε όρθβη θέση No: Oppbevares stående Ja: 立てて保管してください
EC REF	En: Authorized Representative in the European Community Fr: Représentant agréé pour l'Union européenne De: Autorisierte Vertretung in der Europäischen Union It: Rappresentante autorizzato nella Comunità europea Es: Representante autorizado en la Unión Europea Pt: Representante Autorizado na Comunidade Europeia Da: Autoriseret representant i EU Sv: Auktoriserad representant inom europeiska gemenskapen El: Εξουσιοδοτημένος αντιπρόσωπος στην Ευρωπαϊκή Κοινότητα No: Autorisert representant i EU Ja: ヨーロッパ地区の正規代理店		En: Lower limit of temperature ($\ge 2^{\circ}\text{C}$) Fr: Limite inférieure de température ($\ge 2^{\circ}\text{C}$) De: Mindesttemperatur ($\ge 2^{\circ}\text{C}$) It: Limite inferiore di temperatura ($\ge 2^{\circ}\text{C}$) Es: Temperatura mínima ($\ge 2^{\circ}\text{C}$) Pt: Limite inferior de temperatura ($\ge 2^{\circ}\text{C}$) Da: Nedre temperaturgrense ($\ge 2^{\circ}\text{C}$) Sv: Lägsta temperatur ($\ge 2^{\circ}\text{C}$) El: Κατώτερο όριο θερμοκρασίας ($\ge 2^{\circ}\text{C}$) No: Nedre temperaturgrense ($\ge 2^{\circ}\text{C}$) Ja: 最低保存温度 ($\ge 2^{\circ}\text{C}$)	2008-01	En: Date format (year-month) Fr: Format de la date (année-mois) De: Datumformat (Jahr-Monat) It: Formato data (anno-mese) Es: Formato de fecha (año-mes) Pt: Formato de data (ano-mês) Da: Datoformat (år-måned) Sv: Datumformat (år-månad) El: Μορφή ημερομηνίας (έτος-μήνας) No: Datoformat (år-måned) Ja: 日付形式 (年-月)
CE	En: CE Mark Fr: Marque CE De: CE-Kennzeichen It: Marchio CE Es: Símbolo de la CE Pt: Marca CE Da: CE-mærke Sv: CE-märke El: Σήμαση CE No: CE-merke Ja: CE マーク		En: Do not freeze ($> 0^{\circ}\text{C}$) Fr: Ne pas congeler ($> 0^{\circ}\text{C}$) De: Nicht einfrieren ($> 0^{\circ}\text{C}$) It: Non congelare ($> 0^{\circ}\text{C}$) Es: No congelar ($> 0^{\circ}\text{C}$) Pt: Não congele ($> 0^{\circ}\text{C}$) Da: Må ikke nedfrys ($> 0^{\circ}\text{C}$) Sv: Får ej frysas ($> 0^{\circ}\text{C}$) El: Μην καταψυχετε ($> 0^{\circ}\text{C}$) No: Må ikke fryse ($> 0^{\circ}\text{C}$) Ja: 冷凍を禁じていることを示します ($> 0^{\circ}\text{C}$)		En: Recycle Fr: Recyclage De: Recyceln It: Riciclo Es: Reciclar Pt: Reciclar Da: Genbrug Sv: Kan återvinnas El: Ανακυκλώσει No: Kan gjenvinnas Ja: リサイクル
CE 0088	En: CE Mark with identification number of notified body Fr: Marque CE avec numéro d'identification du corps notifié De: CE-Kennzeichen Identifikationsnummer der benannten Stelle It: Marchio CE con numero identificativo dell'ente notificato Es: Marca de la CE con número de identificación del organismo notificado Pt: Marca CE, com número de identificação do órgão notificado Da: CE-mærke med id-nummer på underrettet myndighed Sv: CE-märke med identifieringsnummer på tillståndsmyndighet El: Σήμαση CE με αριθμό αναγνώρισης του φορέα πιστοποίησης No: CE-merke med ID-nummer for teknisk kontrollorgan Ja: 認定機関 (Notified Body) の認購番号付き CE マーク		En: Keep away from sunlight Fr: Maintenir hors de portée de la lumière du soleil De: Vor Sonneneinstrahlung schützen It: Non esporre alla luce del sole Es: Mantener protegido de la luz solar Pt: Manter protegido da luz solar Da: Undgå direkte sollys Sv: Skyddas mot solljus El: Διατηρείται μακριά από το ηλιακό φως No: Undgå direkte sollys Ja: 日の当たらない場所に保管してください		En: Printed with soy ink Fr: Imprimé avec de l'encre de soja De: Gedruckt mit Sojafarbe It: Stampato con inchiostro di soia Es: Imprimido con tinta de soja Pt: Impresso com tinta de soja Da: Trykt med sojablæk Sv: Tryckt med sojabläck El: Εκτυπώνεται με μελιάνι σόγιας No: Trykt med soyablæk Ja: 大豆インキで印刷されています
LOT	En: Batch code Fr: Numéro de code du lot De: Chargenbezeichnung It: Codice lotto Es: Código de lote Pt: Código de lote Da: Batchkode Sv: Tillverkningskod El: Κωδικός παρτίδας No: Lotnummer Ja: バッチコード		En: Use by Fr: A utiliser avant De: Verwendbar bis It: Usare entro Es: Fecha de caducidad Pt: Use até Da: Brug af Sv: Utgångsdatum El: Ημερομηνία λήξης No: Bruk før Ja: 使用期限		

Suomi



VAROITUS! MAHDOLLINEN TARTUNTAVAARA: Sisältää ihmiskudoksista peräisin olevaa materiaalia. Kaikki tämän tuotteen valmistuksessa käytetyt ihmisseerumi- tai veriplasmaprojektit on testattu FDA-säännösten mukaisin menetelmin. Testeissä todettiin, että yksiköt eivät sisältäneet hepatiitti B -pinta-antigeeniä (HBsAg) tai hepatiitti C (HCV)- tai HIV-1/2-viruksen vasta-aineita. Tästä huolimatta on huomioitava, että kaikkia ihmismateriaaleista valmistettuja tuotteita on käsiteltävä mahdollisesti tartuttavina aineina. Koska yhdelläkään testausmenetelmällä ei voida tunnistaa hepatiitti B-, hepatiitti C- ja HIV-virusta tai muita taudinaiheuttajia täysin varmasti, näitä tuotteita on käsiteltävä hyvien laboratoriotyökäytäntöjen mukaisesti.¹⁻³ Käytä silmäsuojuksia ja suojakäsineitä käsitellessäsi tuotetta, pese kädet käsitteilyn jälkeen. Kontrollit on analysoitu FDA:n hyväksymillä menetelmillä ja havaittu ei-reaktiivisiksi hepatiitti B -pinta-antigeenille (HBsAg), hepatiitti C vasta-aineelle (HCV), HIV-1/2 vasta-aineelle.

Polski



OSTRZEŻENIE! POTENCJALNE ZAGROŻENIE BIOLOGICZNE: Produkt zawiera materiał pochodzenia ludzkiego. Chociaż każda jednostka oddawanej surowicy lub osocza krwi ludzkiej wykorzystywana w produkcji tego produktu została przebadana metodami zatwierdzonymi przez FDA i stwierdzono, że nie są reaktywne w stosunku do antygeny powierzchniowego zapalenia wątroby typu B (HBsAg) oraz stanowią przeciwciała dla wirusa zapalenia wątroby typu C (HCV) i wirusa HIV-1/2, to wszystkie produkty wytwarzane przy wykorzystaniu materiału biologicznego pochodzenia ludzkiego i innego powinny być traktowane jako potencjalnie chorobotwórcze. Ponieważ żadna metoda badań nie daje całkowitej pewności braku obecności wirusa zapalenia wątroby typu B lub C, wirusa HIV czy innego czynnika chorobotwórczego, przy pracy z takimi produktami należy przestrzegać ogólnie przyjętych zasad pracy laboratoryjnej.¹⁻³ Podczas obchodzenia się z produktem należy stosować ochronę oczu i nosić rękawice. Po zakończeniu procedury należy umyć ręce. Kontrole zostały zbadane za pomocą metod zatwierdzonych przez FDA i stwierdzono, że są niereaktywne w zakresie antygeny powierzchniowego wirusowego zapalenia wątroby typu B (HBsAg), przeciwciał przeciwko wirusowemu zapaleniu wątroby typu C (HCV) i przeciwciał przeciwko wirusowi HIV 1/2.

Origin: US



Siemens Healthcare Diagnostics Inc.
Tarrytown, NY 10591-5097 USA



Siemens Healthcare Diagnostics Ltd.
Sir William Siemens Sq.
Firmley, Camberley, UK GU16 8QD

Siemens Healthcare
Diagnostics Pty Ltd
ABN 65 007 436 651
885 Mountain Highway
Bayswater Victoria 3153
Australia

シーメンスヘルスケア
ダイアグノスティクス株式会社
東京都品川区東五反田 3-20-14
Siemens Healthcare Diagnostics
