SIEMENS

CE 0197

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Anti-HBs2 (aHBs2)

Assay for the Detection of Antibodies to Hepatitis B Surface Antigen

Current revision and date [a]	Rev. N, 2021-06	
Product Name	ADVIA Centaur® anti-HBs2 assay	**REF** 04670661
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur anti-HBs2 Quality Control Material ADVIA Centaur Wash 1 (2 x 1500 mL) ADVIA Centaur Wash 1 (2 x 2500 mL)	**REF** 06521435 **REF** 01137199 **REF** 03773025
Specimen Types	Serum, EDTA plasma, Heparinized plasma	
Assay Range	3.1–1000 mIU/mL	
Reagent Storage	2–8°C	
Reagent On-System Stability	90 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® anti-HBs2 (aHBs2) assay is an *in vitro* diagnostic immunoassay for the qualitative and quantitative determination of total antibodies to hepatitis B surface antigen in human serum or plasma (EDTA or heparinized) using the ADVIA Centaur® XP and ADVIA Centaur® XPT 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.

Summary and Explanation

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. 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]

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]

Principles of the Procedure

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

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur aHBs2 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	**Unopened:** Stable until the expiration date on the carton **On-system:** 90 days
ADVIA Centaur aHBs2 ReadyPack primary reagent pack; Solid Phase Reagent	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	**Unopened:** Stable until the expiration date on the carton **On-system:** 90 days
ADVIA Centaur aHBs2 ReadyPack primary reagent pack; Ancillary Reagent	5.0 mL/reagent pack non-magnetic latex particles in tris buffer with surfactant and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 90 days
ADVIA Centaur aHBs2 Calibrator	2.0 mL/vial processed human plasma positive for antibodies to HBsAg with preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 8 hours
ADVIA Centaur aHBs2 Quality Control Material [a]	10.0 mL/vial processed human plasma negative and positive for antibodies to HBsAg with preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 8 hours
ADVIA Centaur Wash 1 [a] 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 [a] 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
ADVIA Centaur ReadyPack ancillary reagent pack; Multi-Diluent 11 [b] M-DIL 11	5.0 mL/pack tris buffer and goat serum with protein stabilizers and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 28 consecutive days after accessing the ancillary reagent pack
ADVIA Centaur Multi-Diluent 11 [b] M-DIL 11	10.0 mL/vial tris buffer and goat serum with protein stabilizers and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial

a See *Materials Required but Not Provided*

b See *Optional Materials*

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 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.

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:** Microprotect; ADVIA Centaur aHBs2 Calibrator

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, efer to the system operating instructions.

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, EDTA plasma, or heparinized plasma 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 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 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 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 2–8°C up to 7 days.
- Store primary tube samples at 2–8°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. 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 7 days or refrigerated up to 7 days demonstrated no qualitative differences. Store samples stoppered at 2–8°C upon arrival. If during shipment, samples may be subjected to temperatures above 25°C, then ship samples 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
04670661	1 ReadyPack primary reagent pack containing ADVIA Centaur anti-HBs2 Lite Reagent, Solid Phase, and Ancillary Reagent ADVIA Centaur and ADVIA Centaur CP anti-HBs2 Master Curve cards 1 vial ADVIA Centaur anti-HBs2 low calibrator CAL L 1 vial ADVIA Centaur anti-HBs2 high calibrator CAL H ADVIA Centaur and ADVIA Centaur CP anti-HBs2 Calibrator Assigned Value cards	200

Materials Required but Not Provided

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

Item	Description	
REF 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
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

Optional Materials

The following materials may be used to perform this assay, but are not provided:

Item	Description	
REF 05699280 (117228)	ADVIA Centaur Multi-Diluent 11 M-DIL 11	2 ReadyPack ancillary reagent packs containing 5 mL/pack
REF 03479704 (111088)	ADVIA Centaur Multi-Diluent 11 M-DIL 11	10 mL/vial

Assay Procedure

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

The 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.

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.

Preparing the System

Ensure that the system has sufficient primary reagent. 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. For detailed information about loading reagents, refer to the system operating instructions.

Preparing the Samples

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, see 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 anti-HBs2 assay reagents are stable unopened until the expiration date on the carton or onboard the system for 90 days.

Performing 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.

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

   Note Each drop from the calibrator vial is approximately 35 to 40 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 42-day calibration interval.

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.

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 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.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

For quality control of the ADVIA Centaur anti-HBs2 assay, use ADVIA Centaur anti-HBs2 quality control material. 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 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.
3. Gently mix the quality control materials and dispense at least 8 to 10 drops into the appropriate sample cups.

   Note Each drop from the control vial is approximately 35 to 40 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 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.

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-HBs antibody results in mIU/mL and as reactive (positive), or nonreactive (negative) or as needing retest:

Dilutions

The following information pertains to dilutions:

- Samples with anti-HBs levels greater than 1000 mIU/mL (Index Value > 100) 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 (Index Value ≤ 100)

  Dilution factor: 2, 5, 10

  For detailed information about automatic dilutions, refer to the system operating instructions.
- 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

- Nonreactive: Samples with an initial value of less than 8 mIU/mL are considered nonreactive (negative) for antibodies to HBsAg.
- Reactive: Samples with an initial value greater than or equal to 12.0 mIU/mL are considered reactive (positive) for antibodies to HBsAg.
- Retest zone: Samples with an initial value greater than or equal to 8 mIU/mL and less than 12.0 mIU/mL will be flagged for retest. These samples should be retested in duplicate. After retesting, if at least two (2) results are greater than or equal to 10.0 mIU/mL, then the sample is considered to be reactive. If at least two (2) results are less than 10.0 mIU/mL, then the sample is considered to be nonreactive.
- Sample results are invalid and must be repeated if the controls are out of range.

Samples with calculated values of 10.0 mIU/mL or greater are considered reactive (positive) in accordance with the CLSI guidelines[7] and based on the WHO International Standard for anti-HBs serum as an indicator of immune status and a cutoff value to detect most seropositive persons. The cutoff for the ADVIA Centaur anti-HBs2 assay was verified based on correlation with WHO standard (1st International Reference Preparation-1977) and data generated from the results of the clinical studies.

Limitations

The following information pertains to limitations of the assay:

- The ADVIA Centaur anti-HBs2 assay is limited to the detection of antibodies to HBsAg in human serum or plasma (EDTA plasma or heparinized plasma).
- Assay performance characteristics have not been established when the ADVIA Centaur anti-HBs2 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 anti-HBs2 assay as an aid in determining susceptibility to HBV infection prior to or following vaccination in infants or children.
- 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.
- The performance of the ADVIA Centaur anti-HBs2 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.

Expected Values

In a population of 525 nonreactive samples, 522 were nonreactive (< 10 mIU/mL) using the ADVIA Centaur anti-HBs2 assay resulting in 99.4% relative specificity. In a population of 215 individuals reactive for anti-HBs (≥ 10.0 mIU/mL using a reference assay), 100% were reactive using the ADVIA Centaur anti-HBs2 assay.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[10]

Performance Characteristics

Analytical Measuring Range

The ADVIA Centaur anti-HBs2 assay measures concentrations of total antibodies to hepatitis B surface antigen from 3.1–1000 mIU/mL.

Clinical Sensitivity and Specificity

The performance of the ADVIA Centaur anti-HBs2 assay was evaluated by testing a total of 740 samples at 1 site. The samples included 105 samples from vaccinated individuals, 105 samples from naturally-infected individuals, and 530 samples from blood donors and hospitalized patients. The ADVIA Centaur anti-HBs2 results were compared to results generated using a commercially available automated anti-HBs assay. Discordant samples were retested in duplicate and if still discordant, the samples were tested using a second commercially available assay for anti-HBs to obtain a consensus result.

216 samples initially tested reactive using a commercially available anti-HBs assay. Of these, 0 required retesting, 215 were reactive, and 1 was nonreactive using the ADVIA Centaur anti-HBs2 assay. The initial relative sensitivity was 99.5%.

519 samples initially tested nonreactive using a commercially available anti-HBs assay. Of these, 5 required retesting, 1 was reactive, and 513 were nonreactive using the ADVIA Centaur anti-HBs2 assay. The initial relative specificity was 99.8%.

Five samples required repeat testing using a commercially available anti-HBs assay. Of these, 2 required further retesting, 0 were reactive, and 3 were nonreactive using the ADVIA Centaur anti-HBs2 assay.

Initial Relative Sensitivity and Relative Specificity

	Reference Anti-HBs Assay			
ADVIA Centaur anti-HBs2 Assay	**Reactive (≥ 12.5 mIU/mL)**	**Retest Zone (7.5–12.4 mIU/mL)**	**Nonreactive (< 7.5 mIU/mL)**	**Total**
Reactive (≥ 12 mIU/mL)	215	0	1	216
Retest Zone (8–11.9 mIU/mL)	0	2	5	7
Nonreactive (< 8 mIU/mL)	1	3	513	517
Total	**216**	**5**	**519**	**740**

Initial Relative Sensitivity = 99.5% (215/216); 95% Confidence Interval (CI) = 97.45–99.99%

Initial Relative Specificity = 99.8% (513/514); 95% CI = 98.92–100%

Total Re-Test Results = 0.95% (7/740)

Samples with discordant results were tested using a second commercially available anti-HBs assay. Consensus method agreement (agreement between 2 of the 3 assays used) determined resolution of the sample result. Samples falling within the Retest Zone (8–11.9 mIU/mL) were re-tested and interpreted as described under Interpretation of Results. After resolution the relative sensitivity and specificity were 100% and 99.4% respectively as shown in the following table:

Consensus (Resolved) Relative Sensitivity and Relative Specificity

	Consensus Anti-HBs Assay Results		
ADVIA Centaur anti-HBs2 Assay	**Reactive (≥ 10 mIU/mL)**	**Nonreactive (< 10 mIU/mL)**	**Total**
Reactive (≥ 10.0 mIU/mL)	215	3	218
Nonreactive (< 10.0 mIU/mL)	0	522	522
Total	**215**	**525**	**740**

Resolved Relative Sensitivity = 100% (215/215); 95% CI = 98.30–100%

Resolved Relative Specificity = 99.4% (522/525); 95% CI = 98.34–99.88%

Precision

Precision was evaluated according to the CLSI protocol EP5-A2.[11] Samples were assayed in 2 replicates 2 times a day for at least 16 days. The following results were obtained from testing performed on 2 ADVIA Centaur systems:

Sample	Mean (mIU/mL)	Within-run		Between run		Total	
		SD	CV(%)	SD	CV(%)	SD	CV(%)
Negative Control	< 1.00	0.52	NA [a]	0.21	NA	0.56	NA
Positive Control	117.88	1.78	1.5	1.61	1.4	2.80	2.4
Serum 1	5.98	0.26	4.3	0.30	5.0	0.47	7.8
Serum 2	10.90	0.36	3.3	0.36	3.3	0.61	5.6
Serum 3	20.81	0.52	2.5	0.53	2.5	0.83	4.0
Serum 4	113.44	2.13	1.9	2.04	1.8	3.19	2.8
Serum 5	373.49	6.02	1.6	6.67	1.8	9.64	2.6
Serum 6	565.07	8.69	1.5	14.50	2.6	18.34	3.2
Lithium heparin plasma 1	6.84	0.31	4.5	0.20	2.9	0.38	5.6
Lithium heparin plasma 2	15.86	0.53	3.3	0.36	2.3	0.78	4.9
Lithium heparin plasma 3	18.15	0.35	2.0	0.45	2.5	0.58	3.2
Lithium heparin plasma 4	148.15	3.29	2.2	7.77	5.2	8.52	5.8
Lithium heparin plasma 5	487.36	9.15	1.9	19.25	4.0	21.51	4.4
Lithium heparin plasma 6	745.50	13.65	1.8	28.85	3.9	32.88	4.4
Sodium heparin plasma 1	4.98	0.23	4.7	0.16	3.2	0.36	7.2
Sodium heparin plasma 2	13.96	0.27	1.9	0.40	2.9	0.55	4.0
Sodium heparin plasma 3	24.04	0.58	2.4	0.75	3.1	0.99	4.1
Sodium heparin plasma 4	176.68	3.57	2.0	5.75	3.3	7.83	4.4
Sodium heparin plasma 5	369.16	6.79	1.8	10.91	3.0	13.08	3.5
Sodium heparin plasma 6	807.96	14.15	1.8	20.88	2.6	25.64	3.2
EDTA plasma 1	13.63	0.37	2.7	0.36	2.6	0.51	3.7
EDTA plasma 2	14.94	0.40	2.7	0.41	2.8	0.59	3.9
EDTA plasma 3	24.06	0.71	3.0	1.54	6.4	1.70	7.0
EDTA plasma 4	154.62	3.29	2.1	7.03	4.5	8.22	5.3
EDTA plasma 5	493.80	8.26	1.7	21.43	4.3	22.96	4.7
EDTA plasma 6	642.37	13.79	2.1	30.05	4.7	33.08	5.2

a NA = Not Applicable

Seroconversion Panels

To demonstrate the ability of the ADVIA Centaur anti-HBs2 assay to detect and monitor the immune response to natural infection, 10 seroconversion panels were tested at the clinical trial sites to determine the seroconversion sensitivity of the assay. The performance of the ADVIA Centaur anti-HBs2 assay on the seroconversion panels closely matched the performance of the reference assay. The following results were obtained:

		Bleed Number of First Result ≥ 10 mIU/mL	
		ADVIA Centaur anti-HBs2 Assay	**Reference Assay**
Panel ID	**Type**	**Bleed Number**	**Bleed Number**
6281	Infected	11	11
6509	Infected	7	7
A	HBV Vaccine Specimen	3	3
B	HBV Vaccine Specimen	3	3
C	HBV Vaccine Specimen	3	3
D	HBV Vaccine Specimen	3	3
E	HBV Vaccine Specimen	3	3
F	HBV Vaccine Specimen	3	3
G	HBV Vaccine Specimen	2	2
PHM935B	Infected	31	31

Interferences

Serum specimens that are or contain...	**Demonstrate a ≤ 15% change in results or have an insignificant effect on the assay 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 [a]
hyper IgG	6 g/dL of immunoglobulin G
biotin	3521 ng/mL of biotin

a Demonstrate ≤ 15% change in results with protein as low as 3.0 g/dL.

Interference testing was determined according to CLSI Document EP7-A2.[12]

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 anti-HBs reference assay. The following results were obtained using the ADVIA Centaur anti-HBs2 assay:

	ADVIA Centaur anti-HBs2 Results		
Clinical Category	**Number Tested**	**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
Toxoplasma gondii 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**

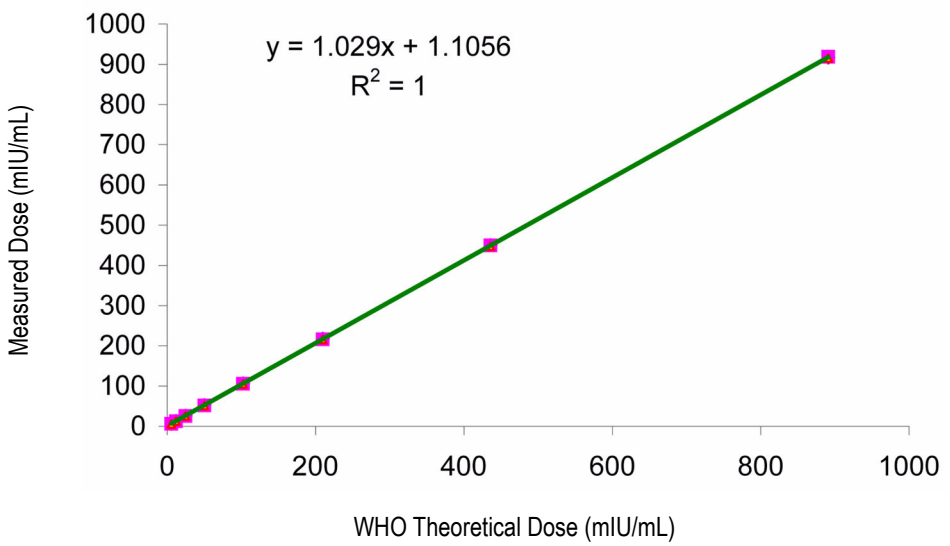
High-Dose Hook Effect

Patient samples with high levels of antibodies to HBsAg can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with levels of antibodies to HBsAg as high as 200,000 mIU/mL will assay greater than 1000 mIU/mL.

Standardization

The ADVIA Centaur anti-HBs2 assay is standardized against the World Health Organization (WHO) 1st International Reference Preparation (1977). The WHO standards were diluted serially in a negative plasma pool. Each dilution was tested in triplicate in the ADVIA Centaur anti-HBs2 assay. A representative correlation is shown with slope, y-intercept, correlation coefficient, and 95% confidence intervals.

Correlation of ADVIA Centaur anti-HBs2 Standards to 1st IRP WHO.



Technical Assistance

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

siemens.com/healthcare

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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 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
0°C	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat	UP	Up
	Use by	Σ (n)	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	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink

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