

# Hepatitis B e Antigen (HBeAg)

## Assay for the Detection of Hepatitis B e Antigen

### Assay Summary

Sample Type	Serum, potassium EDTA plasma, lithium-heparinized or sodium-heparinized plasma
Sample Volume	100 µL
Calibrator	HBeAg

### Contents

REF	Contents	Number of Tests
01512127	1 ReadyPack® primary reagent pack containing ADVIA Centaur® HBeAg Solid Phase, Lite Reagent, and Ancillary Reagent ADVIA Centaur HBeAg Master Curve card 1 vial HBeAg Low Calibrator <input type="checkbox"/> CAL L 1 vial HBeAg High Calibrator <input type="checkbox"/> CAL H ADVIA Centaur HBeAg Calibrator Assigned Value card	50

### Intended Use

The ADVIA Centaur HBeAg assay is an *in vitro* diagnostic immunoassay for the qualitative determination of the hepatitis B e antigen (HBeAg) in human serum and plasma (potassium EDTA, lithium, or sodium heparin) from individuals who have signs and symptoms of hepatitis or who may be at risk for hepatitis B virus (HBV) infection using the ADVIA Centaur and ADVIA Centaur XP systems. This assay, in conjunction with other serological and clinical information, is intended only for the determination of chronic infection with hepatitis B virus.

**CAUTION:** United States federal law restricts this device for sale by or on the order of a physician.

**WARNING:** This assay has not been FDA-approved for the diagnosis of individuals with acute Hepatitis B infection.

This assay should not be used to test cord blood samples.

Assay performance characteristics have not been established for testing of children less than 17 years of age or in populations of immunocompromised or immunosuppressed patients.<sup>1</sup> Users are responsible for establishing their own assay performance characteristics in these populations.

This assay has not been licensed for the screening of blood, plasma, and tissue donors.

### Materials Required but Not Provided

REF	Description	Contents
	ADVIA Centaur or ADVIA Centaur XP system	
06981117	ADVIA Centaur HBeAg quality control material	1 x 10.0 mL Negative Control <input type="checkbox"/> CONTROL - 1 x 10.0 mL Positive Control <input type="checkbox"/> CONTROL + Expected Value card
01137199 (112351)	ADVIA Centaur Wash 1 <input type="checkbox"/> WASH 1	2 x 1500 mL/pack
	or	
03773025	ADVIA Centaur Wash 1 <input type="checkbox"/> WASH 1*	2 x 2500 mL/pack
03333963	ADVIA Centaur Probe Wash 3 <input type="checkbox"/> PW 3	50.0 mL

- \* for use with systems with 2500 mL capacity

## Optional Reagents

REF	Description	Contents
05440554 (117227)	ADVIA Centaur Multi-Diluent 10 <span style="border: 1px solid black; padding: 0 2px;">M-DIL 10</span>	2 ReadyPack ancillary reagent packs containing 5 mL/pack
04302166 (112370)	Multi-Diluent 10 <span style="border: 1px solid black; padding: 0 2px;">M-DIL 10</span>	10 mL/vial

## Summary and Explanation of the Test

The ADVIA Centaur HBeAg assay is an antibody-capture microparticle chemiluminometric immunoassay used to detect human hepatitis B e 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 sexually 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.<sup>1,2,3</sup>

The detection of HBe antigen in serum and plasma is an indicator of active infection and replicating virus. The disappearance of HBeAg and the appearance of anti-HBe together with other HBV markers allow the clinician to determine a prognosis, and to follow the progression of the disease from acute to chronic or recovered status. The HBeAg assay is intended for use as an aid in the diagnosis of patients with hepatitis B viral infection, when used in conjunction with results from other HBV marker assays.<sup>1,4,5</sup>

## Assay Principle

The ADVIA Centaur HBeAg assay is an antibody sandwich (antibodies bridged by an antigen present in a sample) two wash immunoassay. The solid phase contains a preformed complex of streptavidin-coated microparticles and biotinylated anti-HBe monoclonal antibody and is used to capture HBeAg from patient sample. Lite reagent contains anti-HBe monoclonal antibody labeled with acridinium ester and is used to detect HBeAg in the sample.

The system will wash the reagent probe with PW3 to mitigate potential interference between the ADVIA Centaur HBeAg assay and other assays.

Solid phase is added to the sample, followed by Lite reagent. Antibody-antigen complexes form if HBeAg is present in the sample.

The ADVIA Centaur and ADVIA Centaur XP systems automatically perform the following actions:

- Dispenses 100 µL of sample into a cuvette and incubates for 6 minutes at 37°C
- Dispenses 100 µL of ancillary reagent and 250 µL of solid phase reagent and incubates for 18 minutes at 37°C
- Washes the cuvette with Wash 1
- Dispenses 100 µL of Lite reagent, incubates the mixture for 18 minutes at 37°C
- Separates the Solid Phase from the mixture and aspirates the unbound reagent

- Washes the cuvette with Wash 1
- Dispenses 300  $\mu$ L 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 HBeAg activity present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of reactive or nonreactive is determined according to a cutoff of 1.0 Index Value established with the calibrators. Refer to *Interpretation of Results* for a description of the Cutoff Value calculation.

## Specimen Collection and Handling

Serum, potassium EDTA plasma, and lithium-heparinized or sodium-heparinized plasma are the recommended sample types for this assay.

Do not use heat-inactivated specimens. Do not use specimens with obvious microbial contamination. The performance of the ADVIA Centaur HBeAg 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 fluid, or pleural fluid.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS),<sup>6</sup> and augmented with additional sample handling studies using the ADVIA Centaur HBeAg 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 red cells. The centrifugation step may occur up to 24 hours post-draw. When testing 10 samples where the centrifugation step was varied up to 24 hours post-draw, no clinically significant differences were observed.
- Test samples as soon as possible after collecting. Store samples at 2° to 8°C if not tested immediately.
- Store samples in primary tubes or devoid of red blood cells at 2° to 8°C up to 7 days. 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 1 year. Do not store in a frost-free freezer. When 10 samples were subjected to 3 freeze/thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge at 10,000 x g for 2 minutes 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 24 hours or refrigerated up to 7 days demonstrated no qualitative differences. If there is a risk that samples will be subjected to temperatures above 25°C during shipment, 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.<sup>6</sup> (Example: 1500 x g for 10 minutes; follow tube manufacturer's recommendations)
- Samples are free of bubbles or foam.

## 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, see the system operator's guide.



Protect from sunlight.

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 light sources.

Reagent	Reagent	Volume	Ingredients	Storage	Stability
ADVIA Centaur HBeAg ReadyPack primary reagent pack	Solid Phase	14.0 mL/ reagent pack	Streptavidin-coated paramagnetic microparticles preformed with biotinylated mouse monoclonal anti-HBe (1 mg/L) in protein buffer, surfactant, sodium azide (<0.1%), preservatives.	2–8°C	Until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
	Lite Reagent	6.0 mL/ reagent pack	Acridinium ester conjugated mouse monoclonal anti-HBe in protein buffer, surfactant, sodium azide (<0.1%), preservatives.	2–8°C	Until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
	Ancillary Reagent	6.0 mL/ reagent pack	Non-magnetic latex particles in buffer with surfactant, sodium azide (< 0.1%), and preservatives.	2–8°C	Until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
HBeAg calibrator vials	Calibrators Low and High	2.0 mL/ vial	BSA buffer, preservatives, and rHBeAg diluted in a BSA buffer, sodium azide (< 0.1%), preservatives	2–8°C	Until the expiration date on the vial or onboard 8 hours.
HBeAg quality control material vials*	Controls Negative and Positive	10.0 mL/ vial	recalcified human plasma negative and positive for HBeAg, sodium azide (< 0.1%), preservatives	2–8°C	Until the expiration date on the vial or onboard 8 hours.
ADVIA Centaur <b>WASH 1</b> *	Wash 1	1500 mL/ pack or 2500 mL/ pack	phosphate buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	Until the expiration date on the bottle or onboard—1 month.
ADVIA Centaur Probe Wash 3 <b>PW 3</b> *	Probe Wash 3	50.0 mL/ pack	sodium hypochlorite (0.5%), sodium hydroxide (< 0.5%), pH 11.0	2–8°C	Until the expiration date on the pack label or onboard—100 days.

\* See Materials Required but Not Provided.

## Precautions and Warnings

For *in vitro* diagnostic use.

Safety data sheets (MSDS/SDS) available on [www.siemens.com/diagnostics](http://www.siemens.com/diagnostics).

**NOTE:** Sodium azide can react with copper and lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides, if disposal into a drain is in compliance with federal, state, and local requirements.



**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.<sup>7-9</sup>

The negative control has been assayed by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2. The positive control contains human plasma that may be reactive for HBsAg. The units were treated with a BPL-UV inactivation procedure, however, all products manufactured using human source material should be handled as potentially infectious.<sup>7-9</sup>

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

## 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, see 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 Calibrator card provided in this kit is 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
60 days	30 days

Additionally, the ADVIA Centaur HBeAg assay requires a 2-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 HBeAg assay requires a Master Curve calibration when using a new lot number of Lite Reagent, Solid Phase, and Ancillary Well Reagent. For each new lot number of Lite Reagent, Solid Phase, and Ancillary Well Reagent, use the bar-code 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 HBeAg assay, use ADVIA Centaur HBeAg Calibrators provided with each kit. The calibrators provided in this kit are matched to the ReadyPack primary reagent pack.

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

### Using Bar-code Labels

**NOTE:** Calibrator bar-code labels are lot-number specific. Do not use bar-code labels from one lot of calibrators with any other lot of calibrators.

Use the ADVIA Centaur HBeAg Calibrator bar-code labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur HBeAg assay. Place the bar-code 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 bar-code 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 duplicate.

1. Schedule the calibrators to the worklist.
2. Label 2 sample cups with calibrator bar-code labels: one for the low and another for the high.

**NOTE:** Each drop from the calibrator bottle is approximately 50  $\mu$ L.

3. Gently mix the Low and High Calibrators and dispense at least 9 drops into the appropriate sample cups. Avoid bubbles.
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 HBeAg assay, use ADVIA Centaur HBeAg quality control materials. Refer to the Expected Value card for the suggested expected values specific for the lot number of the positive and negative controls.

### Using Bar-code Labels

**NOTE:** Control bar-code labels are lot-number specific. Do not use bar-code labels from one lot of controls with any other lot of controls.

Use the ADVIA Centaur HBeAg quality control bar-code labels to identify the positive and negative sample cups when performing the ADVIA Centaur HBeAg assay. Place the bar-code 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 two levels of quality control material on each day 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 bar-code labels: one for the positive, and another for the negative.

**NOTE:** Each drop from the control vial is approximately 50  $\mu$ L.

3. Gently mix the quality control materials and dispense at least 9 drops into the appropriate sample cups. Avoid bubbles.
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:

- Consider the sample results invalid.
- 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.
- Investigate and determine the cause of the unacceptable control results.
- When the condition is corrected, retest the controls and confirm that the results are within acceptable limits.
- It is advisable to repeat all of the patient specimens before reporting results for this run.
- If necessary, contact your local technical support provider or distributor for assistance.

## **Sample Volume**

This assay requires 100  $\mu\text{L}$  of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, refer to the system operating instructions or to the online help system.

## **Assay Procedure**

For detailed procedural information, refer to the system operating instructions or to the online help system.

## **Procedural Notes**

### **Dilutions**

The following pertains to dilutions:

- Very highly reactive samples may generate a Signal 4 error. If you observe a Signal 4 error, dilute the sample and retest.
- Patient samples can be automatically diluted by the system, or prepared manually.
- For automatic dilutions, ensure that ADVIA Centaur Multi-Diluent 10 is loaded and set the system parameters as follows:

Dilution point:  $\leq 1000$  Index Value

Dilution factor: 100, 1000

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

- Use Multi-Diluent 10 to manually dilute patient samples, and then load the diluted sample in the sample rack, replacing the undiluted sample.

### **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.

## **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 system reports HBeAg results in Index Values and as reactive, nonreactive, or as needing retest.

- **Nonreactive:** Samples with an initial value Index value  $< 0.80$ . The patient is considered nonreactive (negative) for HBeAg. No further testing is necessary.
- **Reactive:** Samples with an initial value  $> 1.2$  Index Value. The patient is considered reactive (positive) for HBeAg. No further testing is necessary.
- **Retest Zone:** Samples with an initial value  $> 0.8$  and  $< 1.2$  Index Value. If results are within the retest zone after initial testing, samples are to be retested in duplicate. After retesting, if 3 results are available and 2 results are  $> 1.0$  Index, then the sample is considered to be reactive (positive). If 3 results are available and 2 results are  $< 1.0$  Index, then the sample is considered to be nonreactive (negative).

Sample results are invalid and must be repeated if the controls are out of range.

The cutoff for the ADVIA Centaur HBeAg assay was verified based on results of Receiver-Operator characteristics (ROC) Curve<sup>10</sup> and clinical agreement generated from clinical studies.

Very highly reactive samples may generate a Signal 4 error. If you observe a Signal 4 error, dilute the sample and retest.

## Limitations

- The ADVIA Centaur HBeAg assay is limited to the detection of antigen to HBV in human serum or plasma (potassium EDTA plasma, lithium-heparinized or sodium-heparinized plasma).
- The results from this or any other diagnostic kit should be used and interpreted only in the context of the overall clinical picture.
- A negative test result does not guarantee that HBeAg is not present. HBV mutants lacking the ability to produce HBeAg have been reported.<sup>x</sup> These may occur as 'escape' mutants in the presence of anti-HBe and such patients may be infectious.
- A reactive HBeAg result does not exclude co-infection by another hepatitis virus.
- The performance of the ADVIA Centaur HBeAg 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 ADVIA Centaur HBeAg assay has not been established for populations of immunocompromised or immunosuppressed patients.
- Do not use specimens with obvious microbial contamination.
- Heterophilic antibodies in human serum or plasma samples can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.<sup>11</sup> Routine exposure to animals or animal serum products can cause interference and anomalous values. Diagnosis may require additional information.

## Expected Results

The study population for the ADVIA Centaur HBeAg assay consisted of 1744 patients. Of these samples, 50 were collected retrospectively and 1694 were collected prospectively. Of the 1694 prospectives, 935 patients (55.2%) were from the population considered at risk for hepatitis (high risk) due to lifestyle, behavior, occupation, or known exposure events, 654 patients (38.6%) were from the signs and symptoms population and 105 patients (6.2%) were from the dialysis population. Fifty retrospectives, (100%) were from chronic patients. The study population was 25.1% Hispanic, 46.2% Caucasian, 17.5% Black, 6.5% Asian, and 4.8% from unknown or other ethnicity. The patients were nearly equally divided by sex (46.9% female, 51.8% male, and 1.4% unknown). The mean age was 44 years (range of 17 to 85 years).

Patients in the study population were from the following geographic regions: Florida (40.5%), Texas (48.5%), California (5.6%), Vietnam (2.9%), and elsewhere (2.6%).

**NOTE:** The data to classify the hepatitis B status was not available for 16 (0.95%) of these patients; they have been excluded from subsequent analyses. In addition, 2 (0.1%) apparently contaminated samples were excluded.

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

**Distribution of Study Population by Age Group and Gender (All Testing Sites)**

Age Range (Years)	Gender	Reactive <sup>a</sup>		Nonreactive <sup>b</sup>		Total
		(N)	(%) <sup>c</sup>	(N)	(%) <sup>c</sup>	(N)
0-16	Male	0		0		0
	Female	0		0		0
	Overall	0		0		0
17-20	Male	1	11.1	8	88.9	9
	Female	5	20.8	19	79.2	24
	Overall	6	18.2	27	81.8	33
21-29	Male	7	6.4	103	93.6	110
	Female	6	4.5	127	95.5	133
	Overall	13	5.3	230	94.7	243
30-39	Male	20	11.4	155	88.6	175
	Female	11	6.5	157	93.5	168
	Overall	31	9.0	312	91.0	343
40-49	Male	24	8.3	264	91.7	288
	Female	4	1.7	233	98.3	237
	Overall	28	5.3	497	94.7	525
50-59	Male	18	8.5	195	91.5	213
	Female	11	6.3	164	93.7	175
	Overall	29	7.5	359	92.5	388
60-69	Male	9	13.0	60	87.0	69
	Female	10	12.0	73	88.0	83
	Overall	19	12.5	133	87.5	152
≥70	Male	3	12.5	21	87.5	24
	Female	0	0	20	100.0	20
	Overall	3	6.8	41	93.2	44
Total	Male	82	9.2	806	90.8	888
	Female	47	5.6	793	94.4	840
	Overall	129	8.1	1599	92.5	1728

- Samples initially above the reportable range, with a result  $\geq 1.2$  Index, or with an initial result  $\geq 0.80$  Index and  $< 1.2$  Index followed by two repeat results where 2 of the 3 results are  $\geq 1.0$  Index.
- Samples initially below the reportable range, with a result  $< 0.80$  Index, or with an initial result  $\geq 0.80$  Index and  $< 1.2$  Index followed by two repeat results where 2 of the 3 results are  $< 1.0$  Index.
- Percents are for the numbers of reactives, equivocals, and nonreactives in a given row. If the total number of samples in the row is zero, - is entered.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.<sup>12</sup>

## Performance Characteristics

### Results by Specimen Classification

A total of 1678 patients was assessed with a serological hepatitis marker panel of commercially available, FDA- approved reference assays. The serological assessment included the following 6 HBV markers: hepatitis B virus surface antigen (HBsAg), hepatitis B virus e antigen (HBeAg), total antibody to hepatitis B virus core antigen (anti-HBc Total), IgM antibody to hepatitis B core antigen (anti-HBc IgM), total antibody to HBeAg (anti-HBe), and total antibody to hepatitis B virus surface antigen (anti-HBs) (quantitative). Testing of these specimens occurred at each study site. The individual ADVIA Centaur HBV assay result was compared to the reference HBV assay result and to the patient classification.

Each patient's HBV infection status was classified based on a single specimen and the reactive (+)/nonreactive(-) patterns of the 6 HBV reference 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 26 unique reference marker patterns observed using the ADVIA Centaur HBeAg assay. These patterns are presented in the following table:

### Classification by Reference Markers (All Testing Sites)

HBV Classification	HBV Reference Markers					
	HBsAg	HBeAg	HBcIgM	HBc Total	Anti-HBe	Anti-HBs
Chronic	+	+	+	+	-	+
Chronic	+	+	-	+	+	-
Chronic	+	+	-	+	-	+
Chronic	+	+	-	+	-	-
Chronic	+	-	-	+	+	+
Chronic	+	-	-	+	+	-
Chronic	+	-	-	+	-	+
Chronic	+	-	-	+	-	-
Early Recovery	-	-	+	+	+	+
Early Recovery	-	-	+	+	+	-
Early Recovery	-	-	+	+	-	-
Early Recovery	-	-	-	+	+	-
HBV Vaccine Response	-	-	-	-	-	+
Not previously infected	-	-	-	-	-	-
Recovered	-	-	-	+	-	+
Recovered	-	-	-	+	-	-
Recovery	-	-	-	+	+	+
Recovery	-	-	-	-	+	+
Uninterpretable	+	-	-	-	-	-
Uninterpretable	-	-	+	-	-	-
Uninterpretable	-	-	-	-	+	-
Uninterpretable	-	+	-	+	+	+
Uninterpretable	-	+	-	+	-	+
Uninterpretable	-	+	-	+	-	-
Uninterpretable	-	+	-	-	-	-
Unknown	+	-	-	-	+	-

\* + = Reactive and - = Nonreactive

NOTE: When the result was equivocal or indeterminate, it was assumed to be nonreactive (-) for classification purposes.

**Comparison of Results by Risk Groups for Hepatitis: ADVIA Centaur HBeAg Assay versus HBeAg Reference Assay (All Testing Sites)**

Risk Groups	Reference HBeAg Nonreactive		Reference HBeAg Reactive		Reference HBeAg Equivocal		Total
	ADVIA Centaur HBeAg Assay		ADVIA Centaur HBeAg Assay		ADVIA Centaur HBeAg Assay		
	Reactive	Nonreactive	Reactive	Nonreactive	Reactive	Nonreactive	
	N	N	N	N	N	N	N
Signs and Symptoms	19	583	42	3	0	0	647
High Risk <sup>a</sup>	11	901	12	2	0	0	926
Dialysis	2	102	0	1	0	0	105
<b>Total</b>	<b>32</b>	<b>1586</b>	<b>54</b>	<b>6</b>	<b>0</b>	<b>0</b>	<b>1678</b>

a. The High Risk Group includes the following subgroups: hepatitis history, hemophiliac, intravenous drug-user, transplant and/or transfusion, high-risk sex, healthcare worker, HIV-infected, other, unspecified.

**Comparison of Results**

A total of 1678 prospective samples were tested using the ADVIA Centaur HBeAg assay and a reference HBeAg assay for each HBV specimen classification. The following results were obtained:

**Comparison of Results in the Prospective Population by HBV Classification: ADVIA Centaur HBeAg Assay versus HBeAg Reference Assay (All Testing Sites)**

HBV Classification	Reference HBeAg Nonreactive		Reference HBeAg Reactive		Reference HBeAg Equivocal		Total <sup>a</sup>
	ADVIA Centaur HBeAg Assay		ADVIA Centaur HBeAg Assay		ADVIA Centaur HBeAg Assay		
	Reactive	Nonreactive	Reactive	Nonreactive	Reactive	Nonreactive	
	N	N	N	N	N	N	N
Chronic	6	57	52	0	0	0	115
Early Recovery	1	58	0	1	0	0	60
Recovery	6	141	0	0	0	0	147
Recovered	8	153	0	0	0	0	161
HBV Vaccine Response	13	352	0	2	0	0	367
Not Previously Infected	25	789	0	0	0	0	814
Uninterpretable	0	8	2	3	0	0	13
Unknown	0	1	0	0	0	0	1
<b>Total</b>	<b>59</b>	<b>1559</b>	<b>54</b>	<b>6</b>	<b>0</b>	<b>0</b>	<b>1678</b>

a. Total number of test results by HBV categories

A total of 50 chronic prospective samples were tested using the ADVIA Centaur HBeAg assay and a reference HBeAg assay. The following results were obtained:

**Comparison of Results in the Retrospective Population by HBV Classification: ADVIA Centaur HBeAg Assay versus HBeAg Reference Assay (All Testing Sites)**

HBV Classification	Reference HBeAg Nonreactive		Reference HBeAg Reactive		Reference HBeAg Equivocal		Total
	ADVIA Centaur HBeAg Assay		ADVIA Centaur HBeAg Assay		ADVIA Centaur HBeAg Assay		
	Reactive	Nonreactive	Reactive	Nonreactive	Reactive	Nonreactive	
Chronic	0	35	15	0	0	0	50

**Percent Agreement**

The agreement between the ADVIA Centaur HBeAg assay and a reference HBeAg assay for each HBV specimen classification is listed in the table, below. The reference assay has an equivocal zone, but the ADVIA Centaur assay does not. Therefore, the single sample equivocal on the reference assay is excluded from the agreement calculations (it was reactive on the ADVIA Centaur system).

**Prospective Population - Percent Agreement and Confidence Intervals: ADVIA Centaur HBeAg Assay versus HBeAg Reference Assay (All Testing Sites)**

HBV Classification	Positive Agreement		Negative Agreement	
	% (x/n) <sup>a</sup>	95% Confidence Interval	% (x/n) <sup>b</sup>	95% Confidence Interval
Chronic	100.0 (52/52)	93.2–100.0	90.5 (57/63)	80.4–96.4
Early Recovery	0.0 (0/1)	0.0–97.5	98.3 (58/59)	90.9–100.0
Recovery	- (0/0)	-	95.9 (141/147)	91.3–98.5
Recovered	- (0/0)	-	95.0 (153/161)	90.4–97.8
HBV Vaccine Response	0.0 (0/2)	0.0–84.2	96.4 (352/365)	94.0–98.1
Not Previously Infected	- (0/0)	-	96.9 (789/814)	95.5–98.0
Uninterpretable	40.0 (2/5)	5.3–85.3	100.0 (8/8)	63.1–100.0
Unknown	- (0/0)	-	100.0 (1/1)	2.5–100.0
<b>Total</b>	<b>90.0 (54/60)</b>	<b>79.5–96.2</b>	<b>96.4 (1559/1618)</b>	<b>95.3–97.2</b>

- a. x = the number of ADVIA Centaur HBeAg results that are confirmed reactive in agreement with the Reference HBeAg assay; n = the number of reactive Reference HBeAg results
- b. x = the number of ADVIA Centaur HBeAg results that are nonreactive in agreement with the Reference HBeAg assay; n = the number of nonreactive Reference HBeAg results

**Retrospective Population - Percent Agreement and Confidence Intervals: ADVIA Centaur HBeAg Assay versus HBeAg Reference Assay (All Testing Sites)**

HBV Classification	Positive Agreement		Negative Agreement	
	% (x/n) <sup>a</sup>	95% Confidence Interval	% (x/n) <sup>b</sup>	95% Confidence Interval
Chronic	100.0 (15/15)	78.2–100.0	100.0(35/35)	90.0–100.0

- a. x = the number of ADVIA Centaur HBeAg results that are confirmed reactive in agreement with the Reference HBeAg assay; n = the number of reactive Reference HBeAg results
- b. x = the number of ADVIA Centaur HBeAg results that are nonreactive in agreement with the Reference HBeAg assay; n = the number of nonreactive Reference HBeAg results

**Seroconversion Panels**

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

Panel ID	HBeAg Reactive Result From Initial Draw Date		Reference Assay vs ADVIA Centaur Assay
	Reference Assay (Days)	ADVIA Centaur Assay (Days)	Difference in Bleed Numbers <sup>a</sup>
RP-009	56	56	0
RP-016	11	11	0
11015	71	71	0
11024	50	50	0
6278	17	17	0
11004	49	49	0

- a. The difference in bleed numbers is relative to the reference assay. For example, a +2 means that the reference assay required 2 additional bleeds before reactivity was determined as compared to the time-point when ADVIA Centaur assay confirmed reactive.

**NOTE:** Panel PHM935B was also tested but both the Centaur and reference assays were positive for HBeAg on the first bleed date tested.

**Analytical Sensitivity**

To examine the analytical sensitivity of the ADVIA Centaur HBeAg assay, the Paul Ehrlich Institute (PEI) HBeAg reference sample was used to prepare a dilution series that was assayed using 2 ADVIA Centaur HBeAg reagent lots. Linear regression was used to determine the concentration of PEI reference sample that corresponds to the ADVIA Centaur HBeAg cut-off (Index Value = 1.00). The PEI International Unit (IU) concentration at the assay cut-off is less than 0.10 IU/mL.

**Precision**

Precision was evaluated according to the CLSI protocol EP5-A2.<sup>13</sup> A four-member panel and controls were assayed in 3 replicates 2 times per day for 20 days (n=120 for each sample) on two ADVIA Centaur systems. The following results were obtained:

Panel Member	Mean Index	Within Run		Between Run		Between Days		Total		Number of Observations
		SD	CV%	SD	CV%	SD	CV%	SD	CV%	
Control Negative	0.12	0.10	NA	0.11	NA	0.01	NA	0.15	NA	120
Control Positive	8.18	0.24	2.9	0.23	2.9	0.14	1.7	0.36	4.4	120
Panel Member 1	0.73	0.09	12.5	0.1	13.8	0	0	0.14	18.6	120
Panel Member 2	1.19	0.08	6.5	0.09	8	0.03	2.6	0.13	10.6	120
Panel Member 3	1.76	0.1	5.7	0.09	4.9	0.07	3.8	0.15	8.4	120
Panel Member 4	27.02	1.11	4.1	0.52	1.9	0.91	3.4	1.53	5.7	120
Panel Member 5	165.31	6.52	3.9	7.32	4.4	0	0	9.8	5.9	120

\* NA = Not applicable

**System Reproducibility**

System reproducibility was determined by testing a five member panel using three reagent lots, on three ADVIA Centaur systems at three sites over five days with two runs per day. Panel members were run in replicates of four in each run. The analysis of data was based on guidance from the CLSI document EP5-A2. Standard deviation and percent coefficient of variation (CV) were calculated for within run, between run, between testing site, between lot, and total precision component. The following results were obtained:

Panel Member	Mean Index	Within Run		Between Run		Among Site		Among Lot		Total		Number of Observations
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	
1	0.47	0.18	39.1	0.02	4.5	0.04	9.3	0.15	31.7	0.25	52.1	354*
2	1.10	0.15	13.5	0.06	5.1	0.04	3.2	0.08	7.4	0.19	17.1	360
3	1.89	0.20	10.5	0.06	3.2	0.09	4.8	0.02	1.2	0.23	12.2	360
4	28.30	1.10	3.9	0.32	1.1	1.21	4.3	2.02	7.1	2.65	9.4	360
5	216.98	7.74	3.6	2.17	1.0	9.72	4.5	19.52	9.0	23.38	10.8	360

\* Six replicates were below the range of the assay.

**Cross-Reactivity**

The ADVIA Centaur HBeAg assay was evaluated for potential cross-reactivity with viral antibodies and disease state specimens. The nonreactive HBeAg status of each specimen was verified using an HBeAg reference assay. The following results were obtained using the ADVIA Centaur HBeAg assay:

Clinical Category	Number Tested	ADVIA Centaur HBeAg Results	
		Nonreactive	Reactive
Hepatitis A Infection (HAV)	10	10	0
Hepatitis C Infection (HCV)	10	10	0
Autoimmune Disease (Rheumatoid Arthritis/ Systemic Lupus)	10	10	0
Epstein-Barr Virus (EBV) IgM	10	10	0
Herpes Simplex Virus (HSV) IgM	10	10	0
Syphilis IgM	10	10	0
Human Immunodeficiency Virus (HIV-1)	10	10	0
Varicella Zoster Virus (VZV) IgM	10	10	0
Rubella IgM	10	10	0
Cytomegalovirus (CMV) IgM	10	10	0
Toxoplasma	10	10	0
Flu Vaccine Recipients	10	10	0
Human anti-mouse antibody (HAMA)	10	10	0
Total Samples Tested	130	130	0

**Interference**

Interference testing was determined according to CLSI Document EP7-A2.<sup>14</sup>

The following endogenous substances were added to human based samples at the concentrations listed and evaluated for potential interference in the ADVIA Centaur HBeAg assay. The results demonstrate a  $\leq 10\%$  interference from each substance.

Serum and plasma specimens that are . . .	Demonstrate $\leq 10\%$ change in results up to . . .
icteric	60 mg/dL of conjugated bilirubin
icteric	40 mg/dL of unconjugated bilirubin
lipemic	3000 mg/dL of Intralipid
hemolyzed	500 mg/dL of hemoglobin
hypoproteinemic	3.5 g/dL of protein*
hyperproteinemic	12.0 g/dL of protein
biotin	100 mg/dL of biotin

\* Demonstrates  $\leq 10\%$  change in results with protein as low as 3.5 g/dL.

In addition, the following bacterial and recombinant viral antigens were spiked into HBeAg negative and positive serum and plasma specimens:

Spiked Material	Reactivity Before Spike	Reactivity After Spike
<b>Negative samples spiked with bacterial cross-reactants</b>		
<i>S. aureus</i> 1000 CFU/mL	Nonreactive	Nonreactive
<i>S. aureus</i> 10,000 CFU/mL	Nonreactive	Nonreactive
<i>P. aeruginosa</i> 1000 CFU/mL	Nonreactive	Nonreactive
<i>P. aeruginosa</i> 10,000 CFU/mL	Nonreactive	Nonreactive
<i>E. coli</i> 1000 CFU/mL	Nonreactive	Nonreactive
<i>E. coli</i> 10,000 CFU/mL	Nonreactive	Nonreactive
<b>HBeAg-positive samples spiked with bacterial cross-reactants</b>		
<i>S. aureus</i> 1000 CFU/mL	Reactive	Reactive
<i>S. aureus</i> 10,000 CFU/mL	Reactive	Reactive
<i>P. aeruginosa</i> 1000 CFU/mL	Reactive	Reactive
<i>P. aeruginosa</i> 10,000 CFU/mL	Reactive	Reactive
<i>E. coli</i> 1000 CFU/mL	Reactive	Reactive
<i>E. coli</i> 10,000 CFU/mL	Reactive	Reactive
<b>Negative samples spiked with viral cross-reactants</b>		
EBV 1 µg/mL	Nonreactive	Nonreactive
EBV 1 ng/mL	Nonreactive	Nonreactive
CMV 1 µg/mL	Nonreactive	Nonreactive
CMV 1 ng/mL	Nonreactive	Nonreactive
VZV 1 µg/mL	Nonreactive	Nonreactive
VZV 1 ng/mL	Nonreactive	Nonreactive
Rubella 1 µg/mL	Nonreactive	Nonreactive
Rubella 1 ng/mL	Nonreactive	Nonreactive
<b>HBeAg-positive samples spiked with viral cross-reactants</b>		
EBV 1 µg/mL	Reactive	Reactive
EBV 1 ng/mL	Reactive	Reactive
CMV 1 µg/mL	Reactive	Reactive
CMV 1 ng/mL	Reactive	Reactive
VZV 1 µg/mL	Reactive	Reactive
VZV 1 ng/mL	Reactive	Reactive
Rubella 1 µg/mL	Reactive	Reactive
Rubella 1 ng/mL	Reactive	Reactive

## Standardization

The ADVIA Centaur HBeAg assay standardization is based upon relative clinical agreement with commercially available HBeAg assays. The ADVIA Centaur HBeAg assay cutoff is set to detect acute, recent (usually 6 months or less), or chronic hepatitis B infection. Refer to *Performance Characteristics*. Assigned values for calibrators and controls are traceable to this standardization.

### Alternative Sample Types

The ADVIA Centaur HBeAg assay can use plasma specimens collected using either potassium EDTA, sodium heparin, or lithium heparin anticoagulants.

Fifty negative samples were collected in various tube types. Fifteen sets were spiked to obtain Index values between 1 and 10. Fifteen specimens were spiked to obtain Index values between 10 and 50 Index. Twenty sets remained negative (below Index 1.0). The percent difference between the serum Index value and the matched plasma Index value was calculated for each sample pair. The number of samples within a range of percent differences was then tabulated. The table below provides the number of positive sample pairs within each percent difference range. The percent differences were not tabulated for the negative samples because the values for the negative samples ranged from below the lower end of the assay range to 0.38 Index.

Distribution of Percent Difference to Serum (%)	Collection Tube Type		
	Potassium EDTA	Lithium Heparin	Sodium Heparin
>-20	0	0	0
-20 to -10	16.7% (5/30)	13.3% (4/30)	13.3% (4/30)
-10 to -5	26.7% (8/30)	33.3% (10/30)	33.3% (10/30)
-5 to 0	33.3% (10/30)	26.6% (8/30)	30% (9/30)
0 to 5	16.7% (5/30)	13.3% (4/30)	13.3% (4/30)
5 to 10	6.6% (2/30)	3.3% (1/30)	6.6% (2/30)
10 to 20	0	6.6% (2/30)	3.3% (1/30)
>20	0	3.3% (1/30)	0

### Technical Assistance

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

[www.siemens.com/diagnostics](http://www.siemens.com/diagnostics)

## Understanding the Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
	<i>In vitro</i> diagnostic medical device	<b>REF</b>	Catalog number
	Manufacturer		Authorized Representative in the European Community
	CE Mark		CE Mark with identification number of notified body
	Consult instructions for use		Caution! Potential Biohazard
	Do not freeze ( $> 0^{\circ}\text{C}$ )		Temperature limitation ( $2-8^{\circ}\text{C}$ )
	Lower limit of temperature ( $\geq 2^{\circ}\text{C}$ )		Upper limit of temperature ( $\leq -10^{\circ}\text{C}$ )
	Keep away from sunlight		Use by
	Store upright		Shake the reagent pack vigorously. Refer to <i>Loading Reagents</i> in the assay-specific ADVIA Centaur product instructions for detailed information.
	Batch code		Contains sufficient for (n) tests
<b>2010-01</b>	Date format (year-month)		Printed with soy ink
	Green dot		Recycle

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13. 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. NCCLS Document EP5-A2.
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US Pats 5,110,932; 5,656,426; 5,609,822; 5,788,928

Origin: US

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

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



# HBeAg (HBe)

## Contents

REF	Contents
06981117	1 vial of Negative Control <b>CONTROL -</b> 1 vial of Positive Control <b>CONTROL +</b> Expected Values Card and barcode labels

07044486 Rev. C, 2011-DRAFT

## Intended Use

The controls are used for monitoring the performance of the HBeAg assay on the ADVIA Centaur® systems. The performance of the HBeAg quality control material has not been established with any other HBeAg assay.

**WARNING:** United States federal law restricts this device to sale by or on the order of a physician.

## Control Description

Volume	Ingredients	Storage	Stability
10.0 mL/vial	Recalcified human plasma negative and positive for HBeAg, sodium azide (<0.1%), preservatives	2-8°C	Until the expiration date on the vial label or onboard-8 hours

### WARNINGS:

For *in vitro* diagnostic use.



- R43 Irritant! May cause sensitization by skin contact. Avoid contact with skin.
- S24 Wear suitable gloves. Contains: 5-chloro-2-methyl-2H-isothiazol-3-one and
- S37 2-methyl-2H-isothiazol-3-one



**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.<sup>1,3</sup> Use eye protection and gloves when handling this product; wash hands after handling.

The negative control has been assayed by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2. The positive control contains human plasma that is reactive for HBsAg and has been assayed by FDA-approved methods and found nonreactive for antibodies to HCV and antibody to HIV-1/2. The units were treated with a BPL-UV inactivation procedure, however, all products manufactured using human source material should be handled as potentially infectious.

**NOTE:** Sodium azide can react with copper and lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides, if disposal into a drain is in compliance with federal, state, and local 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 all federal, state, and local requirements.

The results obtained using the HBeAg quality control material depend on several factors. Erroneous results can occur from improper storage, inadequate mixing, or other sample handling errors.

The controls are not calibrators and should not be used for assay calibration.

## 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 HBeAg quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur HBeAg 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 in the HBeAg assay.

- 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 50 µL.

- Gently mix the quality control materials and dispense at least 9 drops into the appropriate sample cups. Avoid bubbles.
- 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.

**CAUTION:** 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.

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

## 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 HBeAg quality control material. For additional information, refer to the reagent instructions for use.

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

Assay values have not been established for assays other than the ADVIA Centaur HBeAg Assay. If the user wishes to use this control material with other assays, it is their responsibility to establish appropriate ranges.

## Technical Assistance

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

[www.siemens.com/diagnostics](http://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. NCCLS Document M29-A3.

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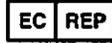
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Symbol	Definition	Symbol	Definition	Symbol	Definition
	En: <i>In vitro</i> diagnostic medical device Fr: Dispositif médical de diagnostic <i>in vitro</i> De: Medizinisches Gerät zur <i>In-vitro</i> Diagnose It: Dispositivo medico per diagnostica <i>in vitro</i> Es: Dispositivo médico para diagnóstico <i>in vitro</i> Pt: Dispositivo médico para diagnóstico <i>in vitro</i> Da: Medicinsk <i>in vitro</i> -diagnostiseringsenhed Sv: Medicinsk utrustning för <i>in vitro</i> -diagnostik El: <i>In vitro</i> διαγνωστική ιατρική συσκευή No: Medisinsk utstyr til <i>in vitro</i> diagnostikk Ja: 体外診断用医薬品		En: Caution! Potential Biohazard Fr: Attention! Risque biologique potentiel De: Vorsicht! Biologisches Risikomaterial It: Attenzione! Potenziale Pericolo Biologico Es: ¡Precaución! Peligro Biológico Potencial Pt: Precaução! Potenciais Riscos Biológicos Da: Forsigtigt! Potentielt biologisk smittetare Sv: Viktigt! Potentiellt biologisk smittorisk El: Προσοχή! Διυνητικός βιολογικός κίνδυνος No: Forsiktig! Potensiell biologisk smittetare 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: Sufisant pour (n) tests Da: 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: Περιέχόμενο 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: Limite di temperatura (2-8°C) Es: Limitación de la temperatura (2-8°C) Pt: Limites de temperatura (2-8°C) Da: Temperaturbegrænsning (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 Da: Grüner Punkt It: Punto verde Es: Punto verde Pt: Ponto Verde Da: Der Grüne Punkt Sv: Gröna punkten El: Πράσινη κουκίδα 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: Κατασκευαστής No: Produsent Ja: 製造元		En: Upper limit of temperature (≤ -20°C) Fr: Limite supérieure de température (≤ -20°C) De: Obere Temperaturgrenze (≤ -20°C) It: Limite superiore di temperatura (≤ -20°C) Es: Limitación superior de la temperatura (≤ -20°C) Pt: Limite máximo de temperatura (≤ -20°C) Da: Øvre temperaturbegrænsning (≤ -20°C) Sv: Högsta temperatur (≤ -20°C) El: Ανώτερο όριο θερμοκρασίας (≤ -20°C) No: Øvre temperaturgrense (≤ -20°C) Ja: 最高保存温度 (≤ -20°C)		En: Store upright Fr: Conserver en position verticale Da: Aufrecht lagem It: Conservare in posizione verticale Es: Conservar en posición vertical Pt: Armazenar em posição vertical Da: Opbevares oprejst Sv: Förvaras stående El: Φυλάσσεται σε όρθια θέση No: Oppbevares stående Ja: 立てて保管してください
EC REP	En: Authorized Representative in the European Community Fr: Représentant agréé pour l'Union européenne De: Autorisierter Vertreter 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 repræsentant i EU Sv: Autoriserad representant inom europeiska gemenskapen El: Εξουσιοδοτημένος αντιπρόσωπος στην Ευρωπαϊκή Κοινότητα No: Autoriseret representant i EU Ja: ヨーロッパ地区の正規代理店		En: Lower limit of temperature (≥ 2°C) Fr: Limite inférieure de température (≥ 2°C) De: Mindesttemperatur (≥ 2°C) It: Limite inferiore di temperatura (≥ 2°C) Es: Temperatura mínima (≥ 2°C) Pt: Limite inferior de temperatura (≥ 2°C) Da: Nedre temperaturgrense (≥ 2°C) Sv: Lågsta temperatur (≥ 2°C) El: Κατώτερο όριο θερμοκρασίας (≥ 2°C) No: Nedre temperaturgrense (≥ 2°C) Ja: 最低保存温度 (≥ 2°C)	2008-01	En: Date format (year-month) Fr: Format de la date (année-mois) Da: 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: Έμφανση CE No: CE-merke Ja: CE マーク		En: Do not freeze (> 0°C) Fr: Ne pas congeler (> 0°C) De: Nicht einfrieren (> 0°C) It: Non congelare (> 0°C) Es: No congelar (> 0°C) Pt: Não congele (> 0°C) Da: Må ikke nedfryses (> 0°C) Sv: Får ej frysas (> 0°C) El: Μην καταψύξετε (> 0°C) No: Må ikke fryse (> 0°C) Ja: 冷凍を避けていることを示します (> 0°C)		En: Recycle Fr: Recyclage Da: Recyclen It: Riciclo Es: Reciclar Pt: Reciclar Da: Genbrug Sv: Kan återvinnas El: Ανακυκλώσιτε 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: Έμφανση CE με αριθμό αναγνώρισης του φορέα πιστοποίησης No: CE-merke med ID-nummer for teknisk kontrollorgan Ja: 認定機関 (Notified Body) の認定番号付き CE マーク		En: Keep away from sunlight Fr: Maintenir hors de portée de la lumière du soleil De: Vor Sonnenelstrahlung 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 sojabænk Sv: Tryckt med sojabänk El: Εκτυπώνεται με μελάνη σόγιας No: Trykt med soyabænk Ja: 大豆油インキで印刷されています
	En: Consult instructions for use Fr: Consulter le mode d'emploi De: Bedienungsanweisung beachten It: Consultare le istruzioni per l'uso Es: Consulte las instrucciones de uso Pt: Consulte as instruções de utilização Da: Se den medfølgende betjeningsvejledning Sv: Läs igenom användarinstruktionerna El: Συμβουλευτείτε τις οδηγίες λειτουργίας No: Se bruksanvisningen Ja: 取扱上の指示に従ってください	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: 製造番号		En: Use by Fr: A utiliser avant Da: 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

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