SIEMENS

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

HBc Total 2 (HBcT2)

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

Current Revision and Date[a]	Rev. C, 2023-04	
Product Name	ADVIA Centaur HBc Total 2 (HBcT2)	REF 10376698 (100 tests)
Abbreviated Product Name	ADVIA Centaur HBcT2	
Test Name/ID	HBcT2	
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur HBcT2 QC	REF 10376699
	ADVIA Centaur Ancillary Probe Wash 1	REF 03395373
	ADVIA Centaur Probe Wash 3	REF 03333963
	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199 (112351)
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
Specimen Types	Serum, EDTA plasma, lithium heparin plasma, sodium heparin plasma	
Sample Volume	50 µL	
Measuring Interval	0.07–10.00 Index	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

Intended Use

The ADVIA Centaur® HBc Total 2 (HBcT2) assay is an *in vitro* diagnostic immunoassay for use in the qualitative determination of total antibodies to the core antigen of the hepatitis B virus (HBV) in human pediatric (2–21 years old) and adult serum and plasma (EDTA, lithium heparin, and sodium heparin) using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems.

This assay can be used as an aid in the diagnosis of acute or chronic hepatitis B virus (HBV) infection, and in the determination of the clinical status of HBV-infected individuals in conjunction with other HBV serological markers, for the laboratory diagnosis of HBV disease associated with HBV infection. This assay can also be used as an aid in the differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown.

This assay is not intended for screening donors of blood or blood products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).

Summary and Explanation

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 6–8 weeks (range 1–6 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%–95% of patients with HBV infection completely recover from acute illness and clear the virus. Approximately 5%–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.[1-3]

Hepatitis B core antigen (HBcAg), found in liver cells, does not circulate in the bloodstream. However, IgM and IgG antibodies to HBcAg can be detected serologically in HBV-infected individuals. Anti-HBc IgM is detectable first and remains detectable for approximately 6 months. Shortly after the IgM response, anti-HBc IgG appears and can remain detectable indefinitely. The presence of anti-HBc IgM is characteristic of acute infection, while the presence of anti-HBc IgG is characteristic of chronic or recovered stages of HBV infection.

Anti-HBc total assays detect both IgM and IgG anti-HBc responses. Most often levels of anti-HBc will coincide with detectable levels of other HBV markers. Rarely, anti-HBc may be the only detectable HBV marker. This may occur during the brief period when hepatitis B surface antigen (HBsAg) has been cleared from the bloodstream and before antibodies to hepatitis B surface antigen (anti-HBs) become detectable. For this reason, the use of anti-HBc total assays to detect acute infection is not recommended. Anti-HBc total assays should be used in conjunction with other marker assays to assess current or past exposure to HBV.[1,2,4,5]

Principles of the Procedure

The ADVIA Centaur HBcT2 assay is a 2-wash antigen sandwich immunoassay in which antigens are bridged by antibody present in the patient sample. The Solid Phase contains a preformed complex of streptavidin-coated microparticles and biotinylated recombinant HBc antigen, and is used to capture anti-HBc in the patient sample.

The Lite Reagent contains recombinant HBc antigen labeled with acridinium ester and anti-human IgG Fab monoclonal antibody labeled with acridinium ester, and is used to detect anti-HBc in the sample. The Ancillary Reagent, Solid Phase, and Ancillary Well Reagent are added to the sample, followed by Lite Reagent. Antibody-antigen complexes will form if anti-HBc antibodies (IgM and IgG) are present in the sample.

A direct relationship exists between the amount of anti-HBc antibodies 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 the Index Value established with the calibrators. Refer to *Interpretation of Results*.

Reagents

Material Description	Storage	Stability
ADVIA Centaur HBcT2 ReadyPack® primary reagent pack[a, b] **Lite Reagent** 10.0 mL/reagent pack Recombinant hepatitis B core antigen (~0.03 µg/mL) labeled with acridinium ester; mouse anti-human IgG Fab fragment (~3.5 ng/mL) labeled with acridinium ester; bovine serum albumin (BSA); buffer; surfactant; sodium azide (< 0.1%) **Solid Phase** 12.5 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated recombinant HBcAg (~1.0 µg/mL) in buffer; potassium thiocyanate (5.0%); BSA; surfactant; sodium azide (< 0.1%) **Ancillary Well Reagent** 10.0 mL/reagent pack Buffer; potassium thiocyanate (12.5%); non-magnetic particles; BSA; surfactant; sodium azide (< 0.1%)	Unopened at 2–8° C Onboard	Until expiration date on product 42 days
ADVIA Centaur HBcT2 ReadyPack ancillary reagent pack[a, b] 10.0 mL/reagent pack Buffer; potassium thiocyanate (5.0%); surfactant; sodium azide (< 0.1%)	Unopened at 2–8° C Onboard	Until expiration date on product 42 days
ADVIA Centaur HBcT2 CAL[a] 2.0 mL/vial Processed human plasma positive for HBc antibodies; sodium azide (< 0.1%); preservatives	Unopened at 2–8° C Opened at 2–8° C At room temperature	Until expiration date on product 60 days 8 hours
ADVIA Centaur Ancillary Probe Wash 1 ReadyPack ancillary reagent pack[a, c] 25.0 mL/pack 0.4 N sodium hydroxide	Unopened at 2–8° C Onboard	Until expiration date on product 14 days
ADVIA Centaur PW3 ReadyPack primary reagent pack[a, c] 50.0 mL/pack Sodium hypochlorite (0.5%); sodium hydroxide (< 0.5%); pH 11.0	Unopened at 2–8° C Onboard	Until expiration date on product 100 days
ADVIA Centaur Wash 1[a, c] 1500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%); surfactant	Unopened at 2–25° C Onboard	Until expiration date on product 1 month
ADVIA Centaur Wash 1[a, c] 2500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%); surfactant	Unopened at 2–25° C Onboard	Until expiration date on product 1 month

[a] Store in an upright position.

[b] Prevent exposure to sunlight and heat.

- c Refer to *Materials Required but Not Provided*.

Warnings and Precautions

For *in vitro* diagnostic

use.

For Professional Use.

For Prescription Use Only.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens-healthineers.com.

H317, H412
P280, P273, P302+P352, P333+P313, P362+P364, P501

Warning!
May cause an allergic skin reaction. Harmful to aquatic life with long lasting effects.
Wear protective gloves/protective clothing/eye protection/face protection. Avoid release to the environment. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Take off contaminated clothing and wash it before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2- methyl-2H-isothiazol-3-one (3:1) (in ADVIA Centaur HBcT2 CAL)

H290, H319, H315
P234, P264, P280, P337+P313, P390, P501

Warning!
May be corrosive to metals. Causes serious eye irritation. Causes skin irritation.
Keep only in original container. Wash hands thoroughly after handling. Wear protective gloves/protective clothing/eye protection/face protection. If eye irritation persists: Get medical advice/attention. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hydroxide (in ADVIA Centaur APW1)

H412
P273, P501

Harmful to aquatic life with long lasting effects.
Avoid release to the environment.
Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hypochlorite (in ADVIA Centaur PW3)

Warning! Potential Biohazard

Contains human source material.

No known test method can ensure that products derived from human source materials will not transmit infection. These materials should be handled using good laboratory practices and universal precautions.[6-8]

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.

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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

Specimen Collection and Handling

Serum and plasma (EDTA, lithium heparin and sodium heparin) are the recommended specimen types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[8]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[9]
- Follow the instructions provided with your specimen collection device for use and processing.[10]
- Allow blood specimens to clot completely before centrifugation.[11]
- Keep tubes capped at all times.[11]
- Specimens are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post-draw. When testing 12 specimens, and the centrifugation step was varied up to 24 hours post-draw, no clinically significant differences were observed.

Storing the Specimen

- After centrifugation, specimens in the primary collection device are stable for up to 7 days at 2–8° C. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel-barrier tubes.
- Separated samples are stable for up to 3 days at room temperature, and for up to 7 days at 2–8° C.
- Separated samples are stable at ≤ -20° C for up to 12 months. When 10 samples were subjected to 5 freeze-thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge them before using.

The handling and storage information provided here is based on data or references maintained by the manufacturer. 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.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

If during shipment, specimens may be subjected to temperatures > 25° C, then ship specimens frozen.

Preparing the Samples

This assay requires 50 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[11]

Procedure

Materials Provided

The following materials are provided:

REF	Content	Number of Tests
10376698	1 ReadyPack primary reagent pack containing ADVIA Centaur HBcT2 Lite Reagent, Solid Phase, and Ancillary Well Reagent 1 ReadyPack ancillary reagent pack containing ADVIA Centaur HBcT2 Ancillary Reagent ANC ADVIA Centaur HBcT2 master curve card 1 vial ADVIA Centaur HBcT2 CAL low calibrator 1 vial ADVIA Centaur HBcT2 CAL high calibrator	100

Materials Required but Not Provided

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

REF	Description	
	ADVIA Centaur XP System[a] ADVIA Centaur XPT System[a]	
10376699	ADVIA Centaur HBcT2 QC	2 x 7.0 mL negative quality control, level 1 CONTROL - 1 2 x 7.0 mL positive quality control, level 2 CONTROL + 2 Quality control assigned value card and barcode labels
03333963	ADVIA Centaur PW3 (probe wash)	50.0 mL/pack PW 3
03395373	ADVIA Centaur Ancillary Probe Wash 1	2 ReadyPack ancillary reagent packs containing 25.0 mL/ pack WASH

REF	Description	
01137199 (112351)	ADVIA Centaur Wash 1 (wash)	2 x 1500 mL/pack WASH 1
03773025	ADVIA Centaur Wash 1 (wash)	2 x 2500 mL/pack WASH 1

[a] Additional system fluids are required to operate the system: ADVIA Centaur Acid Reagent, ADVIA Centaur Base Reagent, and ADVIA Centaur Cleaning Solution.

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 100 µL of Ancillary Reagent into a cuvette, then incubates for 6 minutes at 37° C.
3. Dispenses 100 µL of Ancillary Well Reagent and 125 µL of Solid Phase, then incubates for 18 minutes at 37° C.

   Note The ADVIA Centaur HBcT2 Ancillary Well Reagent is milky white in color.
4. Performs a wash sequence using ADVIA Centaur Wash 1.
5. Resuspends the particles in 250 µL of ADVIA Centaur Wash 1
6. Dispenses 100 µL of Lite Reagent, then incubates for 18 minutes at 37° C.
7. Performs a wash sequence using ADVIA Centaur Wash 1.
8. Dispenses 300 µL each of ADVIA Centaur Acid Reagent and ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
9. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

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

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve values by scanning the master curve card. For information about defining the master curve, refer to the system online help.

Performing Calibration

For calibration of the ADVIA Centaur HBcT2 assay, use the calibrators provided with each kit.

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- At the end of the 21-day calibration interval.
- When changing lot numbers of primary reagent packs.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Calibrators are liquid and ready to use. Allow the calibrators to equilibrate to room temperature. Gently mix and invert the vials to ensure homogeneity of the material.

Use calibrators within the stability limits specified in *Reagents* and discard any remaining material.

Calibration Procedure

The calibrators are provided in dropper vials. Each dispensed drop is approximately 50 µL.

Perform the calibration procedure using the following steps:

1. Ensure that the appropriate master curve and calibrator assigned values are entered on the system. For information about defining the master curve and entering calibrator values, refer to the system online help.
2. Load the required reagents for the assay.
3. Schedule the calibrators.
4. Label two sample containers with barcode labels: one container for the low calibrator and one container for the high calibrator. Place the barcode labels on the sample containers with the readable characters oriented vertically.

   Note Barcode labels are lot-specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.
5. Gently mix the product and dispense a sufficient volume of each calibrator into the appropriate sample containers. Avoid bubbles.

   The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the system online help.
6. Load the samples according to the system online help.

Note Dispose of any calibrator that remains in the sample container after 8 hours. Do not refill or reuse sample containers. Do not return any calibrator material back into the original container.

Performing Quality Control

For quality control of the ADVIA Centaur HBcT2 assay, use the ADVIA Centaur HBcT2 QC at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use. For the assigned values, refer to the quality control assigned value sheet provided.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

Taking Corrective Action

If the quality control results do not fall within the expected control interval, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the system online help.

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system online help. Refer to *Interpretation of Results*.

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Interpretation of Results

The system reports ADVIA Centaur HBcT2 assay results in Index Values and as Nonreactive or Reactive:

- Nonreactive: < 1.00 Index. These samples are considered negative.
- Reactive: ≥ 1.00 Index. These samples are considered positive.

The cut-off value for the ADVIA Centaur HBcT2 assay was verified based on the clinical agreement of results generated from clinical studies.

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

Limitations

The following information pertains to limitations of the assay:

- The ADVIA Centaur HBcT2 assay is limited to the detection of total antibodies to hepatitis B core antigen in human serum or plasma. Assays for the detection of anti-HBc may not identify all patient samples that contain hepatitis B virus.
- Performance characteristics have not been established for the assay used in conjunction with other manufacturers' assays for specific HBV serological markers. Laboratories are responsible for establishing their own performance characteristics.
- Performance characteristics have not been established for the use of the ADVIA Centaur HBcT2 assay as an aid in determining susceptibility to HBV infection prior to or following vaccination in infants, children, or adolescents.

- Results obtained with the assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- The performance of the assay has not been established with cadaver specimens, heat- inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- A nonreactive test result does not exclude the possibility of exposure to or infection with HBV. Human anti-HBc total may be undetectable in some stages of the infection and in some clinical conditions.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[12,13] Additional information may be required for diagnosis.

Expected Values

The study was designed to test samples from patients with general signs and symptoms of hepatitis B or a high risk of HBV infection, including pregnant women, transplant recipients, and dialysis patients.

The analysis included 1595 samples in the following classifications: acute, chronic, early recovery, recovered, recovery, HBV vaccine response, not previously infected with HBV, and unclassified. The study population was 30.3% Caucasian, 61.0% Black, 2.4% Asian, and 6.3% from unknown or other race. The patients were nearly equally divided by sex (53.0% female and 47.0% male). The mean age was 47 years. Patients in the study population were from the following geographic regions: Florida (36.5%), California (27.2%), Minnesota (33.6%), and Arizona, Massachusetts, Michigan, North Dakota, New Jersey, Nevada, Texas, Virginia, Wisconsin, and other locations combined (2.7 %).

The test results for the prospective population for all sites, combined by age group and gender, are summarized in the following table.

Comparison of results in the signs-and-symptoms prospective population: ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

		Reactive		Nonreactive		Total
Age (Years)	**Gender**	**N[a]**	**(%)**	**N**	**(%)**	**N**
21-30	Male	3	4.2	69	95.8	72
	Female	4	2	193	98.0	197
	Overall	7	2.6	262	97.4	269
31-40	Male	13	15.5	71	84.5	84
	Female	31	16.2	161	83.9	192
	Overall	44	15.9	232	84.1	276
41-50	Male	48	34.3	92	65.7	140
	Female	35	24.8	106	75.2	141
	Overall	83	29.5	198	70.5	281
51-60	Male	115	40.9	166	59.1	281
	Female	78	40.0	117	60.0	195
	Overall	193	40.5	283	59.5	476

		Reactive		Nonreactive		Total
Age (Years)	**Gender**	**N[a]**	**(%)**	**N**	**(%)**	**N**
61-70	Male	72	47.4	80	52.6	152
	Female	38	39.2	59	60.8	97
	Overall	110	44.2	139	55.8	249
71-92	Male	11	37.9	18	62.1	29
	Female	5	33.3	10	66.7	15
	Overall	16	36.4	28	63.6	44
Total	Male	262	34.6	496	65.4	758
	Female	191	22.8	646	77.2	837
	Overall	453	28.4	1142	71.6	1595

[a] Number of measurements.

Results are representative of the population tested. Consider this information as guidance only.

Performance Characteristics

Measuring Interval

0.07–10.00 Index is reported as nonreactive or reactive.

Clinical Performance

Results by Specimen Classification

Patients were assessed for hepatitis markers using commercially available, FDA-approved reference assays using the ADVIA Centaur XP system. The serological assessment included the following 6 HBV markers: hepatitis B virus surface antigen (HBsAg), hepatitis B e antigen (HBeAg), IgM antibody to hepatitis B core antigen (anti-HBc IgM), total antibody to hepatitis B virus core antigen (anti-HBc Total), hepatitis B e antibody (anti-HBe), and antibody to hepatitis B virus surface antigen (anti-HBs).

Testing of these specimens occurred at 3 study sites. Patients had the following hepatitis marker profiles: acute, chronic, early recovery, recovery, recovered, HBV vaccine response, not previously infected with HBV, and unclassified.

Each patient's HBV infection status was classified based on a single specimen and the reactive (+) or nonreactive (-) patterns of the 6 HBV reference serological markers. The 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 30 unique reference marker patterns observed using the FDA-approved assays.

Classification by HBV Reference Markers (All Testing Sites)

HBV Classification	HBsAg[a]	HBeAg	Anti-HBc IgM	Anti-HBc Total	Anti-HBe	Anti-HBs[b]
Acute	+[c]	+	+	+	+	–[d]
Acute	+	+	+	+	–	–
Chronic	+	+	–	+	+	–

HBV Classification	HBsAg[a]	HBeAg	Anti-HBc IgM	Anti-HBc Total	Anti-HBe	Anti-HBs[b]
Chronic	+	+	–	+	–	–
Chronic	+	–	–	+	+	–
Chronic	+	–	–	+	–	+
Chronic	+	–	–	+	–	–
Early Recovery	–	–	+	+	+	+
Early Recovery	–	–	+	+	–	+
Early Recovery	–	–	–	+	+	–
Recovery	–	–	–	+	+	+
Recovery	–	–	–	–	+	+
Recovered	–	–	–	+	–	+
Recovered	–	–	–	+	–	–
HBV Vaccine Response	–	–	–	–	–	+
Not Previously Infected	–	–	–	–	–	–
Unclassified	+	–	–	–	–	+
Unclassified	+	–	–	–	–	–
Unclassified	–	+	–	–	–	+
Unclassified	–	+	–	–	–	–
Unclassified	–	–	+	–	–	–
Unclassified	–	–	–	–	+	–
Unclassified	+	+	–	–	–	+
Unclassified	+	+	–	–	–	–
Unclassified	–	–	Equivocal	–	–	–
Unclassified	–	–	Equivocal	+	+	–
Unclassified	–	–	Equivocal	+	+	+
Unclassified	+	–	Equivocal	+	+	–
Unclassified	Conf Invalid[e]	–	–	–	–	–
Unclassified	–	+	–	+	+	+

[a] Reactive (+) = reference HBsAg assay result was reactive and confirmed to be positive by neutralization. nonreactive (-) = reference HBsAg assay result was nonreactive or reactive but not confirmed positive by neutralization.

[b] > 10 mIU/mL

[c] + = Reactive.

[d] - = Nonreactive.

[e] Test result was invalid based on confirmatory testing.

Comparison of Results: Prospective Population by HBV Category

A total of 1595 samples from patients with general signs and symptoms of hepatitis B or with a high risk of HBV infection were tested using the ADVIA Centaur HBcT2 assay and a reference anti-HBc total assay. Subgroups within this population included pregnant women, transplant recipients, and dialysis patients.

Comparison of results in the signs-and-symptoms prospective population: ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay		
ADVIA Centaur HBcT2 Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	189	12	201
Nonreactive	5	570	575
Total	**194**	**582**	**776**

Positive Percent Agreement: 97.4% (189/194); 95% Confidence Interval: 94.1%–98.9%

Negative Percent Agreement: 97.9% (570/582); 95% Confidence Interval: 96.4%–98.8%

Comparison of results in the high-risk prospective population: ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay		
ADVIA Centaur HBcT2 Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	245	7	252
Nonreactive	4	563	567
Total	**249**	**570**	**819**

Positive Percent Agreement: 98.4% (245/249); 95% Confidence Interval: 95.9%–99.4%

Negative Percent Agreement: 98.8% (563/570); 95% Confidence Interval: 97.5%–99.4%

The agreement between the ADVIA Centaur HBcT2 assay and a reference anti-HBc total assay for each HBV category is summarized in the following table.

Prospective Population by HBV Category - ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
HBV Category	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Signs and symptoms	256	4	6	362	628
High risk	140	5	6	468	619
Pregnant	10	0	1	182	193
Transplant	8	0	1	41	50

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
HBV Category	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Dialysis	20	0	5	80	105
Total	**434**	**9**	**19**	**1133**	**1595**

Percent agreement and confidence intervals by HBV category (all test sites)

	Positive Agreement		Negative Agreement	
HBV Category	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
Signs and symptoms	98.5 (256/260)	96.1–99.4	98.4 (362/368)	96.5–99.3
High risk	96.6 (140/145)	92.2–98.5	98.7 (468/474)	97.3–99.4
Pregnant	100 (10/10)	72.2–100.0	99.5 (182/183)	97.0–99.9
Transplant	100 (8/8)	67.6–100.0	97.6 (41/42)	87.7–99.6
Dialysis	100 (20/20)	83.9–100.0	94.1 (80/85)	87.0–97.5
Total, N = 1595	**98.0 (434/443)**	**96.2–98.9**	**98.4 (1133/1152)**	**97.4–98.9**

[a] x = the number of ADVIA Centaur HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of ADVIA Centaur HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

Comparison of Results: Prospective Population by HBV Serological Classification

A total of 1595 prospective samples were tested using the ADVIA Centaur HBcT2 assay and a reference anti-HBc total assay for each HBV serological classification (all testing sites).

Comparison of results in the prospective population by HBV serological classification; ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur IM HBcT2 Assay		
HBV Classification	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Acute	3	0	–	–	3
Chronic	77	0	–	–	77
Early recovery	15	0	–	–	15
Recovery	101	0	1	3	105
Recovered	207	2	8	6	223
HBV vaccine response	20	5	5	509	539

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
HBV Classification	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Not previously infected	3	2	3	591	599
Unclassified	8	0	2	24	34
Total	**434**	**9**	**19**	**1133**	**1595**

Percent agreement and confidence intervals by HBV classification (all testing sites)

	Positive Agreement		Negative Agreement	
HBV Classification	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
Acute	100.0 (3/3)	43.9–100.0	–[d]	–
Chronic	100.0 (77/77)	95.2–100.0	–	–
Early recovery	100.0 (15/15)	79.6–100.0	–	–
Recovery	100.0 (101/101)	96.3–100.0	75.0 (3/4)	30.1–95.4
Recovered	99.0 (207/209)	96.6–99.7	42.9 (6/14)	21.4–67.4
HBV vaccine response	80.0 (20/25)	60.9–91.1	99.0 (509/514)	97.7–99.6
Not previously infected	60.0 (3/5)	23.1–88.2	99.5 (591/594)	98.5–99.8
Unclassified	100.0 (8/8)	67.6–100.0	92.3 (24/26)	75.9–97.9
Total, N = 1595	**98.0 (434/443)**	**95.9–98.8**	**98.4 (1133/1152)**	**97.4–98.9**

[a] x = the number of ADVIA Centaur HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of ADVIA Centaur HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

[d] Percentages are for the numbers of reactive and nonreactive samples in a given row. If the total number of samples in the row is zero, a dash (–) is displayed.

Prenatal Population

Serum samples from United States were included in the study (N = 193). Samples were tested from pregnant women with either signs and symptoms of hepatitis B or with risk factors for HBV infection, who were in the first (62/193, 32.1%), second (61/193, 31.6%), or third trimester (70/193, 36.3%) of pregnancy. Results of the testing (reactive and nonreactive) were compared using the ADVIA Centaur HBcT2 assay and the reference anti-HBc total assay for the prenatal population in their first, second, and third trimester, for all testing sites:

Comparison of results: prenatal population (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
Trimester	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
First	2	0	0	60	62
Second	6	0	1	54	61
Third	2	0	0	68	70
Total	**10**	**0**	**1**	**182**	**193**

Percent agreement and confidence intervals: prenatal population (all test sites)

	Positive Agreement		Negative Agreement	
Trimester	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
First	100 (2/2)	34.2–100	100 (60/60)	94.0–100
Second	100 (6/6)	61.0–100	98.2 (54/55)	90.4–99.7
Third	100 (2/2)	34.2–100	100 (68/68)	94.7–100
Total	**100 (10/10)**	**72.2–100**	**99.5 (182/183)**	**97.0–99.9**

[a] x = the number of ADVIA Centaur HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of ADVIA Centaur HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

Pediatric and Adolescent Population

Pediatric and adolescent (non-pregnant) samples were prospectively collected (N = 139) and tested using the ADVIA Centaur XP system. The population analysis was stratified by the following age groups: 2–12 years and 13–21 years.

	Reference Assay - Reactive		Reference Assay - Nonreactive		
Age Range (Years)	**HBcT2 Assay - Reactive**	**HBcT2 Assay - Nonreactive**	**HBcT2 Assay - Reactive**	**HBcT2 Assay - Nonreactive**	**Total**
2–12	1	0	0	29	30
13–21	3	0	1	105	109
Total	4	0	1	134	139

Age Range (Years)	**Positive Percent Agreement % (x/n)[a]**	**95% Confidence Interval**	**Negative Percent Agreement % (x/n)[b]**	**95% Confidence Interval**
2–12	100 (1/1)	20.7–100	100 (29/29)	88.3–100
13–21	100 (3/3)	43.9–100	99.1 (105/106)	94.8–99.8
Total	**100 (4/4)**	**51.0–100**	**99.3 (134/135)**	**95.9–99.9**

[a] x = the number of ADVIA Centaur HBcT2 results using the ADVIA Centaur XP system that are reactive in agreement with the reference HBcT2 assay; n = the total number of reference HBcT2 results that are reactive.

[b] x = the number of ADVIA Centaur HBcT2 results using the ADVIA Centaur XP system that are nonreactive in agreement with the reference HBcT2 assay; n = the total number of reference HBcT2 results that are nonreactive.

Because few positives were identified, a study was conducted to evaluate the results observed when pediatric samples are tested with the ADVIA Centaur HBcT2 assay using the ADVIA Centaur XP system. A total of 60 pediatric (age 2–21 years) and 60 adult serum samples were spiked with unique native anti- HBc positive samples. Out of 60 samples tested, 59 samples showed bias less than 20% (98.3% samples). The distribution of percent bias between the Index values of the spiked pediatric serum samples and the paired adult serum samples are summarized in the following table:

	Distribution of Percent Bias			
Age Range (Years)	**N[a]**	**≤ 10%**	**> 10%– ≤ 20%**	**> 20%– ≤ 30%**
2–12	20	45.0 (9/20)	50.0 (10/20)	5.0 (1/20)
13–21	40	72.5 (29/40)	27.5 (11/40)	0.0 (0/40)
Total	60	63.3 (38/60)	35.0 (21/60)	1.7 (1/60)

[a] Number tested.

Seroconversion Panels

Commercially available HBV patient seroconversion panels were tested using the ADVIA Centaur HBcT2 assay to determine the seroconversion sensitivity of the assay. The performance of the ADVIA Centaur HBcT2 assay on the seroconversion panels matched or exceeded the performance of the reference assay.

	Reference Anti-HBc Total Assay - Reactive From Initial Draw Date		ADVIA Centaur HBcT2 Assay versus Reference Anti-HBc Total Assay
Panel ID	ADVIA Centaur HBcT2 Assay (Days)	Reference Assay (Days)	Differenc in Bleed Numbers[a] e
HBV6278	41	41	0
HBV6281	41	41	0
HBV9093	49	49	0
HBV9099	74	74	0

Panel ID	Reference Anti-HBc Total Assay - Reactive From Initial Draw Date		ADVIA Centaur HBcT2 Assay versus Reference Anti-HBc Total Assay
	ADVIA Centaur HBcT2 Assay (Days)	Reference Assay (Days)	Difference in Bleed Numbers[a]
PHM941	99	99	0
SCPHBV1	29	29	0
SCPHBV4	65	71	+1

[a] The difference in bleed numbers is relative to the reference assay. For example, a "+1" means that the reference assay required 1 additional bleed before reactivity was determined as compared to the time point when the ADVIA Centaur HBcT2 assay confirmed as reactive.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[14] Samples were assayed in duplicate in 2 runs per day for 20 days. The following results were obtained using 1 reagent lot and stored calibration curves.

Specimen Type	N[a]	Mean (Index)	Repeatability SD[b] (Index)	Repeatability CV[c] (%)	Within-Laboratory Precision SD (Index)	Within-Laboratory Precision CV (%)
Plasma A	80	0.39	0.02	N/A[d]	0.09	N/A
Plasma B	80	0.78	0.03	N/A	0.06	N/A
Plasma C	80	1.56	0.07	4.6	0.10	6.7
Plasma D	80	2.38	0.11	4.5	0.15	6.3
Plasma E	80	6.71	0.33	4.9	0.64	9.6
Serum A	80	0.30	0.02	N/A	0.09	N/A
Serum B	80	0.63	0.04	N/A	0.06	N/A
Serum C	80	1.53	0.09	5.8	0.10	6.4
Serum D	80	2.30	0.09	4.0	0.16	7.1
Serum E	80	6.13	0.34	5.6	0.57	9.3
Control 1 (negative)	80	0.31	0.02	N/A	0.08	N/A
Control 2 (positive)	80	3.49	0.18	5.2	0.25	7.2

[a] Number of measurements.
[b] Standard deviation.
[c] Coefficient of variation.
[d] N/A = not applicable. The results remained nonreactive throughout the study.

The assay is designed to have the following precision.

Concentration Interval (Index)	Precision	
	Repeatability (Within-Run)	Within-Laboratory (Total Precision)
0.80–10.00	≤ 10.0% CV	≤ 12.0% CV

For specimens < 0.80 Index, the assay must not show a change in clinical interpretation.

Reproducibility

Reproducibility was evaluated according to CLSI document EP05-A3.[14] A reproducibility study was conducted at 3 sites, with each site evaluating 3 reagent lots. The protocol was run over 5 days, 2 runs per day. There were 3 replicates per run for each sample, for a total 270 replicates per sample (N = 270). The following results are representative of the performance of the assay:

Sample Type (N = 270)	Mean (Index)	Repeatability (Within-Run)		Between Run		Between Day		Between Lot		Within Laboratory		Between Site		Reproducibility	
		SD[a] (Index)	CV[b] (%)	SD (Index)	CV (%)	SD (Index)	CV (%)	SD (Index)	CV (%)	SD (Index)	CV (%)	SD (Index)	CV (%)	SD (Index)	CV (%)
Serum A	0.50	0.03	N/A[c]	0.03	N/A	0.00	N/A	0.01	N/A	0.04	N/A	0.03	N/A	0.05	N/A
Serum B	0.83	0.03	4.2	0.03	3.9	0.00	N/A	0.03	4.2	0.05	5.7	0.06	7.2	0.08	10.1
Serum C	1.47	0.06	4.0	0.02	1.7	0.02	1.5	0.12	7.9	0.07	4.6	0.11	7.2	0.17	11.7
Serum D	2.56	0.11	4.4	0.04	1.7	0.03	1.2	0.21	8.3	0.12	4.9	0.19	7.5	0.31	12.2
Serum E	5.48	0.26	4.7	0.06	1.2	0.07	1.3	0.48	8.8	0.28	5.1	0.40	7.3	0.68	12.5
Serum F[d]	8.71	0.38	4.4	0.16	1.8	0.00	0.0	0.66	7.6	0.41	4.7	0.61	7.0	0.98	11.3
Control 1 (negative)[e]	0.25	0.02	N/A	0.03	N/A	0.00	N/A	0.02	N/A	0.04	N/A	0.03	N/A	0.05	N/A
Control 2 (positive)	3.28	0.14	4.3	0.09	2.8	0.00	0.0	0.18	5.4	0.17	5.1	0.25	7.7	0.35	10.7

[a] Standard deviation.

[b] Coefficient of variation.

[c] N/A = not applicable. The results remained nonreactive throughout the study.

[d] 23 samples outside of the measuring interval were calculated offline and were included in analysis.

[e] 4 samples outside of the measuring interval were calculated offline and were included in analysis.

The assay is designed to have the following reproducibility:

Concentration Interval (Index)	Reproducibility
0.80–10.00	≤ 20.0% CV

For specimens < 0.80 Index, the assay must not show a change in clinical interpretation.

Assay Comparison

The percent agreement between the ADVIA Centaur XPT system and the ADVIA Centaur XP system was evaluated by testing 1595 samples at 3 clinical testing sites. Each site used 1 ADVIA Centaur XPT system and 1 ADVIA Centaur XP system, and tested 3 lots of reagents. The samples were obtained from subjects with general signs and symptoms of hepatitis B or with a high risk of HBV infection, inclusive of pregnant women, transplant recipients, and dialysis patients.

	ADVIA Centaur XPT		
ADVIA Centaur XP	**Reactive**	**Nonreactive**	**Total**
Reactive	452	1	453
Nonreactive	5	1137	1142
Total	**457**	**1138**	**1595**

Positive Percent Agreement: 98.9% (452/457); 95% Confidence Interval: 97.5%–99.5%

Negative Percent Agreement: 99.9% (1137/1138); 95% Confidence Interval: 99.5%–99.9%

Specimen Equivalency

Specimen equivalency was determined with the linear regression model in accordance with CLSI Document EP09-A2.[15] Results were established using the ADVIA Centaur XP system.

The ADVIA Centaur HBcT2 results ranged from 0.11–9.99 Index. No significant difference between the tube types was observed. Agreement of the specimen types may vary depending on the study design and sample population used.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Gel-barrier tube (serum)	y = 0.96 (x) + 0.04	0.29–9.42 Index	50	0.983
Dipotassium EDTA plasma	y = 0.98 (x) + 0.03	0.24–9.24 Index	50	0.981
Lithium heparin plasma	y = 1.00 (x) - 0.05	0.12–9.54 Index	50	0.968
Sodium heparin plasma	y = 1.04 (x) - 0.09	0.11–9.99 Index	50	0.971

[a] Number of samples tested.

[b] Correlation coefficient.

The assay is designed to have a correlation coefficient of ≥ 0.95, a slope of test tube type (y) versus reference (x) of 1.0 ± 0.15, and an intercept of < 0.90 Index.

Interferences

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2.[16]

Substance	Substance Test Concentration
Hemoglobin	500 mg/dL
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	40 mg/dL
Lipemia	1000 mg/dL

Substance	Substance Test Concentration
Biotin	3500 ng/mL
Cholesterol	500 mg/dL
Hyper IgG	60 mg/mL
Hyperproteinemic	12.0 g/dL
Hypoproteinemic	3.5 g/dL

The assay was designed to have ≤ 10% interference up to the concentration of the substances tested.

Cross-Reactivity

The assay was evaluated for potential cross-reactivity with other viral and microbial antibodies and disease state specimens. The anti-HBc status of each sample was assessed using the ADVIA Centaur HBcT2 assay and an anti-HBc reference assay. Results were established using the ADVIA Centaur XP system. The following results are representative of the performance of the assay:

		Number of Reactive Anti-HBc Total Results	
Substance	Number Tested	ADVIA Centaur HBcT2 Assay	Reference Assay
Anti-nuclear antibody (ANA)	32	2	2
Cytomegalovirus (CMV) IgG	15	0	0
Cytomegalovirus (CMV) IgM	15	0	0
Epstein-Barr virus (EBV) IgG	15	0	0
Epstein-Barr virus (EBV) IgM	15	0	0
Flu vaccine recipient	15	0	0
Human anti-mouse antibody (HAMA)	15	2	2
Hepatitis A infection (HAV)	20	4	4
Hepatitis C infection (HCV)	15	7	7
Herpes simplex virus (HSV) IgG	15	0	0
Herpes simplex virus (HSV) IgM	14	0	0
Human immunodeficiency virus (HIV 1/2)	15	6	6
Multiparity	25	1	1
Non-viral liver disease	15	1	0
Rheumatoid arthritis	15	2	1
Rubella IgG	15	0	0
Syphilis IgG	15	3	3
Systemic lupus erythematosus (SLE)	20	1	1
Toxoplasma IgG	21	0	0

Substance	Number Tested	Number of Reactive Anti-HBc Total Results	
		ADVIA Centaur HBcT2 Assay	Reference Assay
Toxoplasma IgM	11	0	0
Varicella zoster virus (VZV) IgG	15	1	1

Analytical Sensitivity

To examine the analytical sensitivity of the ADVIA Centaur HBcT2 assay, the WHO Anti-hepatitis B virus core antigen (anti-HBc) 1st International Standard 95/522, was used to prepare a dilution series that was tested using 3 ADVIA Centaur HBcT2 reagent lots. Linear regression was used to determine the concentration of the WHO 95/522 reference sample value, which corresponds to the ADVIA Centaur HBcT2 cut-off (Index Value = 1.00). The WHO 95/522 International Unit per milliliter (IU/mL) concentration at the assay cut-off was determined to be 0.28 IU/mL.

Standardization

The ADVIA Centaur HBcT2 assay traceability is based on the relative clinical agreement with commercially available anti-HBc total assays. Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or

distributor. siemens-healthineers.com

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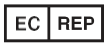
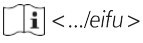
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]		Authorized representative in the European Community	5.1.2[a]
	Use-by date	5.1.4[a]		Authorized representative in Switzerland	Proprietary
	Catalog number	5.1.6[a]		Batch code	5.1.5[a]
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
	Internet URL address to access the electronic instructions for use	Proprietary		Version of Instructions for Use	Proprietary
	*In vitro* diagnostic medical device	5.5.1[a]	Rev.	Revision	Proprietary
	Prescription device (US only)	FDA[b]		Unique Device Identifier	5.7.10[c]
	CE Marking with Notified Body	EU IVDR[d]		CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of tempera-	5.3.5[a]

ture

Symbol	Symbol	Sourc	Symbol	Symbol	Sourc
	Do not re-	5.4.2[a]		Do not	Proprietar
	Recycl	1135[e]		This way	0623[e]
	Biological	5.4.1[a]		Caution	5.4.4[a]
UNITS C	Common	Proprietar	UNITS SI	International System of	Proprietar
YYYY-MM-	Date format (year-month- day)	N/	YYYY-	Date format (year-month)	
	Document face	1952[e]		Targe	Proprietar
	Handheld barcode scanner			Interval	Proprietar
LOT DTL	Lot	Proprietar	CHECKSUM	Variable hexadecimal y number that ensures the Master Curve and Cali- brator definition	Proprietar
CAL LOT VAL	Calibrator lot	Proprietar	MC DEF	Master Curve definition	
CONTROL LOT VAL	Quality control lot value				

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.

[b] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.

[c] ISO 15223-1:2020-04

[d] IVDR REGULATION (EU) 2017/746

[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.

[f] Indicates Assay-*e*Note

Legal Information

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SIEMENS

ADVIA Centaur® CP
Immunoassay System

HBc Total 2 (HBcT2)

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

Current Revision and Date[a]	Rev. C, 2023-DRAFT	
Product Name	ADVIA Centaur HBc Total 2 (HBcT2)	REF 10376698 (100 tests)
Abbreviated Product Name	ADVIA Centaur HBcT2	
Test Name/ID	HBcT2	
Systems	ADVIA Centaur CP system	
Materials Required but Not Provided	ADVIA Centaur HBcT2 QC	REF 10376699
	ADVIA Centaur Ancillary Probe Wash 1	REF 03395373
	ADVIA Centaur Probe Wash 3	REF 03333963
	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199 (112351)
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
Specimen Types	Serum, EDTA plasma, lithium heparin plasma, sodium heparin plasma	
Sample Volume	50 µL	
Measuring Interval	0.07–10.00 Index	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

Intended Use

The ADVIA Centaur® HBc Total 2 (HBcT2) assay is an *in vitro* diagnostic immunoassay for use in the qualitative determination of total antibodies to the core antigen of the hepatitis B virus (HBV) in human pediatric (2–21 years old) and adult serum and plasma (EDTA, lithium heparin, and sodium heparin) using the ADVIA Centaur® CP system.

This assay can be used as an aid in the diagnosis of acute or chronic hepatitis B virus (HBV) infection, and in the determination of the clinical status of HBV-infected individuals in conjunction with other HBV serological markers, for the laboratory diagnosis of HBV disease associated with HBV infection. This assay can also be used as an aid in the differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown.

This assay is not intended for screening donors of blood or blood products or human cells,

tissues, and cellular and tissue-based products (HCT/Ps).

Summary and Explanation

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 6–8 weeks (range 1–6 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%–95% of patients with HBV infection completely recover from acute illness and clear the virus. Approximately 5%–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.[1-3]

Hepatitis B core antigen (HBcAg), found in liver cells, does not circulate in the bloodstream. However, IgM and IgG antibodies to HBcAg can be detected serologically in HBV-infected individuals. Anti-HBc IgM is detectable first and remains detectable for approximately
6 months. Shortly after the IgM response, anti-HBc IgG appears and can remain detectable indefinitely. The presence of anti-HBc IgM is characteristic of acute infection, while the presence of anti-HBc IgG is characteristic of chronic or recovered stages of HBV infection.

Anti-HBc total assays detect both IgM and IgG anti-HBc responses. Most often levels of anti-HBc will coincide with detectable levels of other HBV markers. Rarely, anti-HBc may be the only detectable HBV marker. This may occur during the brief period when hepatitis B surface antigen (HBsAg) has been cleared from the bloodstream and before antibodies to hepatitis B surface antigen (anti-HBs) become detectable. For this reason, the use of anti-HBc total assays to detect acute infection is not recommended. Anti-HBc total assays should be used in conjunction with other marker assays to assess current or past exposure to HBV.[1,2,4,5]

Principles of the Procedure

The ADVIA Centaur HBcT2 assay is a 2-wash antigen sandwich immunoassay in which antigens are bridged by antibody present in the patient sample. The Solid Phase contains a preformed complex of streptavidin-coated microparticles and biotinylated recombinant HBc antigen, and is used to capture anti-HBc in the patient sample.

The Lite Reagent contains recombinant HBc antigen labeled with acridinium ester and anti-human IgG Fab monoclonal antibody labeled with acridinium ester, and is used to detect anti-HBc in the sample. The Ancillary Reagent, Solid Phase, and Ancillary Well Reagent are added to the sample, followed by Lite Reagent. Antibody-antigen complexes will form if anti-HBc antibodies (IgM and IgG) are present in the sample.

A direct relationship exists between the amount of anti-HBc antibodies 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 the Index Value established with the calibrators. Refer to *Interpretation of Results*.

Reagents

Material Description	Storage	Stability
ADVIA Centaur HBcT2 ReadyPack® primary reagent pack[a, b] **Lite Reagent** 10.0 mL/reagent pack Recombinant hepatitis B core antigen (~0.03 µg/mL) labeled with acridinium ester; mouse anti-human IgG Fab fragment (~3.5 ng/mL) labeled with acridinium ester; bovine serum albumin (BSA); buffer; surfactant; sodium azide (< 0.1%) **Solid Phase** 12.5 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated recombinant HBcAg (~1.0 µg/mL) in buffer; potassium thiocyanate (5.0%); BSA; surfactant; sodium azide (< 0.1%) **Ancillary Well Reagent** 10.0 mL/reagent pack Buffer; potassium thiocyanate (12.5%); non-magnetic particles; BSA; surfactant; sodium azide (< 0.1%)	Unopened at 2–8° C Onboard	Until expiration date on product 42 days
ADVIA Centaur HBcT2 ReadyPack ancillary reagent pack[a, b] 10.0 mL/reagent pack Buffer; potassium thiocyanate (5.0%); surfactant; sodium azide (< 0.1%)	Unopened at 2–8° C Onboard	Until expiration date on product 42 days
ADVIA Centaur HBcT2 CAL[a] 2.0 mL/vial Processed human plasma positive for HBc antibodies; sodium azide (< 0.1%); preservatives	Unopened at 2–8° C Opened at 2–8° C At room temperature	Until expiration date on product 60 days 8 hours
ADVIA Centaur Ancillary Probe Wash 1 ReadyPack ancillary reagent pack[a, c] 25.0 mL/pack 0.4 N sodium hydroxide	Unopened at 2–8° C Onboard	Until expiration date on product 14 days
ADVIA Centaur PW3 ReadyPack primary reagent pack[a, c] 50.0 mL/pack Sodium hypochlorite (0.5%); sodium hydroxide (< 0.5%); pH 11.0	Unopened at 2–8° C Onboard	Until expiration date on product 60 days
ADVIA Centaur Wash 1[a, c] 1500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%); surfactant	Unopened at 2–25° C Onboard	Until expiration date on product 1 month
ADVIA Centaur Wash 1[a, c] 2500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%); surfactant	Unopened at 2–25° C Onboard	Until expiration date on product 1 month

[a] Store in an upright position.

[b] Prevent exposure to sunlight and heat.

[c] Refer to *Materials Required but Not Provided*.

Warnings and Precautions

For *in vitro* diagnostic

use.

For Professional Use.

For Prescription Use Only.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens-healthineers.com.

H317, H412
P280, P273, P302+P352, P333+P313, P362+P364, P501

Warning!
May cause an allergic skin reaction. Harmful to aquatic life with long lasting effects.
Wear protective gloves/protective clothing/eye protection/face protection. Avoid release to the environment. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Take off contaminated clothing and wash it before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2- methyl-2H-isothiazol-3-one (3:1) (in ADVIA Centaur HBcT2 CAL)

H290, H319, H315
P234, P264, P280, P337+P313, P390, P501

Warning!
May be corrosive to metals. Causes serious eye irritation. Causes skin irritation.
Keep only in original container. Wash hands thoroughly after handling. Wear protective gloves/protective clothing/eye protection/face protection. If eye irritation persists: Get medical advice/attention. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hydroxide (in ADVIA Centaur APW1)

H412
P273, P501

Harmful to aquatic life with long lasting effects.
Avoid release to the environment.
Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hypochlorite (in ADVIA Centaur PW3)

Warning! Potential Biohazard

Contains human source material.

No known test method can ensure that products derived from human source materials will not transmit infection. These materials should be handled using good laboratory practices and universal precautions.[6-8]

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.

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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

Specimen Collection and Handling

Serum and plasma (EDTA, lithium heparin and sodium heparin) are the recommended specimen types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[8]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[9]
- Follow the instructions provided with your specimen collection device for use and processing.[10]
- Allow blood specimens to clot completely before centrifugation.[11]
- Keep tubes capped at all times.[11]
- Specimens are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post-draw. When testing 12 specimens, and the centrifugation step was varied up to 24 hours post-draw, no clinically significant differences were observed.

Storing the Specimen

- After centrifugation, specimens in the primary collection device are stable for up to 7 days at 2–8° C. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel-barrier tubes.
- Separated samples are stable for up to 3 days at room temperature, and for up to 7 days at 2–8° C.
- Separated samples are stable at ≤ -20° C for up to 12 months. When 10 samples were subjected to 5 freeze-thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge them before using.

The handling and storage information provided here is based on data or references maintained by the manufacturer. 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.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

If during shipment, specimens may be subjected to temperatures > 25° C, then ship specimens frozen.

Preparing the Samples

This assay requires 50 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[11]

Procedure

Materials Provided

The following materials are provided:

REF	Content	Number of Tests
10376698	1 ReadyPack primary reagent pack containing ADVIA Centaur HBcT2 Lite Reagent, Solid Phase, and Ancillary Well Reagent 1 ReadyPack ancillary reagent pack containing ADVIA Centaur HBcT2 Ancillary Reagent ANC ADVIA Centaur HBcT2 master curve card 1 vial ADVIA Centaur HBcT2 CAL low calibrator 1 vial ADVIA Centaur HBcT2 CAL high calibrator ADVIA Centaur HBcT2 CAL calibrator assigned value cards and barcode labels	100

Materials Required but Not Provided

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

REF	Description	
	ADVIA Centaur CP System[a]	
10376699	ADVIA Centaur HBcT2 QC	2 x 7.0 mL negative quality control, level 1 CONTROL - 1 2 x 7.0 mL positive quality control, level 2 CONTROL + 2 Quality control assigned value card and barcode labels
03333963	ADVIA Centaur PW3 (probe wash)	50.0 mL/pack PW 3
03395373	ADVIA Centaur Ancillary Probe Wash 1	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH

REF	Description	
01137199 (112351)	ADVIA Centaur Wash 1 (wash)	2 x 1500 mL/pack WASH 1
03773025	ADVIA Centaur Wash 1 (wash)	2 x 2500 mL/pack WASH 1

[a] Additional system fluids are required to operate the system: ADVIA Centaur Acid Reagent, ADVIA Centaur Base Reagent, and ADVIA Centaur Cleaning Solution.

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 100 µL of Ancillary Reagent into a cuvette, then incubates for 4 minutes at 37° C.
3. Dispenses 100 µL of Ancillary Well Reagent and 125 µL of Solid Phase, then incubates for 17 minutes at 37° C.

   Note The ADVIA Centaur HBcT2 Ancillary Well Reagent is milky white in color.
4. Performs a wash sequence using ADVIA Centaur Wash 1.
5. Resuspends the particles in 250 µL of ADVIA Centaur Wash 1
6. Dispenses 100 µL of Lite Reagent, then incubates for 18 minutes at 37° C.
7. Performs a wash sequence using ADVIA Centaur Wash 1.
8. Dispenses 300 µL each of ADVIA Centaur Acid Reagent and ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
9. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

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

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve values by scanning the master curve card. For information about defining the master curve, refer to the system online help.

Performing Calibration

For calibration of the ADVIA Centaur HBcT2 assay, use the calibrators provided with each kit.

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- At the end of the 21-day calibration interval.
- When changing lot numbers of primary reagent packs.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Calibrators are liquid and ready to use. Allow the calibrators to equilibrate to room temperature. Gently mix and invert the vials to ensure homogeneity of the material.

Use calibrators within the stability limits specified in *Reagents* and discard any remaining material.

Calibration Procedure

The calibrators are provided in dropper vials. Each dispensed drop is approximately 50 µL.

Perform the calibration procedure using the following steps:

1. Ensure that the appropriate master curve and calibrator assigned values are entered on the system. For information about defining the master curve and entering calibrator values, refer to the system online help.
2. Load the required reagents for the assay.
3. Schedule the calibrators.
4. Label two sample containers with barcode labels: one container for the low calibrator and one container for the high calibrator. Place the barcode labels on the sample containers with the readable characters oriented vertically.

   Note Barcode labels are lot-specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.
5. Gently mix the product and dispense a sufficient volume of each calibrator into the appropriate sample containers. Avoid bubbles.

   The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the system online help.
6. Load the samples according to the system online help.

Note Dispose of any calibrator that remains in the sample container after 8 hours. Do not refill or reuse sample containers. Do not return any calibrator material back into the original container.

Performing Quality Control

For quality control of the ADVIA Centaur HBcT2 assay, use the ADVIA Centaur HBcT2 QC at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use. For the assigned values, refer to the quality control assigned value sheet provided.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

Taking Corrective Action

If the quality control results do not fall within the expected control interval, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the system online help.

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system online help. Refer to *Interpretation of Results*.

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Interpretation of Results

The system reports ADVIA Centaur HBcT2 assay results in Index Values and as Nonreactive or Reactive:

- Nonreactive: < 1.00 Index. These samples are considered negative.
- Reactive: ≥ 1.00 Index. These samples are considered positive.

The cut-off value for the ADVIA Centaur HBcT2 assay was verified based on the clinical agreement of results generated from clinical studies.

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

Limitations

The following information pertains to limitations of the assay:

- The ADVIA Centaur HBcT2 assay is limited to the detection of total antibodies to hepatitis B core antigen in human serum or plasma. Assays for the detection of anti-HBc may not identify all patient samples that contain hepatitis B virus.
- Performance characteristics have not been established for the assay used in conjunction with other manufacturers' assays for specific HBV serological markers. Laboratories are responsible for establishing their own performance characteristics.
- Performance characteristics have not been established for the use of the ADVIA Centaur HBcT2 assay as an aid in determining susceptibility to HBV infection prior to or following vaccination in infants, children, or adolescents.

- Results obtained with the assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- The performance of the assay has not been established with cadaver specimens, heat- inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- A nonreactive test result does not exclude the possibility of exposure to or infection with HBV. Human anti-HBc total may be undetectable in some stages of the infection and in some clinical conditions.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[12,13] Additional information may be required for diagnosis.

Expected Values

The study was designed to test samples from patients with general signs and symptoms of hepatitis B or a high risk of HBV infection, including pregnant women, transplant recipients, and dialysis patients.

The analysis included 1595 samples in the following classifications: acute, chronic, early recovery, recovered, recovery, HBV vaccine response, not previously infected with HBV, and unclassified. The study population was 30.3% Caucasian, 61.0% Black, 2.4% Asian, and 6.3% from unknown or other race. The patients were nearly equally divided by sex (53.0% female and 47.0% male). The mean age was 47 years. Patients in the study population were from the following geographic regions: Florida (36.5%), California (27.2%), Minnesota (33.6%), and Arizona, Massachusetts, Michigan, North Dakota, New Jersey, Nevada, Texas, Virginia, Wisconsin, and other locations combined (2.7 %).

Results were established using the ADVIA Centaur CP system. The test results for the prospective population for all sites, combined by age group and gender, are summarized in the following table.

Comparison of results in the signs-and-symptoms prospective population: ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

		Reactive		Nonreactive		Total
Age (Years)	**Gender**	**N[a]**	**(%)**	**N**	**(%)**	**N**
21-30	Male	2	2.8	70	97.2	72
	Female	4	2.0	193	98.0	197
	Overall	6	2.2	263	97.8	269
31-40	Male	14	16.7	70	83.3	84
	Female	31	16.2	161	83.9	192
	Overall	45	16.3	231	83.7	276
41-50	Male	48	34.3	92	65.7	140
	Female	35	24.8	106	75.2	141
	Overall	83	29.5	198	70.5	281
51-60	Male	114	40.6	167	59.4	281
	Female	78	40.0	117	60.0	195
	Overall	192	40.3	284	59.7	476

		Reactive		Nonreactive		Total
Age (Years)	Gender	N[a]	(%)	N	(%)	N
61-70	Male	72	47.4	80	52.6	152
	Female	37	38.1	60	61.9	97
	Overall	109	43.8	140	56.2	249
71-92	Male	10	34.5	19	65.5	29
	Female	5	33.3	10	66.7	15
	Overall	15	34.1	29	65.9	44
Total	Male	260	34.3	498	65.7	758
	Female	190	22.7	647	77.3	837
	Overall	450	28.2	1145	71.8	1595

[a] Number of measurements.

Results are representative of the population tested. Consider this information as guidance only.

Performance Characteristics

Measuring Interval

0.07–10.00 Index is reported as nonreactive or reactive.

Clinical Performance

Results by Specimen Classification

Patients were assessed for hepatitis markers using commercially available, FDA-approved reference assays using the ADVIA Centaur XP system. The serological assessment included the following 6 HBV markers: hepatitis B virus surface antigen (HBsAg), hepatitis B e antigen (HBeAg), IgM antibody to hepatitis B core antigen (anti-HBc IgM), total antibody to hepatitis B virus core antigen (anti-HBc Total), hepatitis B e antibody (anti-HBe), and antibody to hepatitis B virus surface antigen (anti-HBs).

Testing of these specimens occurred at 3 study sites. Patients had the following hepatitis marker profiles: acute, chronic, early recovery, recovery, recovered, HBV vaccine response, not previously infected with HBV, and unclassified.

Each patient's HBV infection status was classified based on a single specimen and the reactive (+) or nonreactive (-) patterns of the 6 HBV reference serological markers. The 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 30 unique reference marker patterns observed using the FDA-approved assays.

Classification by HBV Reference Markers (All Testing Sites)

HBV Classification	HBsAg[a]	HBeAg	Anti-HBc IgM	Anti-HBc Total	Anti-HBe	Anti-HBs[b]
Acute	+[c]	+	+	+	+	–[d]
Acute	+	+	+	+	–	–
Chronic	+	+	–	+	+	–

HBV Classification	HBsAg[a]	HBeAg	Anti-HBc IgM	Anti-HBc Total	Anti-HBe	Anti-HBs[b]
Chronic	+	+	–	+	–	–
Chronic	+	–	–	+	+	–
Chronic	+	–	–	+	–	+
Chronic	+	–	–	+	–	–
Early Recovery	–	–	+	+	+	+
Early Recovery	–	–	+	+	–	+
Early Recovery	–	–	–	+	+	–
Recovery	–	–	–	+	+	+
Recovery	–	–	–	–	+	+
Recovered	–	–	–	+	–	+
Recovered	–	–	–	+	–	–
HBV Vaccine Response	–	–	–	–	–	+
Not Previously Infected	–	–	–	–	–	–
Unclassified	+	–	–	–	–	+
Unclassified	+	–	–	–	–	–
Unclassified	–	+	–	–	–	+
Unclassified	–	+	–	–	–	–
Unclassified	–	–	+	–	–	–
Unclassified	–	–	–	–	+	–
Unclassified	+	+	–	–	–	+
Unclassified	+	+	–	–	–	–
Unclassified	–	–	Equivocal	–	–	–
Unclassified	–	–	Equivocal	+	+	–
Unclassified	–	–	Equivocal	+	+	+
Unclassified	+	–	Equivocal	+	+	–
Unclassified	Conf Invalid[e]	–	–	–	–	–
Unclassified	–	+	–	+	+	+

[a] Reactive (+) = reference HBsAg assay result was reactive and confirmed to be positive by neutralization. nonreactive (-) = reference HBsAg assay result was nonreactive or reactive but not confirmed positive by neutralization.

[b] > 10 mIU/mL

[c] + = Reactive.

[d] - = Nonreactive.

[e] Test result was invalid based on confirmatory testing.

Comparison of Results: Prospective Population by HBV Category

A total of 1595 samples from patients with general signs and symptoms of hepatitis B or with a high risk of HBV infection were tested using the ADVIA Centaur HBcT2 assay and a reference anti-HBc total assay. Subgroups within this population included pregnant women, transplant recipients, and dialysis patients. Results were established using the ADVIA Centaur CP system.

Comparison of results in the signs-and-symptoms prospective population: ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay		
ADVIA Centaur HBcT2 Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	189	11	200
Nonreactive	5	571	576
Total	**194**	**582**	**776**

Positive Percent Agreement: 97.4% (189/194); 95% Confidence Interval: 94.1%–98.9%

Negative Percent Agreement: 98.1% (571/582); 95% Confidence Interval: 96.6%–98.9%

Comparison of results in the high-risk prospective population: ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay		
ADVIA Centaur HBcT2 Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	244	6	250
Nonreactive	5	564	569
Total	**249**	**570**	**819**

Positive Percent Agreement: 98.0% (244/249); 95% Confidence Interval: 95.4%–99.1%

Negative Percent Agreement: 98.9% (564/570); 95% Confidence Interval: 97.7%–99.5%

The agreement between the ADVIA Centaur HBcT2 assay and a reference anti-HBc total assay for each HBV category is summarized in the following table.

Prospective Population by HBV Category - ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		**Reference Anti-HBc Total Nonreactive**		
	ADVIA Centaur HBcT2 Assay		**ADVIA Centaur HBcT2 Assay**		
HBV Category	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Signs and symptoms	256	4	3	365	628
High risk	139	6	7	467	619
Pregnant	10	0	1	182	193
Transplant	8	0	1	41	50

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
HBV Category	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Dialysis	20	0	5	80	105
Total	**433**	**10**	**17**	**1135**	**1595**

Percent agreement and confidence intervals by HBV category (all test sites)

	Positive Agreement		Negative Agreement	
HBV Category	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
Signs and symptoms	98.5 (256/260)	96.1–99.4	99.2 (365/368)	97.6–99.7
High risk	95.9 (139/145)	91.3–98.1	98.5 (467/474)	97.0–99.3
Pregnant	100 (10/10)	72.2–100	99.5 (182/183)	97.0–99.9
Transplant	100 (8/8)	67.6–100	97.6 (41/42)	87.7–99.6
Dialysis	100 (20/20)	83.9–100	94.1 (80/85)	87.0–97.5
Total, N = 1595	**97.7 (433/443)**	**95.9–98.8**	**98.5 (1135/1152)**	**97.6–99.1**

[a] x = the number of ADVIA Centaur HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of ADVIA Centaur HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

Comparison of Results: Prospective Population by HBV Serological Classification

A total of 1595 prospective samples were tested using the ADVIA Centaur HBcT2 assay and a reference anti-HBc total assay for each HBV serological classification (all testing sites). Results were established using the ADVIA Centaur CP system.

Comparison of results in the prospective population by HBV serological classification; ADVIA Centaur HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
HBV Classification	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Acute	3	0	–	–	3
Chronic	77	0	–	–	77
Early recovery	15	0	–	–	15
Recovery	101	0	1	3	105
Recovered	207	2	9	5	223
HBV vaccine response	19	6	3	511	539

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	ADVIA Centaur HBcT2 Assay		ADVIA Centaur HBcT2 Assay		
HBV Classification	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Not previously infected	3	2	3	591	599
Unclassified	8	0	1	25	34
Total	**433**	**10**	**17**	**1135**	**1595**

Percent agreement and confidence intervals by HBV classification (all testing sites)

	Positive Agreement		Negative Agreement	
HBV Classification	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
Acute	100 (3/3)	43.9–100	–[d]	–
Chronic	100 (77/77)	95.2–100	–	–
Early recovery	100 (15/15)	79.6–100	–	–
Recovery	100 (101/101)	96.3–100	75.0 (3/4)	30.1–95.4
Recovered	99.0 (207/209)	96.6–99.7	35.7 (5/14)	16.3–61.2
HBV vaccine response	76.0 (19/25)	56.6–88.5	99.4 (511/514)	98.3–99.8
Not previously infected	60.0 (3/5)	23.1–88.2	99.5 (591/594)	98.5–99.8
Unclassified	100 (8/8)	67.6–100	96.2 (25/26)	81.1–99.3
Total, N = 1595	**97.7 (433/443)**	**95.9–98.8**	**98.5 (1135/1152)**	**97.6–99.1**

[a] x = the number of ADVIA Centaur HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of ADVIA Centaur HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

[d] Percentages are for the numbers of reactive and nonreactive samples in a given row. If the total number of samples in the row is zero, a dash (–) is displayed.

Prenatal Population

Serum samples from United States were included in the study (N = 193). Samples were tested from pregnant women with either signs and symptoms of hepatitis B or with risk factors for HBV infection, who were in the first (62/193, 32.1%), second (61/193, 31.6%), or third trimester (70/193, 36.3%) of pregnancy. Results of the testing (reactive and nonreactive) were compared using the ADVIA Centaur HBcT2 assay and the reference anti-HBc total assay for the prenatal population in their first, second, and third trimester, for all testing sites. Results were established using the ADVIA Centaur CP system.

Comparison of results: prenatal population (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		**Reference Anti-HBc Total Nonreactive**		
	ADVIA Centaur HBcT2 Assay		**ADVIA Centaur HBcT2 Assay**		
Trimester	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
First	2	0	0	60	62
Second	6	0	1	54	61
Third	2	0	0	68	70
Total	**10**	**0**	**1**	**182**	**193**

Percent agreement and confidence intervals: prenatal population (all test sites)

	Positive Agreement		**Negative Agreement**	
Trimester	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
First	100 (2/2)	34.2–100	100 (60/60)	94.0–100
Second	100 (6/6)	61.0–100	98.2 (54/55)	90.4–99.7
Third	100 (2/2)	34.2–100	100 (68/68)	94.7–100
Total	**100 (10/10)**	**72.2–100**	**99.5 (182/183)**	**97.0–99.9**

[a] x = the number of ADVIA Centaur HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of ADVIA Centaur HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

Pediatric and Adolescent Population

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Pediatric and adolescent (non-pregnant) samples were prospectively collected (N = 139) and tested using the ADVIA Centaur XP system. The population analysis was stratified by the following age groups: 2–12 years and 13–21 years.

	Reference Assay - Reactive		Reference Assay - Nonreactive		
Age Range (Years)	**HBcT2 Assay - Reactive**	**HBcT2 Assay - Nonreactive**	**HBcT2 Assay - Reactive**	**HBcT2 Assay - Nonreactive**	**Total**
2–12	1	0	0	29	30
13–21	3	0	1	105	109
Total	4	0	1	134	139

Age Range (Years)	**Positive Percent Agreement % (x/n)[a]**	**95% Confidence Interval**	**Negative Percent Agreement % (x/n)[b]**	**95% Confidence Interval**
2–12	100 (1/1)	20.7–100	100 (29/29)	88.3–100
13–21	100 (3/3)	43.9–100	99.1 (105/106)	94.8–99.8
Total	**100 (4/4)**	**51.0–100**	**99.3 (134/135)**	**95.9–99.9**

[a] x = the number of ADVIA Centaur HBcT2 results using the ADVIA Centaur XP system that are reactive in agreement with the reference HBcT2 assay; n = the total number of reference HBcT2 results that are reactive.

[b] x = the number of ADVIA Centaur HBcT2 results using the ADVIA Centaur XP system that are nonreactive in agreement with the reference HBcT2 assay; n = the total number of reference HBcT2 results that are nonreactive.

Because few positives were identified, a study was conducted to evaluate the results observed when pediatric samples are tested with the ADVIA Centaur HBcT2 assay using the ADVIA Centaur XP system. A total of 60 pediatric (age 2–21 years) and 60 adult serum samples were spiked with unique native anti- HBc positive samples. Out of 60 pediatric samples tested 59 samples showed bias less than 20% (98.3% samples). The distribution of percent bias between the Index values of the spiked pediatric serum samples and the paired adult serum samples are summarized in the following table:

	Distribution of Percent Bias			
Age Range (Years)	**N[a]**	**≤ 10%**	**> 10%– ≤ 20%**	**> 20%– ≤ 30%**
2–12	20	45.0 (9/20)	50.0 (10/20)	5.0 (1/20)
13–21	40	72.5 (29/40)	27.5 (11/40)	0.0 (0/40)
Total	60	63.3 (38/60)	35.0 (21/60)	1.7 (1/60)

[a] Number tested.

Seroconversion Panels

Commercially available HBV patient seroconversion panels were tested using the ADVIA Centaur HBcT2 assay to determine the seroconversion sensitivity of the assay. Results were established using the ADVIA Centaur CP system. The performance of the ADVIA Centaur HBcT2 assay on the seroconversion panels matched or exceeded the performance of the reference assay.

	Reference Anti-HBc Total Assay - Reactive From Initial Draw Date		ADVIA Centaur HBcT2 Assay versus Reference Anti-HBc Total Assay
Panel ID	**ADVIA Centaur HBcT2 Assay (Days)**	**Reference Assay (Days)**	**Difference in Bleed Numbers[a]**
HBV6278	41	41	0
HBV6281	41	41	0
HBV9093	49	49	0
HBV9099	74	74	0

	Reference Anti-HBc Total Assay - Reactive From Initial Draw Date		ADVIA Centaur HBcT2 Assay versus Reference Anti-HBc Total Assay
Panel ID	ADVIA Centaur HBcT2 Assay (Days)	Reference Assay (Days)	Difference in Bleed Numbers[a]
PHM941	99	99	0
SCPHBV1	29	29	0
SCPHBV4	65	71	+1

[a] The difference in bleed numbers is relative to the reference assay. For example, a "+1" means that the reference assay required 1 additional bleed before reactivity was determined as compared to the time point when the ADVIA Centaur HBcT2 assay confirmed as reactive.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[14] Samples were assayed in duplicate in 2 runs per day for 20 days. Results were established using the ADVIA Centaur CP system. The following results were obtained using 1 reagent lot and stored calibration curves.

			Repeatability		Within-Laboratory Precision	
Specimen Type	N[a]	Mean (Index)	SD[b] (Index)	CV[c] (%)	SD (Index)	CV (%)
Plasma A	80	0.21	0.02	N/A[d]	0.05	N/A
Plasma B	80	0.68	0.04	N/A	0.08	N/A
Plasma C	80	1.60	0.07	4.4	0.14	8.9
Plasma D	80	2.22	0.09	4.1	0.21	9.6
Plasma E	80	7.66	0.39	5.1	0.89	11.6
Serum A	80	0.13	0.02	N/A	0.06	N/A
Serum B	80	0.56	0.03	N/A	0.07	N/A
Serum C	80	1.49	0.07	4.4	0.15	10.3
Serum D	80	2.22	0.09	3.9	0.20	9.0
Serum E	80	6.71	0.36	5.3	0.68	10.1
Control 1 (negative)	80	0.21	0.02	N/A	0.06	N/A
Control 2 (positive)	80	3.12	0.13	4.2	0.27	8.5

[a] Number of measurements.
[b] Standard deviation.
[c] Coefficient of variation.
[d] N/A = not applicable. The results remained nonreactive throughout the study.

The assay is designed to have the following precision.

	Precision	
Concentration Interval (Index)	Repeatability (Within-Run)	Within-Laboratory (Total Precision)

0.80–10.00	≤ 10.0% CV	≤ 12.0% CV

For specimens < 0.80 Index, the assay must not show a change in clinical interpretation.

Reproducibility

Reproducibility was evaluated according to CLSI document EP05-A3.[14] A reproducibility study was conducted at 3 sites, with each site evaluating 3 reagent lots. The protocol was run over 5 days, 2 runs per day. There were 3 replicates per run for each sample, for a total 270 replicates per sample (N = 270). Results were established using the ADVIA Centaur CP system. The following results are representative of the performance of the assay:

Sample Type (N = 270)	Mean (Index)	Repeatability (Within-Run) SD[a] (Index)	Repeatability (Within-Run) CV[b] (%)	Between Run SD (Index)	Between Run CV (%)	Between Day SD (Index)	Between Day CV (%)	Between Lot SD (Index)	Between Lot CV (%)	Within Laboratory SD (Index)	Within Laboratory CV (%)	Between Site SD (Index)	Between Site CV (%)	Reproducibility SD (Index)	Reproducibility CV (%)
Serum A[c]	0.40	0.02	N/A[d]	0.02	N/A	0.02	N/A	0.06	N/A	0.04	N/A	0.00	N/A	0.07	N/A
Serum B[e]	0.71	0.03	N/A	0.03	N/A	0.03	N/A	0.06	N/A	0.05	N/A	0.00	N/A	0.08	N/A
Serum C	1.34	0.05	3.6	0.04	2.8	0.04	2.8	0.12	8.8	0.07	5.3	0.02	1.5	0.14	10.4
Serum D	2.41	0.08	3.3	0.07	3.1	0.08	3.4	0.18	7.4	0.14	5.6	0.02	0.7	0.23	9.3
Serum E	5.28	0.22	4.1	0.19	3.6	0.16	3.1	0.36	6.8	0.33	6.2	0.12	2.2	0.50	9.5
Serum F[f]	8.66	0.33	3.9	0.27	3.1	0.37	.3	0.56	6.5	0.38	4.4	0.12	1.4	0.69	8.0
Control 1 (negative)	0.19	0.02	N/A	0.02	N/A	0.01	N/A	0.03	N/A	0.04	N/A	0.02	N/A	0.05	N/A
Control 2 (positive)	3.28	0.11	3.4	0.06	1.8	0.11	3.4	0.23	7.1	0.17	5.1	0.08	2.3	0.30	9.1

[a] Standard deviation.

[b] Coefficient of variation

[c] 1 sample outside of the measuring interval(N = 1) was calculated offline and was included in analysis .

[d] N/A = not applicable. The results remained nonreactive throughout the study.[e] 10 samples outside of the measuring interval(N = 10) were calculated offline and were included in analysis.

f 133 samples outside of the measuring interval(N = 137) were calculated offline and were included in analysis.

The assay is designed to have the following reproducibility:

Concentration Interval (Index)	Reproducibility
0.80–10.00	≤ 20.0% CV

For specimens < 0.80 Index, the assay must not show a change in clinical interpretation.

Assay Comparison

The percent agreement between the ADVIA Centaur CP system and the ADVIA Centaur XP system was evaluated by testing 1595 samples at 3 clinical testing sites. Each site used 1 ADVIA Centaur CP system and 1 ADVIA Centaur XP system, and tested 3 lots of reagents. The samples were obtained from subjects with general signs and symptoms of hepatitis B or with a high risk of HBV infection, inclusive of pregnant women, transplant recipients, and dialysis patients.

	ADVIA Centaur CP		
ADVIA Centaur XP	**Reactive**	**Nonreactive**	**Total**
Reactive	448	5	453
Nonreactive	2	1140	1142
Total	**450**	**1145**	**1595**

Positive Percent Agreement: 99.6% (448/450); 95% Confidence Interval: 98.4%–99.9%

Negative Percent Agreement: 99.6% (1140/1145); 95% Confidence Interval: 99.0%–99.8%

Specimen Equivalency

Specimen equivalency was determined with the linear regression model in accordance with CLSI Document EP09-A2.[15] Results were established using the ADVIA Centaur XP system.

The ADVIA Centaur HBcT2 results ranged from 0.11–9.99 Index. No significant difference between the tube types was observed. Agreement of the specimen types may vary depending on the study design and sample population used.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Gel-barrier tube (serum)	y = 0.96 (x) + 0.04	0.29–9.42 Index	50	0.983
Dipotassium EDTA plasma	y = 0.98 (x) + 0.03	0.24–9.24 Index	50	0.981
Lithium heparin plasma	y = 1.00 (x) - 0.05	0.12–9.54 Index	50	0.968
Sodium heparin plasma	y = 1.04 (x) - 0.09	0.11–9.99 Index	50	0.971

[a] Number of samples tested.

[b] Correlation coefficient.

The assay is designed to have a correlation coefficient of ≥ 0.95, a slope of test tube type (y) versus reference (x) of 1.0 ± 0.15, and an intercept of < 0.90 Index.

Interferences

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2[16] using the ADVIA Centaur XP system.

Substance	Substance Test Concentration
Hemoglobin	500 mg/dL
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	40 mg/dL
Lipemia	1000 mg/dL

Substance	Substance Test Concentration
Biotin	3500 ng/mL
Cholesterol	500 mg/dL
Hyper IgG	60 mg/mL
Hyperproteinemic	12.0 g/dL
Hypoproteinemic	3.5 g/dL

The assay was designed to have ≤ 10% interference up to the concentration of the substances tested.

Cross-Reactivity

The assay was evaluated for potential cross-reactivity with other viral and microbial antibodies and disease state specimens. The anti-HBc status of each sample was assessed using the ADVIA Centaur HBcT2 assay and an anti-HBc reference assay. Results were established using the ADVIA Centaur XP system. The following results are representative of the performance of the assay:

		Number of Reactive Anti-HBc Total Results	
Substance	Number Tested	ADVIA Centaur HBcT2 Assay	Reference Assay
Anti-nuclear antibody (ANA)	32	2	2
Cytomegalovirus (CMV) IgG	15	0	0
Cytomegalovirus (CMV) IgM	15	0	0
Epstein-Barr virus (EBV) IgG	15	0	0
Epstein-Barr virus (EBV) IgM	15	0	0
Flu vaccine recipient	15	0	0
Human anti-mouse antibody (HAMA)	15	2	2
Hepatitis A infection (HAV)	20	4	4
Hepatitis C infection (HCV)	15	7	7
Herpes simplex virus (HSV) IgG	15	0	0
Herpes simplex virus (HSV) IgM	14	0	0
Human immunodeficiency virus (HIV 1/2)	15	6	6
Multiparity	25	1	1
Non-viral liver disease	15	1	0
Rheumatoid arthritis	15	2	1
Rubella IgG	15	0	0
Syphilis IgG	15	3	3
Systemic lupus erythematosus (SLE)	20	1	1
Toxoplasma IgG	21	0	0

Substance	Number Tested	Number of Reactive Anti-HBc Total Results	
		ADVIA Centaur HBcT2 Assay	Reference Assay
Toxoplasma IgM	11	0	0
Varicella zoster virus (VZV) IgG	15	1	1

Analytical Sensitivity

To examine the analytical sensitivity of the ADVIA Centaur HBcT2 assay, the WHO Anti-hepatitis B virus core antigen (anti-HBc) 1st International Standard 95/522, was used to prepare a dilution series that was tested using 3 ADVIA Centaur HBcT2 reagent lots. Linear regression was used to determine the concentration of the WHO 95/522 reference sample value, which corresponds to the ADVIA Centaur HBcT2 cut-off (Index Value = 1.00). The WHO 95/522 International Unit per milliliter (IU/mL) concentration at the assay cut-off was determined to be 0.26 IU/mL.

Standardization

The ADVIA Centaur HBcT2 assay traceability is based on the relative clinical agreement with commercially available anti-HBc total assays. Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or

distributor. siemens-healthineers.com

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16. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP07-A2.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]	EC REP	Authorized representative in the European Community	5.1.2[a]
REF	Use-by date	5.1.4[a]	CH REP	Authorized representative in Switzerland	Proprietary
	Catalog number	5.1.6[a]	Σ	Batch code	5.1.5[a]
<.../eifu>	Consult Instructions for Use	5.4.3[a]	Rev. XX	Contains sufficient for <n> tests	5.5.5[a]
IVD	Internet URL address to access the electronic instructions for use	Proprietary		Version of Instructions for Use	Proprietary
RxOnly	*In vitro* diagnostic medical device	5.5.1[a]	UDI	Unique Device Identifier	5.7.10[c]
CE XXXX	CE Marking with Notified Body	EU IVDR[d]	Rev. REVISION	Revision	Proprietary
	Prescription device (US only)	FDA[b]		CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of tempera-	5.3.5[a]

ture

Symbol	Symbol	Sourc	Symbol	Symbol	Sourc
	Do not re-	5.4.2[a]		Do not	Proprietar
	Recycl	1135[e]		This way	0623[e]
	Biological	5.4.1[a]		Caution	5.4.4[a]
	Common	Proprietar		International System of	Proprietar
YYYY-MM-	Date format (year-month- day)	N/	**YYYY-**	Date format (year-month)	
	Document face	1952[e]		Targe	Proprietar
	Handheld barcode scanner			Interval	Proprietar
	Lot	Proprietar		Variable hexadecimal y number that ensures the Master Curve and Cali- brator definition	Proprietar
	Calibrator lot	Proprietar		Master Curve definition	
	Quality control lot value				

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.
[b] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.
[c] ISO 15223-1:2020-04
[d] IVDR REGULATION (EU) 2017/746
[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.
[f] Indicates Assay-*e*Note

Legal Information

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HBc Total 2 (HBcT2)

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

Current Revision and Date[a]	Rev. 03, 2023-04	
Product Name	Atellica IM HBc Total 2 (HBcT2)	REF 11200739 (100 tests)
Abbreviated Product Name	Atellica IM HBcT2	
Test Name/ID	HBcT2	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM HBcT2 QC	REF 11200740
Specimen Types	Serum, EDTA plasma, lithium heparin plasma, sodium heparin plasma	
Sample Volume	50 µL	
Measuring Interval	0.07–10.00 Index	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

Intended Use

The Atellica® IM HBc Total 2 (HBcT2) assay is an *in vitro* diagnostic immunoassay for use in the qualitative determination of total antibodies to the core antigen of the hepatitis B virus (HBV) in human pediatric (2–21 years old) and adult serum and plasma (EDTA, lithium heparin, and sodium heparin) using the Atellica® IM Analyzer.

This assay can be used as an aid in the diagnosis of acute or chronic hepatitis B virus (HBV) infection and in the determination of the clinical status of HBV-infected individuals in conjunction with other HBV serological markers, for the laboratory diagnosis of HBV disease associated with HBV infection. This assay can also be used as an aid in the differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown.

This assay is not intended for screening donors of blood or blood products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).

Summary and Explanation

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 6–8 weeks (range 1–6 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%–95% of patients with HBV infection completely recover from acute illness and clear the virus. Approximately 5%–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.[1-3]

Hepatitis B core antigen (HBcAg), found in liver cells, does not circulate in the bloodstream. However, IgM and IgG antibodies to HBcAg can be detected serologically in HBV-infected individuals. Anti-HBc IgM is detectable first and remains detectable for approximately
6 months. Shortly after the IgM response, anti-HBc IgG appears and can remain detectable indefinitely. The presence of anti-HBc IgM is characteristic of acute infection, while the presence of anti-HBc IgG is characteristic of chronic or recovered stages of HBV infection.

Anti-HBc total assays detect both IgM and IgG anti-HBc responses. Most often levels of anti-HBc will coincide with detectable levels of other HBV markers. Rarely, anti-HBc may be the only detectable HBV marker. This may occur during the brief period when hepatitis B surface antigen (HBsAg) has been cleared from the bloodstream and before antibodies to hepatitis B surface antigen (anti-HBs) become detectable. For this reason, the use of anti-HBc total assays to detect acute infection is not recommended. Anti-HBc total assays should be used in conjunction with other marker assays to assess current or past exposure to HBV.[1,2,4,5]

Principles of the Procedure

The Atellica IM HBcT2 assay is a 2-wash antigen sandwich immunoassay in which antigens are bridged by antibody present in the patient sample. The Solid Phase contains a preformed complex of streptavidin-coated microparticles and biotinylated recombinant HBc antigen, and is used to capture anti-HBc in the patient sample.

The Lite Reagent contains recombinant HBc antigen labeled with acridinium ester and anti-human IgG Fab monoclonal antibody labeled with acridinium ester, and is used to detect anti-HBc in the sample. The Ancillary Reagent, Solid Phase, and Ancillary Well Reagent are added to the sample, followed by Lite Reagent. Antibody-antigen complexes will form if anti-HBc antibodies (IgM and IgG) are present in the sample.

A direct relationship exists between the amount of anti-HBc antibodies 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 the Index Value established with the calibrators. Refer to *Interpretation of Results*.

Reagents

Material Description	Storage	Stability
Atellica IM HBcT2 ReadyPack® primary reagent pack[a, b]	Unopened at 2–8° C	Until expiration date on product
Lite Reagent 10.0 mL/reagent pack Recombinant hepatitis B core antigen (~0.03 µg/mL) labeled with acridinium ester; mouse anti-human IgG Fab fragment (~3.5 ng/mL) labeled with acridinium ester; bovine serum albumin (BSA); buffer; surfactant; sodium azide (< 0.1%) **Solid Phase** 12.5 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated recombinant HBcAg (~1.0 µg/mL) in buffer; potassium thiocyanate (5.0%); BSA; surfactant; sodium azide (< 0.1%) **Ancillary Well Reagent** 10.0 mL/reagent pack Buffer; potassium thiocyanate (12.5%); non-magnetic particles; BSA; surfactant; sodium azide (< 0.1%)	Onboard	84 days
Atellica IM HBcT2 ReadyPack ancillary reagent pack[a, b] 10.0 mL/reagent pack Buffer; potassium thiocyanate (5.0%); surfactant; sodium azide (< 0.1%)	Unopened at 2–8° C	Until expiration date on product
	Onboard	84 days
Atellica IM HBcT2 CAL[a] 2.0 mL/vial Processed human plasma positive for HBc antibodies; sodium azide (< 0.1%); preservatives	Unopened at 2–8° C	Until expiration date on product
	Opened at 2–8° C	60 days
	At room temperature	8 hours

[a] Store in an upright position.

[b] Prevent exposure to sunlight and heat.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

For Prescription Use Only.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens-healthineers.com.

H317, H412
P280, P273,
P302+P352,
P333+P313,
P362+P364,
P501

Warning!
May cause an allergic skin reaction. Harmful to aquatic life with long lasting effects.
Wear protective gloves/protective clothing/eye protection/face protection. Avoid release to the environment. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Take off contaminated clothing and wash it before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2- methyl-2H-isothiazol-3-one (3:1) (in Atellica IM HBcT2 CAL)

Warning! Potential Biohazard

Contains human source material.

No known test method can ensure that products derived from human source materials will not transmit infection. These materials should be handled using good laboratory practices and universal precautions.[6-8]

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.

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.

Storage and Stability

Store all reagents in an upright position, away from light and heat. Do not use products beyond the expiration date printed on the product labeling.

For information about product storage and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

For information about product onboard stability, refer to *Reagents*.

Specimen Collection and Handling

Serum and plasma (EDTA, lithium heparin, and sodium heparin) are the recommended specimen types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[8]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[9]

- Follow the instructions provided with your specimen collection device for use and processing.[10]
- Allow blood specimens to clot completely before centrifugation.[11]
- Keep tubes capped at all times.[11]
- Specimens are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post-draw. When testing 12 specimens, and the centrifugation step was varied up to 24 hours post-draw, no clinically significant differences were observed.

Storing the Specimen

- After centrifugation, specimens in the primary collection device are stable for up to 7 days at 2–8° C. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel-barrier tubes.
- Separated samples are stable for up to 3 days at room temperature, and for up to 7 days at 2–8° C.
- Separated samples are stable at ≤ -20° C for up to 12 months. When 10 samples were subjected to 5 freeze-thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge them before using.

The handling and storage information provided here is based on data or references maintained by the manufacturer. 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.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

If during shipment, specimens may be subjected to temperatures > 25° C, then ship specimens frozen.

Preparing the Samples

This assay requires 50 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[11]

Procedure

Materials Provided

The following materials are provided:

REF	Content	Number of Tests
11200739	1 ReadyPack primary reagent pack containing Atellica IM HBcT2 Lite Reagent, Solid Phase, and Ancillary Well Reagent 1 ReadyPack ancillary reagent pack containing Atellica IM HBcT2 Ancillary Reagent ANC Atellica IM HBcT2 master curve and test definition MC TDEF 1 vial Atellica IM HBcT2 CAL low calibrator 1 vial Atellica IM HBcT2 CAL high calibrator CAL LOT VAL Atellica IM HBcT2 CAL calibrator assigned value sheet	100

Materials Required but Not Provided

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

REF	Description	
	Atellica IM Analyzer[a]	
11200740	Atellica IM HBcT2 QC (quality control material) 1 2	2 x 7.0 mL negative quality control, level 1 CONTROL - 1 2 x 7.0 mL positive quality control, level 2 CONTROL + 2 Quality control assigned value sheet CONTROL LOT VAL

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 50 µL of sample into a cuvette.
2. Dispenses 100 µL of Ancillary Reagent into a cuvette, then incubates for 6 minutes at 37° C.
3. Dispenses 100 µL of Ancillary Well Reagent and 125 µL of Solid Phase, then incubates for 18 minutes at 37° C.

   Note The Atellica IM HBcT2 Ancillary Well Reagent is milky white in color.
4. Performs a wash sequence using Atellica IM Wash.
5. Resuspends the particles in 250 µL of Atellica IM Wash.
6. Dispenses 100 µL of Lite Reagent, then incubates for 18 minutes at 37° C.
7. Performs a wash sequence using Atellica IM Wash.
8. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
9. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

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

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Materials Required but Not Provided* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve and test definition by scanning the 2D barcodes. For information about entering the master curve and test definition, refer to the system online help.

Performing Calibration

For calibration of the Atellica IM HBcT2 assay, use the calibrators provided with each kit.

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

Note When loading a new primary reagent pack, a calibration is not required if there is a valid lot calibration. For information about lot calibration and pack calibration, refer to the system online help.

Stability Interval	Days
Lot Calibration	63
Pack Calibration	42
Reagent Onboard Stability	84

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Calibrators are liquid and ready to use. Allow the calibrators to equilibrate to room temperature. Gently mix and invert the vials to ensure homogeneity of the material.

Use calibrators within the stability limits specified in *Reagents* and discard any remaining material.

Calibration Procedure

The calibrators are provided in dropper vials. Each dispensed drop is approximately 50 µL.

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the system online help.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the lot-specific value sheet provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the system online help.

Performing Quality Control

For quality control of the Atellica IM HBcT2 assay, use the Atellica IM HBcT2 QC at least once during each day that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use. For the assigned values, refer to the quality control assigned value sheet provided .

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

Taking Corrective Action

If the quality control results do not fall within the expected control interval, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the system online help.

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system online help. Refer to *Interpretation of Results*.

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Interpretation of Results

The system reports Atellica IM HBcT2 assay results in Index Values and as Nonreactive or Reactive:

- Nonreactive: < 1.00 Index. These samples are considered negative.
- Reactive: ≥ 1.00 Index. These samples are considered positive.

The cut-off value for the Atellica IM HBcT2 assay was verified based on the clinical agreement of results generated from clinical studies.

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

Limitations

The following information pertains to limitations of the assay:

- The Atellica IM HBcT2 assay is limited to the detection of total antibodies to hepatitis B core antigen in human serum or plasma. Assays for the detection of anti-HBc may not identify all patient samples that contain hepatitis B virus.
- Performance characteristics have not been established for the assay used in conjunction with other manufacturers' assays for specific HBV serological markers. Laboratories are responsible for establishing their own performance characteristics.
- Performance characteristics have not been established for the use of the Atellica IM HBcT2 assay as an aid in determining susceptibility to HBV infection prior to or following vaccination in infants, children, or adolescents.
- Results obtained with the assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- The performance of the assay has not been established with cadaver specimens, heat- inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- A nonreactive test result does not exclude the possibility of exposure to or infection with HBV. Human anti-HBc total may be undetectable in some stages of the infection and in some clinical conditions.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[12,13] Additional information may be required for diagnosis.

Expected Values

The study was designed to test samples from patients with general signs and symptoms of hepatitis B or a high risk of HBV infection, including pregnant women, transplant recipients, and dialysis patients.

The analysis included 1595 samples in the following classifications: acute, chronic, early recovery, recovered, recovery, HBV vaccine response, not previously infected with HBV, and unclassified. The study population was 30.3% Caucasian, 61.0% Black, 2.4% Asian, and 6.3% from unknown or other race. The patients were nearly equally divided by sex (53.0% female and 47.0% male). The mean age was 47 years. Patients in the study population were from the following geographic regions: Florida (36.5%), California (27.2%), Minnesota (33.6%), and Arizona, Massachusetts, Michigan, North Dakota, New Jersey, Nevada, Texas, Virginia, Wisconsin, and other locations combined (2.7 %).

The test results for the prospective population for all sites, combined by age group and gender, are summarized in the following table.

Comparison of results in the signs-and-symptoms prospective population: Atellica IM HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

		Reactive		Nonreactive		Total
Age (Years)	**Gender**	**N[a]**	**(%)**	**N**	**(%)**	**N**
21-30	Male	3	4.2	69	95.8	72
	Female	4	2.0	193	98.0	197
	Overall	7	2.6	262	97.4	269
31-40	Male	13	15.5	71	84.5	84
	Female	31	16.2	161	83.9	192
	Overall	44	15.9	232	84.1	276
41-50	Male	48	34.3	92	65.7	140
	Female	35	24.8	106	75.2	141
	Overall	83	29.5	198	70.5	281
51-60	Male	114	40.6	167	59.4	281
	Female	78	40.0	117	60.0	195
	Overall	192	40.3	284	59.7	476
61-70	Male	70	46.1	82	54.0	152
	Female	38	39.2	59	60.8	97
	Overall	108	43.4	141	56.6	249
71-92	Male	10	34.5	19	65.5	29
	Female	5	33.3	10	66.7	15
	Overall	15	34.1	29	65.9	44
Total	Male	258	34.0	500	66.0	758
	Female	191	22.8	646	77.2	837
	Overall	449	28.2	1146	71.9	1595

[a] Number of measurements.

Results are representative of the population tested. Consider this information as guidance only.

Performance Characteristics

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur systems. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur XP system.

Measuring Interval

0.07–10.00 Index is reported as nonreactive or reactive.

Clinical Performance

Results by Specimen Classification

Patients were assessed for hepatitis markers using commercially available, FDA-approved reference assays using the ADVIA Centaur XP system. The serological assessment included the following 6 HBV markers: hepatitis B virus surface antigen (HBsAg), hepatitis B e antigen (HBeAg), IgM antibody to hepatitis B core antigen (anti-HBc IgM), total antibody to hepatitis B virus core antigen (anti-HBc Total), hepatitis B e antibody (anti-HBe), and antibody to hepatitis B virus surface antigen (anti-HBs).

Testing of these specimens occurred at 3 study sites. Patients had the following hepatitis marker profiles: acute, chronic, early recovery, recovery, recovered, HBV vaccine response, not previously infected with HBV, and unclassified.

Each patient's HBV infection status was classified based on a single specimen and the reactive (+) or nonreactive (-) patterns of the 6 HBV reference serological markers. The 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 30 unique reference marker patterns observed using the FDA-approved assays.

Classification by HBV Reference Markers (All Testing Sites)

HBV Classification	HBsAg[a]	HBeAg	Anti-HBc IgM	Anti-HBc Total	Anti-HBe	Anti-HBs[b]
Acute	+[c]	+	+	+	+	–[d]
Acute	+	+	+	+	–	–
Chronic	+	+	–	+	+	–
Chronic	+	+	–	+	–	–
Chronic	+	–	–	+	+	–
Chronic	+	–	–	+	–	+
Chronic	+	–	–	+	–	–
Early Recovery	–	–	+	+	+	+
Early Recovery	–	–	+	+	–	+
Early Recovery	–	–	–	+	+	–
Recovery	–	–	–	+	+	+
Recovery	–	–	–	–	+	+
Recovered	–	–	–	+	–	+
Recovered	–	–	–	+	–	–
HBV Vaccine Response	–	–	–	–	–	+
Not Previously Infected	–	–	–	–	–	–
Unclassified	+	–	–	–	–	+
Unclassified	+	–	–	–	–	–
Unclassified	–	+	–	–	–	+
Unclassified	–	+	–	–	–	–
Unclassified	–	–	+	–	–	–

HBV Classification	HBsAg[a]	HBeAg	Anti-HBc IgM	Anti-HBc Total	Anti-HBe	Anti-HBs[b]
Unclassified	–	–	–	–	+	–
Unclassified	–	+	–	+	+	+
Unclassified	+	+	–	–	–	+
Unclassified	+	+	–	–	–	–
Unclassified	–	–	Equivocal	–	–	–
Unclassified	–	–	Equivocal	+	+	–
Unclassified	–	–	Equivocal	+	+	+
Unclassified	+	–	Equivocal	+	+	–
Unclassified	Conf Invalid[e]	–	–	–	–	–

[a] Reactive (+) = reference HBsAg assay result was reactive and confirmed to be positive by neutralization. nonreactive (-) = reference HBsAg assay result was nonreactive or reactive but not confirmed positive by neutralization.

[b] > 10 mIU/mL

[c] + = Reactive.

[d] - = Nonreactive.

[e] Test result was invalid based on confirmatory testing.

Comparison of Results: Prospective Population by HBV Category

A total of 1595 samples from patients with general signs and symptoms of hepatitis B or with a high risk of HBV infection was tested using the Atellica IM HBcT2 assay and a reference anti- HBc total assay. Subgroups within this population included pregnant women, transplant recipients, and dialysis patients.

Comparison of results in the signs-and-symptoms prospective population: Atellica IM HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay		
Atellica IM HBcT2 Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	189	11	200
Nonreactive	5	571	576
Total	**194**	**582**	**776**

Positive Percent Agreement: 97.4% (189/194); 95% Confidence Interval: 94.1%–98.9%

Negative Percent Agreement: 98.1% (571/582); 95% Confidence Interval: 96.6%–98.9%

Comparison of results in the high-risk prospective population: Atellica IM HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay		
Atellica IM HBcT2 Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	244	5	249
Nonreactive	5	565	570
Total	**249**	**570**	**819**

Positive Percent Agreement: 98.0% (244/249); 95% Confidence Interval: 95.4%–99.1%

Negative Percent Agreement: 99.1% (565/570); 95% Confidence Interval: 98.0%–99.6%

The agreement between the Atellica IM HBcT2 assay and a reference anti-HBc total assay for each HBV category is summarized in the following table.

Prospective Population by HBV Category - Atellica IM HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	Atellica IM HBcT2 Assay		Atellica IM HBcT2 Assay		
HBV Category	**Reactive[a]**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Signs and symptoms	256	4	4	364	628
High risk	139	6	5	469	619
Pregnant	10	0	1	182	193
Transplant	8	0	1	41	50
Dialysis	20	0	5	80	105
Total	**433**	**10**	**16**	**1136**	**1595**

[a] Number tested.

Percent agreement and confidence intervals by HBV category (all test sites)

	Positive Agreement		Negative Agreement	
HBV Category	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
Signs and symptoms	98.5 (256/260)	96.1–99.4	98.9 (364/368)	97.2–99.6
High risk	95.9 (139/145)	91.3–98.1	98.9 (469/474)	97.6–99.5
Pregnant	100.0 (10/10)	72.2–100.0	99.5 (182/183)	97.0–99.9
Transplant	100.0 (8/8)	67.6–100.0	97.6 (41/42)	87.7–99.6
Dialysis	100.0 (20/20)	83.9–100.0	94.1 (80/85)	87.0–97.5
Total, N = 1595	**97.7 (433/443)**	**95.9–98.8**	**98.6 (1136/1152)**	**97.8–99.1**

[a] x = the number of Atellica IM HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of Atellica IM HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

Comparison of Results: Prospective Population by HBV Serological Classification

A total of 1595 prospective samples were tested using the Atellica IM HBcT2 assay and a reference anti-HBc total assay for each HBV serological classification (all testing sites).

Comparison of results in the prospective population by HBV serological classification; Atellica IM HBcT2 assay versus a reference anti-HBc total assay (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	Atellica IM HBcT2 Assay		Atellica IM HBcT2 Assay		
HBV Classification	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
Acute	3	0	–	–	3
Chronic	77	0	–	–	77
Early recovery	15	0	–	–	15
Recovery	101	0	1	3	105
Recovered	207	2	7	7	223
HBV vaccine response	19	6	3	511	539
Not previously infected	3	2	3	591	599
Unclassified	8	0	2	24	34
Total	**433**	**10**	**16**	**1136**	**1595**

Percent agreement and confidence intervals by HBV classification (all testing sites)

	Positive Agreement		Negative Agreement	
HBV Classification	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
Acute	100.0 (3/3)	43.9–100.0	–[d]	–
Chronic	100.0 (77/77)	95.2–100.0	–	–
Early recovery	100.0 (15/15)	79.6–100.0	–	–
Recovery	100.0 (101/101)	96.3–100.0	75.0 (3/4)	30.1–95.4
Recovered	99.0 (207/209)	96.6–99.7	50.0 (7/14)	26.8–73.2
HBV vaccine response	76.0 (19/25)	56.6–88.5	99.4 (511/514)	98.3–99.8
Not previously infected	60.0 (3/5)	23.1–88.2	99.5 (591/594)	98.5–99.8
Unclassified	100.0 (8/8)	67.6–100.0	92.3 (24/26)	75.9–97.9
Total, N = 1595	**97.7 (433/443)**	**95.9–98.8**	**98.6 (1136/1152)**	**97.8–99.1**

[a] x = the number of Atellica IM HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of Atellica IM HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

[d] Percentages are for the numbers of reactive and nonreactive samples in a given row. If the total number of samples in the row is zero, a dash (–) is displayed.

Prenatal Population

Serum samples from United States were included in the study (N = 193). Samples were tested from pregnant women with either signs and symptoms of hepatitis B or with risk factors for HBV infection, who were in the first (62/193, 32.1%), second (61/193, 31.6%), or third trimester (70/193, 36.3%) of pregnancy. Results of the testing (reactive and nonreactive) were compared using the Atellica IM HBcT2 assay and the reference anti-HBc total assay for the prenatal population in their first, second, and third trimester, for all testing sites:

Comparison of results: prenatal population (all testing sites)

	Reference Anti-HBc Total Assay - Assay - Reactive		Reference Anti-HBc Total Nonreactive		
	Atellica IM HBcT2 Assay		Atellica IM HBcT2 Assay		
Trimester	**Reactive**	**Nonreactive**	**Reactive**	**Nonreactive**	**Total**
First	2	0	0	60	62
Second	6	0	1	54	61
Third	2	0	0	68	70
Total	**10**	**0**	**1**	**182**	**193**

Percent agreement and confidence intervals: prenatal population (all test sites)

	Positive Agreement		Negative Agreement	
Trimester	**% (x/n)[a]**	**95% CI[b]**	**% (x/n)[c]**	**95% CI**
First	100 (2/2)	34.2–100	100 (60/60)	94.0–100
Second	100 (6/6)	61.0–100	98.2 (54/55)	90.4–99.7
Third	100 (2/2)	34.2–100	100 (68/68)	94.7–100
Total	**100 (10/10)**	**72.2–100**	**99.5 (182/183)**	**97.0–99.9**

[a] x = the number of Atellica IM HBcT2 results that are reactive in agreement with the reference anti-HBc total assay. n = the number of reactive reference anti-HBc total results.

[b] Confidence Interval

[c] x = the number of Atellica IM HBcT2 results that are nonreactive in agreement with the reference anti-HBc total assay. n = the number of nonreactive reference anti-HBc total results.

Pediatric and Adolescent Population

Pediatric and adolescent (non-pregnant) samples were prospectively collected (N = 139) and tested using the ADVIA Centaur XP system. The population analysis was stratified by the following age groups: 2–12 years and 13–21 years.

	Reference Assay - Reactive		Reference Assay - Nonreactive		
Age Range (Years)	**HBcT2 Assay - Reactive**	**HBcT2 Assay - Nonreactive**	**HBcT2 Assay - Reactive**	**HBcT2 Assay - Nonreactive**	**Total**
2–12	1	0	0	29	30
13–21	3	0	1	105	109
Total	4	0	1	134	139

Age Range (Years)	**Positive Percent Agreement % (x/n)[a]**	**95% Confidence Interval**	**Negative Percent Agreement % (x/n)[b]**	**95% Confidence Interval**
2–12	100 (1/1)	20.7–100	100 (29/29)	88.3–100
13–21	100 (3/3)	43.9–100	99.1 (105/106)	94.8–99.8
Total	**100 (4/4)**	**51.0–100**	**99.3 (134/135)**	**95.9–99.9**

[a] x = the number of ADVIA Centaur HBcT2 results using the ADVIA Centaur XP system that are reactive in agreement with the reference HBcT2 assay; n = the total number of reference HBcT2 results that are reactive.

[b] x = the number of ADVIA Centaur HBcT2 results using the ADVIA Centaur XP system that are nonreactive in agreement with the reference HBcT2 assay; n = the total number of reference HBcT2 results that are nonreactive.

Because few positives were identified, a study was conducted to evaluate the results observed when pediatric samples are tested with the ADVIA Centaur HBcT2 assay using the ADVIA Centaur XP system. A total of 60 pediatric (age 2–21 years) and 60 adult serum samples were spiked with unique native anti- HBc positive samples. Out of 60 pediatric samples tested 59 samples showed bias less than 20% (98.3% samples). The distribution of percent bias between the Index values of the spiked pediatric serum samples and the paired adult serum samples are summarized in the following table:

	Distribution of Percent Bias			
Age Range (Years)	**N[a]**	**≤ 10%**	**> 10%– ≤ 20%**	**> 20%– ≤ 30%**
2–12	20	45.0 (9/20)	50.0 (10/20)	5.0 (1/20)
13–21	40	72.5 (29/40)	27.5 (11/40)	0.0 (0/40)
Total	60	63.3 (38/60)	35.0 (21/60)	1.7 (1/60)

[a] Number tested.

Seroconversion Panels

Commercially available HBV patient seroconversion panels were tested using the Atellica IM HBcT2 assay to determine the seroconversion sensitivity of the assay. The performance of the Atellica IM HBcT2 assay on the seroconversion panels matched or exceeded the performance of the reference assay.

	Reference Anti-HBc Total Assay - Reactive From Initial Draw Date		Atellica IM HBcT2 Assay versus Reference Anti-HBc Total Assay
Panel ID	**Atellica IM HBcT2 Assay (Days)**	**Reference Assay (Days)**	**Differenc in Bleed Numbers[a] e**
HBV6278	41	41	0
HBV6281	41	41	0
HBV9093	49	49	0
HBV9099	74	74	0
PHM941	99	99	0

	Reference Anti-HBc Total Assay - Reactive From Initial Draw Date		Atellica IM HBcT2 Assay versus Reference Anti-HBc Total Assay
Panel ID	**Atellica IM HBcT2 Assay Assay (Days)**	**Reference (Days)**	**Difference in Bleed Numbers[a]**
SCPHBV1	29	29	0
SCPHBV4	65	71	+1

[a] The difference in bleed numbers is relative to the reference assay. For example, a "+1" means that the reference assay required 1 additional bleed before reactivity was determined as compared to the time point when the Atellica IM HBcT2 assay confirmed as reactive.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[14] Samples were assayed in duplicate in 2 runs per day for 20 days. The following results were obtained using 1 reagent lot and stored calibration curves. The following results are representative of the performance of the assay:

			Repeatability		Within-Laboratory Precision	
Specimen Type	**N[a]**	**Mean (Index)**	**SD[b] (Index)**	**CV[c] (%)**	**SD (Index)**	**CV (%)**
Plasma A	75[d]	0.13	0.03	N/A[e]	0.06	N/A
Plasma B	80	0.62	0.04	N/A	0.06	N/A
Plasma C	80	1.38	0.06	4.3	0.11	8.1
Plasma D	80	2.25	0.06	2.7	0.12	5.3
Plasma E	80	6.42	0.23	3.7	0.34	5.4
Serum A	77[d]	0.10	0.03	N/A	0.05	N/A
Serum B	80	0.46	0.04	N/A	0.07	N/A
Serum C	80	1.41	0.07	4.8	0.12	8.3
Serum D	80	2.17	0.10	4.4	0.16	7.2
Serum E	80	5.73	0.27	4.7	0.39	6.8
Control 1 (negative)	80	0.24	0.02	N/A	0.04	N/A
Control 2 (positive)	80	3.52	0.10	2.9	0.14	3.9

[a] Number of measurements.
[b] Standard deviation.
[c] Coefficient of variation.
[d] Samples recovering below 0.70 Index are not included in the analysis.
[e] N/A = not applicable. The results remained nonreactive throughout the study.

The assay is designed to have the following precision.

	Precision	
Concentration Interval (Index)	**Repeatability (Within-Run)**	**Within-Laboratory (Total Precision)**
0.80–10.00	≤ 10.0% CV	≤ 12.0% CV

For specimens < 0.80 Index, the assay must not show a change in clinical interpretation.

Reproducibility

Reproducibility was evaluated using the Atellica IM Analyzer according to CLSI document EP05-A3.[14] A reproducibility study was conducted at 3 sites, with each site evaluating 3 reagent lots. The protocol was run over 5 days, 2 runs per day. There were 3 replicates per run for each sample, for a total 270 replicates per sample (N = 270). The following results are representative of the performance of the assay:

Sample Type (N = 270)	Mean (Index)	Repeatability (Within Run) SD[a] (Index)	Repeatability (Within Run) CV[b] (%)	Between Run SD (Index)	Between Run CV (%)	Between Day SD (Index)	Between Day CV (%)	Between Lot SD (Index)	Between Lot CV (%)	Within Laboratory SD (Index)	Within Laboratory CV (%)	Between Site SD (Index)	Between Site CV (%)	Reproducibility SD (Index)	Reproducibility CV (%)
Serum A	0.41	0.02	N/A[c]	0.02	N/A	0.00	N/A	0.09	N/A	0.02	N/A	0.00	N/A	0.09	N/A
Serum B	0.76	0.02	N/A	0.01	N/A	0.01	N/A	0.07	N/A	0.03	3.4	0.01	N/A	0.07	N/A
Serum C	1.35	0.04	2.6	0.01	0.6	0.02	1.2	0.13	9.5	0.04	3.0	0.00	0.0	0.13	10.0
Serum D	2.40	0.06	2.4	0.03	1.4	0.02	1.0	0.20	8.4	0.07	3.0	0.00	0.2	0.21	8.9
Serum E	5.09	0.17	3.4	0.12	2.4	0.06	1.2	0.41	8.1	0.22	4.3	0.00	0.0	0.47	9.1
Serum F	8.38	0.21	2.6	0.00	0.0	0.09	1.1	0.43	5.2	0.23	2.8	0.07	0.8	0.50	5.9
Control 1 (negative)[d]	0.21	0.02	N/A	0.01	N/A	0.02	N/A	0.06	N/A	0.03	N/A	0.01	N/A	0.07	N/A
Control 2 (positive)	3.29	0.07	2.1	0.05	1.5	0.03	0.8	0.23	7.0	0.09	2.7	0.04	1.1	0.25	7.6

[a] Standard deviation.

[b] Coefficient of variation.

[c] N/A = not applicable. The results remained nonreactive throughout the study.

[d] 4 samples outside of the measuring interval (N = 4) were calculated offline and were included in analysis.

The assay is designed to have the following reproducibility:

Concentration Interval (Index)	Reproducibility
0.80–10.00	≤ 20.0% CV

For specimens < 0.80 Index, the assay must not show a change in clinical interpretation.

Specimen Equivalency

Specimen equivalency was determined with the linear regression model in accordance with CLSI Document EP09-A2.[15]

The ADVIA Centaur HBcT2 results ranged from 0.11–9.99 Index. No significant difference between the tube types was observed. Results were established using the ADVIA Centaur XP system. Agreement of the specimen types may vary depending on the study design and sample population used.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]

Gel-barrier tube (serum)	y = 0.96 (x) + 0.04	0.29–9.42 Index	50	0.983
Dipotassium EDTA plasma	y = 0.98 (x) + 0.03	0.24–9.24 Index	50	0.981

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Lithium heparin plasma	y = 1.00 (x) - 0.05	0.12–9.54 Index	50	0.968
Sodium heparin plasma	y = 1.04 (x) - 0.09	0.11–9.99 Index	50	0.971

[a] Number of samples tested.

[b] Correlation coefficient.

The ADVIA Centaur HBcT2 assay is designed to have a correlation coefficient of ≥ 0.95, a slope of test tube type (y) versus reference (x) of 1.0 ± 0.15, and an intercept of < 0.90 Index.

Interferences

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

Interference testing was performed in accordance with CLSI Document EP07-A2[16] using the ADVIA Centaur XP system.

Substance	Substance Test Concentration
Hemoglobin	500 mg/dL
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	40 mg/dL
Lipemia	1000 mg/dL
Biotin	3500 ng/mL
Cholesterol	500 mg/dL
Hyper IgG	60 mg/mL
Hyperproteinemic	12.0 g/dL
Hypoproteinemic	3.5 g/dL

The assay was designed to have ≤ 10% interference up to the concentration of the substances tested.

Cross-Reactivity

The assay was evaluated for potential cross-reactivity with other viral and microbial antibodies and disease state specimens using the ADVIA Centaur XP system. The anti-HBc status of each sample was assessed using the ADVIA Centaur HBcT2 assay and an anti-HBc reference assay. The following results are representative of the performance of the assay:

		Number of Reactive Anti-HBc Total Results	
Substance	Number Tested	ADVIA Centaur HBcT2 Assay	Reference Assay
Anti-nuclear antibody (ANA)	32	2	2
Cytomegalovirus (CMV) IgG	15	0	0
Cytomegalovirus (CMV) IgM	15	0	0
Epstein-Barr virus (EBV) IgG	15	0	0
Epstein-Barr virus (EBV) IgM	15	0	0
Flu vaccine recipient	15	0	0

Substance	Number Tested	Number of Reactive Anti-HBc Total Results	
		ADVIA Centaur HBcT2 Assay	Reference Assay
Human anti-mouse antibody (HAMA)	15	2	2
Hepatitis A infection (HAV)	20	4	4
Hepatitis C infection (HCV)	15	7	7
Herpes simplex virus (HSV) IgG	15	0	0
Herpes simplex virus (HSV) IgM	14	0	0
Human immunodeficiency virus (HIV 1/2)	15	6	6
Multiparity	25	1	1
Non-viral liver disease	15	1	0
Rheumatoid arthritis	15	2	1
Rubella IgG	15	0	0
Syphilis IgG	15	3	3
Systemic lupus erythematosus (SLE)	20	1	1
Toxoplasma IgG	21	0	0
Toxoplasma IgM	11	0	0
Varicella zoster virus (VZV) IgG	15	1	1

Analytical Sensitivity

To examine the analytical sensitivity of the Atellica IM HBcT2 assay, the WHO Anti-hepatitis B virus core antigen (anti-HBc) 1st International Standard 95/522, was used to prepare a dilution series that was tested using 3 Atellica IM HBcT2 reagent lots on the Atellica IM Analyzer. Linear regression was used to determine the concentration of the WHO 95/522 reference sample value, which corresponds to the Atellica IM HBcT2 cut-off (Index Value = 1.00). The WHO 95/522 International Unit per milliliter (IU/mL) concentration at the assay cut-off was determined to be 0.25 IU/mL.

Standardization

The Atellica IM HBcT2 assay traceability is based on the relative clinical agreement with commercially available anti-HBc total assays. Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or distributor. siemens-healthineers.com

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16. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP07-A2.

Definition of Symbols

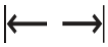
The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]	EC REP	Authorized representative in the European Community	5.1.2[a]
REF			LOT		
	Use-by date	5.1.4[a]	CH REP	Authorized representative in Switzerland	Proprietary

Catalog number	5.1.6[a]	Batch code	5.1.5[a]	

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
<.../eifu>	Internet URL address to access the electronic instructions for use	Proprietary	Rev. XX	Version of Instructions for Use	Proprietary
IVD	*In vitro* diagnostic medical device	5.5.1[a]	Rev.	Revision	Proprietary
			REVISION		
RxOnly	Prescription device (US only)	FDA[b]	UDI	Unique Device Identifier	5.7.10[c]
CE XXXX	CE Marking with Notified Body	EU IVDR[d]	CE	CE Marking IVDR[d]	EU
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of tempera- ture	5.3.6[a]		Lower limit of temperature	5.3.5[a]
	Do not re-use	5.4.2[a]		Do not freeze	Proprietary
	Recycle	1135[e]		This way up	0623[e]
	Biological risks	5.4.1[a]		Caution	5.4.4[a]
UNITS C	Common Units	Proprietary	UNITS SI	International System of Units	Proprietary
YYYY-MM-DD	Date format (year-month-day)	N/A	YYYY-MM	Date format (year-month)	N/A
	Document face up[f]	1952[e]		Handheld barcode scanner	Proprietary
	Target	Proprietary		Mixing of substances	5657[g]
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values			entered are valid.	
MATERIAL ID				Unique material identifica- tion number	

Proprietary



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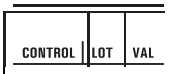
Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Type of control	Proprietary		Name of control	Proprietary
	Quality control lot value	Proprietary		Calibrator lot value	Proprietary

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.
[b] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.
[c] ISO 15223-1:2020-04
[d] IVDR REGULATION (EU) 2017/746
[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.
[f] Indicates Assay-*e*Note
[g] International Electrotechnical Commission (IEC). IEC 60417-1 Graphical symbols for use on equipment – Part 1: Overview and Application

Legal Information

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