

ABBOTT PRISM®
HBcore
List No. 6E66
34-3831/R9



Hepatitis B Virus Core Antigen (*E. coli*, Recombinant)



Customer Service
United States: 1-877-4ABBOTT

Key to symbols used

REF

List Number



Expiration Date

IVD

For *In Vitro* Diagnostic Use

LOT

Lot Number



Consult instructions for use

**ACTIVATOR
DILUENT**

Activator Diluent



Store at 2-8°C

**ACTIVATOR
CONCENTRATE**

Activator Concentrate



Store at 15-30°C

EC REP

Authorized Representative



Legal Manufacturer

U.S. License No. 43



ABBOTT LABORATORIES
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List No. 6E66
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NAME AND INTENDED USE

The ABBOTT PRISM HBcore assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the qualitative detection of total antibody to hepatitis B core antigen (anti-HBc) in human serum and plasma. The ABBOTT PRISM HBcore ChLIA is intended to be used as a screening test for blood and plasma to prevent transmission of hepatitis B virus (HBV) to recipients of blood and blood components.

SUMMARY AND EXPLANATION OF THE TEST

Anti-HBc appears in the serum of patients infected with HBV one to four weeks after the appearance of HBsAg, at the onset of symptoms. Because it generally remains detectable for the remainder of a patient's life, anti-HBc is an indicator of current or previous infection.^{1,2} In the absence of information about any other hepatitis B virus (HBV) markers, it must be considered that an individual with detectable levels of anti-HBc may be actively infected with HBV or that the infection may have resolved.^{3,4} However, as with all immunoassays, the ABBOTT PRISM HBcore assay may yield nonspecific reactivity.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ABBOTT PRISM HBcore assay is a two-step competitive/blocking ChLIA. The reactions occur within the ABBOTT PRISM System in the following sequence:

- Microparticles coated with recombinant HBc antigen (rHBcAg) are incubated with sample (either plasma, serum, calibrator, or control) and Cysteine Solution in the incubation well of the reaction tray. During incubation, anti-HBc present in the sample binds to the rHBcAg on the Microparticles.
- After this first incubation is complete, the reaction mixture is transferred to the glass fiber matrix (matrix) of the reaction tray using the Transfer Wash. The Microparticles are captured by the matrix while the remaining mixture flows through to the absorbent blotter.
- The Acridinium-Labeled Human Anti-HBc Conjugate is added to the Microparticles on the matrix and incubated. The Conjugate will bind to rHBcAg which has not been blocked by human anti-HBc in the sample. After this second incubation, the unbound Conjugate is washed into the blotter with the Conjugate Wash.
- The chemiluminescent signal is generated by addition of an alkaline hydrogen peroxide solution. The resultant photons are counted.

The amount of light emitted is inversely proportional to the amount of anti-HBc in the sample. Anti-HBc in the sample blocks the binding of anti-HBc conjugate to rHBcAg on the microparticles. The presence or absence of anti-HBc in the sample is determined by comparing the number of photons collected from the sample to a cutoff value determined from a calibration performed in the same batch. If the number of photons collected from a test sample is greater than the cutoff value, the sample is considered nonreactive for anti-HBc by the criteria of the ABBOTT PRISM HBcore assay. These specimens need not be further tested. If the number of photons collected from a test sample is less than or equal to the cutoff value, the sample is considered reactive for anti-HBc by the criteria of the ABBOTT PRISM HBcore assay. Specimens that are initially reactive must be handled according to the table in the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert and retested in duplicate. Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive. Reactivity in either or both of these duplicated tests (*i.e.*, repeatedly reactive) is highly predictive of the presence of HBc antibodies in people at risk for HBV infection. For further information regarding ChLIA technology, refer to the ABBOTT PRISM Operations Manual, Section 3.

REAGENTS

NOTE: Each specific component description that follows is accompanied by a unique symbol. These symbols appear on both the component labels and on corresponding instrument tubing identifier labels. They are meant to facilitate identification and installation of reagent bottles within the ABBOTT PRISM System ambient reagent bay and refrigerator.

ABBOTT PRISM HBcore Assay Kit (No. 6E66-68)

NOTE: Do not mix reagents from different bottles. Do not mix or interchange reagents from different ABBOTT PRISM HBcore Assay Kits.

- 1 Bottle (340 mL) Hepatitis B Virus Core Antigen (*E. coli*, Recombinant) Coated Microparticles in TRIS buffered saline with bovine serum albumin and protein stabilizers. Minimum concentration: 0.003% solids. Preservative: 0.1% sodium azide. (Symbol: ●)
- 1 Bottle (335 mL) Antibody to Hepatitis B Virus Core Antigen (Human): Acridinium Conjugate in phosphate buffered saline with calf serum and recalcified, inactivated human plasma, nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, and anti-HIV-1/HIV-2. Minimum concentration: 0.025 µg/mL. Preservative: 0.1% sodium azide. (Symbol: ▲)
- 3 Bottles (10.4 mL each) Negative Calibrator (Human). Recalcified plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, anti-HIV-1/HIV-2, anti-HBc, and anti-HBs. Preservative: 0.1% sodium azide. (Symbol: NC)
- 3 Bottles (10.4 mL each) Positive Calibrator (Human). Recalcified plasma reactive for anti-HBc and anti-HBs, nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, and anti-HIV-1/HIV-2. Minimum concentration: 40 PEI* Units/mL. Preservative: 0.1% sodium azide. (Symbol: PC)
- 1 Bottle (9.5 g) Cysteine Powder. **CAUTION: May be irritating to eyes, respiratory system and skin. Must be reconstituted with Cysteine Diluent and mixed prior to first use.** (Symbol: X)
- 1 Bottle (354 mL) Cysteine Diluent containing 10 mM EDTA. **Must be mixed with Cysteine Powder prior to first use.**

Other Reagents Required

ABBOTT PRISM HBcore Wash Kit (No. 6E66-58)

- 1 Bottle (3422 mL) Transfer Wash. MES {2-(N-morpholino) ethanesulfonic acid} buffered saline. Preservative: 0.1% ProClin[®]** 300. (Symbol: ~)
- 1 Bottle (1757 mL) Conjugate Wash. MES {2-(N-morpholino) ethanesulfonic acid} buffered saline. Preservative: 0.1% ProClin** 300. (Symbol: ★)

ABBOTT PRISM Activator Concentrate (No. 1A75-02)

- 4 Bottles (900 mL each) Activator Concentrate. 0.4% hydrogen peroxide/0.06% diethylenetriaminepentaacetic acid.

ABBOTT PRISM Activator Diluent (No. 1A75-01)

- 4 Bottles (900 mL each) Activator Diluent. 0.3 N sodium hydroxide.

ABBOTT PRISM Run Control Kit (No. 3E60-10)

Or

ABBOTT PRISM Positive Run Control Kit (No. 3E60-11)

NOTE: Each batch **MUST** end in a release control (ABBOTT PRISM Positive Control). The ABBOTT PRISM Positive Control (included in Kit No. 3E60-10 or 3E60-11) must be used as the release control which has been configured to validate the system functionality and release sample results. Refer to the ABBOTT PRISM Run Control Kit package insert or the ABBOTT PRISM Positive Run Control Kit package insert for detailed handling and use instructions.

* Concentration standardized against the reference standard of the Paul Ehrlich Institute (PEI), Langen, Germany.

** ProClin is a registered trademark of Rohm & Haas.

WARNINGS AND PRECAUTIONS

For In Vitro Diagnostic Use.

The performance characteristics of this product have not been established for the laboratory diagnosis of HBV infection.

The ABBOTT PRISM HBcore assay meets FDA potency requirements.

Safety Precautions

CAUTION: This product contains human sourced and/or potentially infectious components. Some components sourced from human blood have been tested and found to be reactive for anti-HBc by FDA licensed tests. Refer to the REAGENTS section of this package insert. No known test method can offer complete assurance that products derived from human sources will not transmit infection. Therefore, all human sourced

materials must be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens,⁵ Biosafety Level 2⁶ or other appropriate biosafety practices^{7,8} should be used for materials that contain or are suspected of containing infectious agents. These precautions include, but are not limited to the following:

- Wear gloves when handling specimens or reagents.
- Do not pipette by mouth.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in work areas where specimens or reagents are handled.
- Clean and disinfect all spills of specimens or reagents using an appropriate disinfectant, such as 0.1% sodium hypochlorite, or other suitable disinfectants.^{8,9,10}
- Decontaminate and dispose of all specimens, reagents and other potentially contaminated materials in accordance with local, state and federal regulations.^{11,12}
- The ABBOTT PRISM Line Cleaner (No. 7A03-31) containing 2% tetraethylammonium hydroxide (TEAH) may cause mild eye irritation. If this solution comes in contact with eyes, rinse immediately with water. For additional information, refer to the ABBOTT PRISM Operations Manual, Section 8.
- Some components of this product contain sodium azide. For a specific listing refer to the **REAGENTS** section of this package insert. Sodium azide has been reported to form lead or copper azide in laboratory plumbing. These azides may explode upon percussion, such as hammering. To prevent formation of lead or copper azide, flush drains thoroughly with water after disposing of solutions containing sodium azide. To remove contamination from old drains suspected of azide accumulation, the National Institute for Occupational Safety and Health recommends the following: (1) siphon liquid from trap using a rubber or plastic hose, (2) fill drain with 10% sodium hydroxide solution, (3) allow to stand for 16 hours, and (4) flush well with water.
- The components containing sodium azide are classified per the applicable European Community (EC) Directives as: Harmful (Xn). The following are the appropriate Risk (R) and Safety (S) phrases.



R22 Harmful if swallowed.
 R32 Contact with acids liberates very toxic gas.
 S35 This material and its container must be disposed of in a safe way.
 S36 Wear suitable protective clothing.
 S46 If swallowed, seek medical advice immediately and show this container or label.

- The ABBOTT PRISM Activator Diluent (No. 1A75-01) contains sodium hydroxide and is classified per the applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



R36 Irritating to eyes.
 S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
 S35 This material and its container must be disposed of in a safe way.
 S46 If swallowed, seek medical advice immediately and show this container or label.

- The ABBOTT PRISM Cysteine Powder (No. 1A77K) is classified per the applicable European Community (EC) Directives as: Harmful (Xn). The following are the appropriate Risk (R) and Safety (S) phrases.



R22 Harmful if swallowed.
 R36/37/38 Irritating to eyes, respiratory system, and skin.
 S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
 S35 This material and its container must be disposed of in a safe way.
 S36 Wear suitable protective clothing.
 S46 If swallowed, seek medical advice immediately and show this container or label.

- The Transfer Wash and Conjugate Wash contain a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (3:1) which is a component of ProClin[®] and is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



R43 May cause sensitization by skin contact.
 S24 Avoid contact with skin.
 S35 This material and its container must be disposed of in a safe way.
 S37 Wear suitable gloves.
 S46 If swallowed, seek medical advice immediately and show this container or label.

- * ProClin is a registered trademark of Rohm & Haas.

Handling Precautions

- Do not use kits beyond the expiration date.
- **Gently** invert each component several times prior to loading the original container on the ABBOTT PRISM System to ensure a homogenous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Each component of the ABBOTT PRISM HBcore Wash Kit should be at room temperature (15-30°C) and then mixed before loading onto the ABBOTT PRISM System.
- Do not mix reagents from different bottles. Do not mix or interchange reagents from different ABBOTT PRISM HBcore Assay Kits.
- Any lot of ABBOTT PRISM HBcore Wash Kit can be used with any lot of ABBOTT PRISM HBcore Assay Kit.
- Any lot of ABBOTT PRISM Activator Concentrate, ABBOTT PRISM Activator Diluent, and Control from ABBOTT PRISM Run Control Kit or ABBOTT PRISM Positive Run Control Kit may be used with any lot of any ABBOTT PRISM Assay Kit.
- Treat Negative and Positive Calibrators and Controls as specimens.
- Avoid microbial and chemical contamination of samples, reagents, and equipment. The use of disposable pipette tips is recommended for any preliminary sample transfer.
- Use accurately calibrated equipment.
- Do not freeze reagents.
- Failure to adhere to instructions in the ABBOTT PRISM Operations Manual or package insert may result in erroneous test results.
- Use caution when handling samples, reagent bottles, and reagent caps to prevent cross contamination.

Additional safety and handling precautions and limitations for the assay kit, calibrators, specimens, controls, and other reagents are described in the ABBOTT PRISM Operations Manual, Sections 7 and 8.

Preparation of Cysteine Solution

1. Carefully empty the entire contents of the ABBOTT PRISM Cysteine Diluent bottle into the ABBOTT PRISM Cysteine Powder bottle. The ABBOTT PRISM Cysteine Powder bottle contains a stir bar.

NOTE: Preparation of cysteine solution does not require the Cysteine Diluent or Cysteine Powder to equilibrate to room temperature prior to combining and mixing.

2. Write the date of dilution and the date of expiration of the prepared cysteine solution, the lot number of the ABBOTT PRISM Cysteine Diluent used, and the preparer's name on the ABBOTT PRISM Cysteine Powder label.

NOTE: The cysteine solution must be used within 8 weeks of preparation.

3. Reseal the ABBOTT PRISM Cysteine Powder bottle and mix for 15-30 minutes using a magnetic stir plate with a plate width of at least three inches. Adjust the speed to create a vortex when mixing the cysteine solution.
4. Place in the ABBOTT PRISM System refrigerator. Verify that the tubing is connected correctly. Refer to the ABBOTT PRISM Operations Manual, Section 5, **PREPARE AND LOAD REAGENTS** for additional information.

Preparation of Activator Solution

Activator solution must be prepared by mixing equal parts of ABBOTT PRISM Activator Concentrate and ABBOTT PRISM Activator Diluent. The activator solution expires 24 hours from preparation. The ABBOTT PRISM Activator Concentrate may be used immediately after removing from the refrigerator. The volume of activator solution required for multiple tests is calculated by the ABBOTT PRISM System software. Refer to the ABBOTT PRISM Operations Manual, Section 5, **PLAN WORK LOAD** for additional information. Use clean pipettes and/or metal-free containers (such as plasticware or acid-washed and purified or equivalent water-rinsed glassware) to measure. Refer to the ABBOTT PRISM Operations Manual Glossary for the definition of purified water. Prepare the activator solution in the bottle provided in the ABBOTT PRISM Accessory Kit (No. 6A36-60). Cover the bottle opening securely with the cap provided and invert gently five to ten times to mix. Load the activator solution on the ABBOTT PRISM System. Refer to the ABBOTT PRISM Operations Manual, Section 5, **PREPARE AND LOAD ACTIVATOR SOLUTION**, for additional information.

NOTE: The activator solution must be used within 24 hours of preparation.

Storage Instructions

- Store the ABBOTT PRISM HBcore Assay Kit, ABBOTT PRISM Run Control Kit, ABBOTT PRISM Positive Run Control Kit, and ABBOTT PRISM Activator Concentrate at 2-8°C.
- Store the ABBOTT PRISM HBcore Wash Kit and ABBOTT PRISM Activator Diluent at room temperature (15-30°C).
- Store ABBOTT PRISM Pipette Tips and ABBOTT PRISM Reaction Trays in their original packaging until use.
- The cysteine solution must be stored at 2-8°C and used within 8 weeks of preparation.
- The activator solution must be stored at 15-30°C and used within 24 hours of preparation.

Indications of Instability or Deterioration of Reagents

The ABBOTT PRISM System will not continue to process samples when calibrator values do not meet specifications. This may indicate either deterioration or contamination of reagents, or instrument failure. Refer to the ABBOTT PRISM Operations Manual, Section 10, for additional information.

INSTRUMENT PROCEDURE

- ABBOTT PRISM software version 2.8 or higher must be used to perform the assay.
- Refer to the ABBOTT PRISM Operations Manual for a detailed description of Instrument Procedures.
- Refer to the ABBOTT PRISM Operations Manual, Section 7, for limitations associated with test management.
- Solutions required for instrument cleaning and maintenance are described in detail in the ABBOTT PRISM Operations Manual, Sections 5 and 9.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ABBOTT PRISM Operations Manual, Section 9.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Either serum (including serum collected in serum separator tubes), plasma collected in EDTA, potassium oxalate, sodium citrate, ACD-A, ACD-B, CP2D, CPD, or CPDA-1 anticoagulants, or plasma collected from segmented tubing may be used with the ABBOTT PRISM HBcore assay. Follow the manufacturer's processing instructions for serum and plasma collection tubes.

CAUTION: Do not use specimens collected in heparin. Use of heparin as an anticoagulant may cause a reduction in Sample Net Counts and in Sample Net Counts/Cutoff Value (S/CO) for ABBOTT PRISM HCV; therefore, heparin is not recommended for any ABBOTT PRISM assay.

- This assay was designed and validated for use with individual human serum and plasma specimens. This assay has not been validated for use with pooled specimens.
- Do not use heat-inactivated specimens.
- Do not use specimens with obvious microbial contamination.

- When shipped, specimens must be packaged and labeled in compliance with applicable regulations covering the transport of clinical specimens and infectious substances. Specimens may be shipped at 30°C or colder for a period not to exceed 7 days. Prior to freezing, the serum or plasma should be removed from the clot or red blood cells.
- Specimens may be stored for up to 14 days at 2-8°C. If storage periods greater than 14 days are anticipated, the serum or plasma should be removed from the clot or red blood cells to avoid hemolysis. Store the serum or plasma frozen (-20°C or colder).
- Previously frozen specimens must be mixed gently and thoroughly after thawing and centrifuged according to Table II in this section.
- Twenty nonreactive and 20 low-level reactive specimens showed no qualitative performance differences when subjected to 6 freeze-thaw cycles. However, some specimens that have undergone multiple freeze-thaw cycles or have been stored frozen for prolonged periods may give erroneous or inconsistent test results.
- Clear, non-hemolyzed specimens should be used when possible. Specimens containing visible particulate matter may give erroneous or inconsistent test results.
- No qualitative performance differences were observed when 20 nonreactive and 19 low-level reactive specimens were spiked with elevated levels of bilirubin (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), red blood cells ($\leq 0.4\%$ v/v), triglycerides (≤ 3000 mg/dL), or protein (≤ 12 g/dL). However, specimens that contain greater concentrations of these potentially interfering substances have not been tested. The impact of greater concentrations of these potentially interfering substances on the ABBOTT PRISM HBcore assay is unknown.
- Performance has not been established using cadaver specimens, umbilical cord blood, or body fluids such as urine, saliva, semen, amniotic fluid, cerebrospinal fluid, or pleural fluid. These specimens should not be tested using the ABBOTT PRISM HBcore assay.
- Specimens collected by plasmapheresis, that have not been frozen, do not require centrifugation. All other specimens (including previously frozen plasmapheresis specimens) must be centrifuged as follows:

Non-frozen specimens (excluding non-frozen plasmapheresis specimens) must be centrifuged such that g-minutes is between 30,000 and 75,000. A refrigerated or non-refrigerated centrifuge is acceptable for use. The acceptable time and force ranges that meet this criterion are listed in Table I.

Table I

Centrifugation Time (minutes)	RCF (x g)	g-minutes
10	3,000	30,000
15	2,000 - 3,000	30,000 - 45,000
20	1,500 - 3,000	30,000 - 60,000
25	1,300 - 3,000	32,500 - 75,000

Convert rpm to RCF as follows: $RCF = 1.12 \times r_{max} (rpm/1000)^2$

Convert RCF to rpm as follows: $rpm = 1000 \times \sqrt{\frac{RCF}{1.12 \times r_{max}}}$

- RCF - The relative centrifugal force generated during centrifugation.
- rpm - The revolutions per minute of the rotor on which the specimens are being spun (usually the digital readout on the centrifuge will indicate the rpm).
- Centrifugation Time - The time should be measured from the time the rotor reaches the required RCF or rpm to the time it begins decelerating.

- r_{max} - Radius of the rotor in millimeters. The radius measured is dependent on whether the rotor is a fixed angle rotor or a swinging bucket rotor. This value is typically provided with the rotor, by the manufacturer. For the fixed angle rotor, r_{max} is a measure of the distance from the rotor axis (center) to the bottom of the tube cavity. For the swinging bucket rotor, r_{max} is a measure of the distance from the rotor axis (center) to the bottom of the tube bucket while it is extended during rotation.
- g-minutes - The unit of measure for the product of RCF (x g) and centrifugation time (minutes).

Previously frozen specimens must be centrifuged such that g-minutes is between 180,000 and 300,000. A refrigerated or non-refrigerated centrifuge is acceptable for use. The acceptable time and force ranges that meet this criterion are listed in Table II.

Table II

Centrifugation Time (minutes)	RCF (x g)	g-minutes
15	12,000	180,000
20	9,000 - 12,000	180,000 - 240,000
25	7,200 - 12,000	180,000 - 300,000

ANY specimen (excluding non-frozen plasmapheresis) not tested within 24 hours of initial centrifugation, must be recentrifuged from 30,000 to 75,000 g-minutes as defined for non-frozen specimens.

NOTE: Specimens retested within 24 hours of initial centrifugation do not require recentrifugation.

FAILURE TO FOLLOW THE SPECIFIED CENTRIFUGATION PROCEDURE MAY GIVE ERRONEOUS OR INCONSISTENT TEST RESULTS.

Specimen Volume

The specimen volume required to perform a single assay on the ABBOTT PRISM System varies according to the number and type of assays, and the different specimen containers. The ABBOTT PRISM HBcore assay requires 100 μ L sample dispense. For ABBOTT PRISM Sample Cups, the minimum specimen volume required for one ABBOTT PRISM HBcore assay is 400 μ L. For either primary or aliquot tubes or additional assay volume requirements, refer to the ABBOTT PRISM Operations Manual, Section 5.

PROCEDURE

Materials Provided

- No. 6E66-68 ABBOTT PRISM HBcore Assay Kit

Materials Required but Not Provided

- No. 6E66-58 ABBOTT PRISM HBcore Wash Kit
- No. 1A75-02 ABBOTT PRISM Activator Concentrate
- No. 1A75-01 ABBOTT PRISM Activator Diluent
- No. 5A07-01 ABBOTT PRISM Reaction Trays
- No. 5A07-10 ABBOTT PRISM Pipette Tips
- No. 6A36-60 ABBOTT PRISM Accessory Kit
- No. 3E60-10 ABBOTT PRISM Run Control Kit
- or
- No. 3E60-11 ABBOTT PRISM Positive Run Control Kit
- No. 6A36-31 ABBOTT PRISM Run Control Adapters
- Magnetic Stir Plate Plate width \geq 3 inches
- Protective Disposable Gloves
- Disinfectant
- Purified Water-rinsed or Clean Disposable Measuring Equipment

Additional Materials Available

- No. 7B36-01 ABBOTT PRISM Sample Cups

ABBOTT PRISM HBcore ASSAY PROCEDURE

Key procedures that require operator interaction for testing samples, are listed below. For detailed information concerning batch time, maximum batch size, reagent handling and loading, and associated procedural steps, refer to the ABBOTT PRISM Operations Manual, Sections 2, 5, and 7.

- Enter a Plan Work Load (refer to the ABBOTT PRISM Operations Manual, Section 5).
- Replace reagents as needed (refer to the ABBOTT PRISM Operations Manual, Sections 5 and 7). Prepare Cysteine Solution, if necessary. Refer to the **Preparation of Cysteine Solution** section of this package insert.

NOTE: Gently invert each component several times prior to loading on the ABBOTT PRISM System to ensure a homogenous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Each component of the ABBOTT PRISM HBcore Wash Kit should be at room temperature (15-30°C) and then mixed before loading onto the ABBOTT PRISM System.

- Verify that all tubing label symbols match the symbols on each reagent label. (Refer to the symbol key in the **REAGENTS** section of this package insert, and the ambient reagent bay and refrigerator diagrams provided with the ABBOTT PRISM System).
 - Verify that all tubing is securely fastened to the corresponding wash and reagent bottles.**
 - Inspect the waste containers. Empty and clean as defined in the ABBOTT PRISM Operations Manual, Section 9, if necessary.
 - Prepare activator solution (Refer to the **Preparation of Activator Solution** section of this package insert) and load onto the ABBOTT PRISM System.
 - Verify that an adequate number of ABBOTT PRISM Reaction Trays are in the Tray Loader.
 - Verify that an adequate number of ABBOTT PRISM Pipette Tips are in the Pipette Tip Racks.
 - Perform the prime procedure (Refer to the ABBOTT PRISM Operations Manual, Section 5).
 - Initiate sample processing. Open the bottles in the calibrator pack and place in the calibrator rack. Load the calibrator rack and sample racks, including the run controls. (Refer to the **QUALITY CONTROL PROCEDURES, Controls**, Control Handling Procedure, in this package insert.)
 - After the calibrators have been automatically pipetted, remove the calibrator rack. Close the calibrator bottles and return them to 2-8°C storage.
 - Each specimen is initially tested once, unless the operator overrides this automatic function of the ABBOTT PRISM System.
 - Sample racks may be removed after the samples have been pipetted.
- NOTE:** No operator interaction is required for the following steps, which are automatically carried out by the ABBOTT PRISM System: reaction tray transport, calibrator/sample/release control pipetting, incubation, reagent dispense, sample reading, data reduction, run validity and result determination.
- After specimen processing is complete, perform the purge procedure (Refer to the ABBOTT PRISM Operations Manual, Section 5).

Refer to the ABBOTT PRISM Operations Manual, Section 3, for a detailed description of ChLIA procedures. The ABBOTT PRISM HBcore assay is a two-step ChLIA procedure.

QUALITY CONTROL PROCEDURES

Calibration

The ABBOTT PRISM HBcore Negative and Positive Calibrators are automatically tested in triplicate at the beginning of each batch. The ABBOTT PRISM System will not generate results when calibrator values do not meet specifications. This may indicate either deterioration or contamination of reagents, or instrument failure.

Controls

1. The ABBOTT PRISM Positive Control **MUST** be included as the last sample in each batch as a release control. The operator is prompted to include this control as the last sample in every batch, and the ABBOTT PRISM Positive Control is then automatically tested as a single replicate. This control must meet specifications defined in the ABBOTT PRISM Run Control Kit package insert or the ABBOTT PRISM Positive Run Control Kit package insert in order to validate the system functionality and release sample results. If this control does not meet specifications defined in the ABBOTT PRISM Run Control Kit package insert or the ABBOTT PRISM Positive Run Control Kit package insert, refer to the ABBOTT PRISM Operations Manual, Section 10, for additional information.
2. Additional controls may be run at the operator's discretion (refer to the ABBOTT PRISM Operations Manual, Section 3).

Invalidate controls: Additional controls may be run anywhere within a batch as an invalidate control. Specifications may be assigned to invalidating controls. If an invalidate control fails to meet assigned specifications, sample processing is shutdown and no sample results are calculated or provided by the instrument. When an invalidate control meets assigned specifications, sample processing continues and a valid release control (ABBOTT PRISM Positive Control) result is required to release data.

Non-validating controls: Additional controls may be run anywhere within a batch as a non-validating control. Specifications may be assigned to non-validating controls. A valid release control (ABBOTT PRISM Positive Control) result is required to release data. If the user-assigned specifications for the non-validating control(s) are not met and the release control specifications are met, there will be no effect on sample processing. In this case, reactive sample results must not be considered invalid.

3. Control Handling Procedure
 - a. Place run control adapters into the sample rack. **The adapters can be placed in any rack position except 1, 2, 27 or 28.**
 - b. Place each run control bottle into an adapter in the sample rack such that when the bottle flip-top cap is opened, it can be snapped into an open position within the adapter.
 - c. As mentioned above, place an ABBOTT PRISM Positive Control after the last sample tested in the batch. **The controls can be placed in any rack position except 1, 2, 27, or 28.**

Refer to the ABBOTT PRISM Operations Manual, Section 3, for additional information on calibrators, assay controls and run controls.

ASSAY PARAMETER SPECIFICATIONS

The ABBOTT PRISM HBcore assay parameter specifications have been factory set. These parameters cannot be printed, displayed, or edited.

RESULTS

Calculation of Cutoff and S/CO Values

The ABBOTT PRISM System calculates the ABBOTT PRISM HBcore assay cutoff value using the following formula:

$$\text{Cutoff Value} = (0.58 \times \text{Mean Negative Calibrator [NC] Net Counts}) + (0.42 \times \text{Mean Positive Calibrator [PC] Net Counts})$$

Example: Mean NC Net Counts = 38,000
Mean PC Net Counts = 1,500
 $(0.58 \times 38,000) + (0.42 \times 1,500) = 22,670$
Cutoff Value = 22,670

The ABBOTT PRISM System calculates the ABBOTT PRISM HBcore assay S/CO for each sample and control using the following formula:

$$\text{S/CO} = \text{Sample Net Counts} \div \text{Cutoff Value}$$

Example: Sample Net Counts = 3,000
Cutoff Value = 22,670
 $3000 \div 22,670 = 0.13$
S/CO = 0.13

Interpretation of Results

- In the ABBOTT PRISM HBcore assay, specimens with Net Counts greater than the cutoff value are nonreactive and need not be tested further. Nonreactive specimens are considered negative for anti-HBc by the criteria of ABBOTT PRISM HBcore.
- Specimens with Net Counts less than or equal to the cutoff value are considered initially reactive by the criteria of the ABBOTT PRISM HBcore assay. All specimens (excluding non-frozen plasmapheresis specimens) that are reactive on initial testing must be centrifuged prior to retesting according to the table in the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert. Initially reactive specimens must be retested in duplicate using the ABBOTT PRISM HBcore Assay Kit.
NOTE: Specimens retested within 24 hours of initial centrifugation do not require recentrifugation.
- If the sample Net Counts for both retests are greater than the cutoff value, the specimen is nonreactive. Nonreactive specimens are considered negative for anti-HBc by the criteria of ABBOTT PRISM HBcore.
- If the sample Net Counts for either duplicate retest are less than or equal to the cutoff value, the specimen is considered repeatedly reactive. Repeatedly reactive results indicate the presence of anti-HBc by the criteria of ABBOTT PRISM HBcore.
- Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive.
- Individuals who are repeatedly reactive may be referred for medical evaluation which may include additional testing.
- Although the association of infectivity of donated blood or plasma and the presence of anti-HBc is strong, it is recognized that presently available methods for anti-HBc detection are not sensitive enough to detect all potentially infectious units of blood or plasma, or possible cases of HBV infection. A nonreactive test result does not exclude infection.

Reading Results

Some S/CO values may be flagged with "<" or ">" symbols. For more information on sample reports, refer to the ABBOTT PRISM Operations Manual, Section 5: Operating Instructions, Reports. The ABBOTT PRISM System reports sample results in Net Counts and S/CO. Net Counts are used by the ABBOTT PRISM System to interpret results. The S/CO value is provided in reports to show reactivity relative to the cutoff value. In the ABBOTT PRISM HBcore assay, specimens with S/CO values of less than or equal to 1.00 are considered reactive. Specimens with an S/CO value of greater than 1.00 are considered nonreactive.

System Errors

For a description of the error codes that appear on ABBOTT PRISM System reports, refer to the ABBOTT PRISM Operations Manual, Section 10.

LIMITATIONS OF THE PROCEDURE

- This assay was designed and validated for use with individual human serum and plasma specimens. This assay has not been validated for use with pooled specimens.
- **Do not use specimens collected in heparin. Use of heparin as an anticoagulant may cause a reduction in Sample Net Counts and in S/CO for ABBOTT PRISM HCV; therefore, heparin is not recommended for any ABBOTT PRISM assay.**
- Serum from heparinized patients may be incompletely coagulated. Erroneous or inconsistent test results may occur due to the presence of fibrin. To prevent this phenomenon, draw specimen prior to heparin therapy.
- False-reactive test results can be expected with any test kit. False-reactive test results have been observed due to nonspecific interactions. Refer to the **SPECIFIC PERFORMANCE CHARACTERISTICS** section of this package insert for assay performance characteristics.
- Some specimens that have undergone multiple freeze-thaw cycles or have been stored frozen for prolonged periods may result in erroneous or inconsistent test results.
- Previously frozen specimens must be centrifuged per the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert prior to running the assay.

- Performance has not been established using cadaver specimens, umbilical cord blood, or body fluids such as urine, saliva, semen, amniotic fluid, cerebrospinal fluid, or pleural fluid. These specimens should not be tested using the ABBOTT PRISM HBcore assay.
- Do not use heat-inactivated specimens.
- Do not use specimens with obvious microbial contamination.

SPECIFIC PERFORMANCE CHARACTERISTICS

ASSAY REPRODUCIBILITY

Assay reproducibility was determined by testing a four-member panel consisting of three diluted specimens reactive or borderline nonreactive for anti-HBc (panel members 1, 2, and 3) and one specimen nonreactive for anti-HBc (panel member 4). Each panel member was tested in replicates of four in five runs over five days with each of three reagent lots at four sites. In addition, each panel member was tested in replicates of four in five runs over five days with one of the three reagent lots at the same four sites. The ABBOTT PRISM Negative and Positive Controls were tested once at the beginning and end of each run on each subchannel. The ABBOTT PRISM HBcore Negative and Positive Calibrators were automatically tested in triplicate at the beginning of each run on each subchannel. The intra-assay and inter-assay standard deviation (SD) and percent coefficient of variation (%CV) were determined with a variance component analysis¹³ for a mixed model¹⁴ (Table III).

Table III

ABBOTT PRISM HBcore Assay Reproducibility

Panel Member or Control	Number of Replicates	Mean S/CO*	Intra-assay SD	%CV	Inter-assay ^a SD	%CV
1	319 ^b	0.24	0.010	4.0	0.012	4.7
2	320	0.50	0.018	3.7	0.020	3.9
3	320	1.15	0.039	3.4	0.039	3.4
4	319 ^c	1.66	0.049	3.0	0.056	3.4
Negative Control	320	1.64	0.050	3.1	0.055	3.3
Positive Control	320	0.53	0.024	4.5	0.034	6.5

*Cutoff Value = (0.58 x Mean Negative Calibrator Net Counts) + (0.42 x Mean Positive Calibrator Net Counts)

Calibrator	Number of Replicates	Mean Net Counts	Intra-assay SD	%CV	Inter-assay SD	%CV
Negative	480	21,682	903.2	4.2	930.5	4.3
Positive	480	1,100	62.8	5.7	112.6	10.2

^a Inter-assay variability contains intra-assay variability.

^b One replicate was invalid due to instrument detection of insufficient sample volume.

^c One replicate was invalid due to instrument detection of a sample dispense error.

ASSAY SPECIFICITY

A total of 16,378 fresh serum and plasma specimens from volunteer whole blood donors were collected and tested at four geographically distinct blood centers (Table IV). Two sites tested a total of 8,234 serum specimens with initial and repeat reactive rates of 0.50% (41/8,234) and 0.45% (37/8,234), respectively. Two sites tested a total of 8,144 plasma specimens with initial and repeat reactive rates of 0.58% (47/8,144). There were a total of 84 repeatedly reactive donor specimens. Based on additional testing, 65 specimens were positive (Table V) and 19 specimens were indeterminate.

Specificity based on assumed zero prevalence of antibody to Hbc in blood donors was estimated in these studies to be 99.88% (16,294/16,313) with a 95% confidence interval of 99.82% to 99.93%. Sixty-five repeatedly reactive specimens that were positive by additional testing were excluded from these calculations.

One site evaluated 318 serum or plasma specimens collected from 318 individuals with medical conditions unrelated to HBV infection or containing potentially interfering substances (Table IV). Seventy-two of the 318 specimens (22.64%) were initially and repeatedly reactive. Sixty-four of the 72 specimens (88.89%) were positive by additional testing. Eight of the remaining 254 specimens were indeterminate by additional testing. The eight specimens included one anti-HCV positive (12 tested), one anti-HIV-1 positive (12 tested), one anti-HIV-2 positive (5 tested), one anti-nuclear antibody positive (12 tested), two influenza vaccine recipients (52 tested), and two patients with non-viral liver diseases (43 tested). The estimated specificity in this population was 96.85% (246/254) and was lower than that observed in the low risk volunteer whole blood donor population (99.88%).

Table IV
Reactivity of the ABBOTT PRISM HBcore Assay in Whole Blood Donors, in Specimens from Individuals with Medical Conditions Unrelated to HBV Infection, and in Specimens Containing Potentially Interfering Substances

Category	Number Tested	IR (% of Total) (95% CI)	RR (% of Total) (95% CI)	Number Positive By Additional Testing ^a (% of RR)
Volunteer Blood Donors				
Serum	8,234	41 (0.50) (0.36 - 0.67)	37 (0.45) (0.32 - 0.62)	25 (67.57)
Plasma	8,144	47 (0.58) (0.42 - 0.77)	47 (0.58) (0.42 - 0.77)	40 (85.11)
Total Donors	16,378	88 (0.54) (0.43 - 0.66)	84 (0.51) (0.41 - 0.63)	65 (77.38)
Medical Conditions Unrelated to HBV Infection and Specimens Containing Potentially Interfering Substances ^b	318	72 (22.64)	72 ^c (22.64)	64 ^d (88.89)

IR = Initially Reactive; RR = Repeatedly Reactive; CI = Confidence Interval

^a Additional tests for the following HBV markers were performed to support a PRISM HBcore reactive test result: HBsAg, anti-HBc detected by a licensed screening assay, IgM anti-HBc, anti-HBs, anti-HBe, and HBV DNA. A PRISM HBcore reactive specimen was defined as anti-HBc positive if any of the following HBV markers were detected: HBsAg, IgM anti-HBc, HBV DNA, anti-HBs and anti-HBe, or anti-HBs and anti-HBc detected by a licensed screening assay (Table V). A specimen was defined as anti-HBc indeterminate according to the following three conditions: 1) reactive for anti-HBs only, 2) reactive for anti-HBc only, 3) negative for all HBV markers tested.

^b Specimens from individuals with medical conditions unrelated to HBV infection and specimens containing potentially interfering substances included the following categories: anti-HCV positive (12), anti-CMV positive (11), anti-EBV positive (10), anti-HSV positive (12), anti-HAV positive (12), anti-HIV-1 positive (12), anti-HIV-2 positive (5), anti-HTLV-I positive (12), anti-HTLV-II positive (12), rubella antibody positive (12), toxoplasma antibody positive (12), *E. coli* infections (5), syphilis serology positive (12), anti-nuclear antibody positive (12), rheumatoid factor positive (12), influenza vaccine recipients (52), elevated IgG (12), elevated IgM (12), elevated triglycerides (12), elevated bilirubin (12), elevated hemoglobin (12), and non-viral liver diseases (43).

^c The 72 repeatedly reactive specimens included the following: anti-HCV positive (4), anti-CMV positive (1), anti-HAV positive (2), anti-HIV-1 positive (10), anti-HIV-2 positive (4), anti-HTLV-I positive (1), anti-HTLV-II positive (2), toxoplasma antibody positive (2), syphilis serology positive (1), anti-nuclear antibody positive (1), influenza vaccine recipients (18), elevated bilirubin (12), and non-viral liver diseases (14).

^d The 64 specimens supported as positive by additional testing included the following: anti-HCV positive (3), anti-CMV positive (1), anti-HAV positive (2), anti-HIV-1 positive (9), anti-HIV-2 positive (3), anti-HTLV-I positive (1), anti-HTLV-II positive (2), toxoplasma antibody positive (2), syphilis serology positive (1), influenza vaccine recipients (16), elevated bilirubin (12), and non-viral liver diseases (12).

Table V

PRISM HBcore Positives by Additional Testing^a

Result	Licensed anti-HBc	HBsAg	IgM anti-HBc	anti-HBs	anti-HBe	HBV DNA
Positive	62	4	2 ^b	56	19	8
Negative	3	61	62	8	24	15

^a Not all PRISM HBcore reactive specimens were tested for all markers as a result of the additional test algorithm and/or available volume of the specimen

^b Two specimens considered gray-zone reactive by the criteria of the assay

ASSAY SENSITIVITY

A total of 1,162 serum and plasma specimens from 251 individuals known to be positive for Total anti-HBc, 250 individuals known to be positive for IgM anti-HBc, 99 individuals with acute HBV infection, 100 individuals with chronic HBV infection, 46 individuals who have recovered from HBV infection, and 416 individuals at increased risk for HBV infection were tested with the ABBOTT PRISM HBcore assay. Of the 1,162 specimens, 982 (84.51%) were determined to be positive for anti-HBc supported by previous HBV serological marker profile testing and additional testing. The ABBOTT PRISM HBcore assay detected 99.49% (977/982) of these specimens (Table VI). The overall sensitivity was estimated in these studies to be 99.49% (977/982) with a 95% confidence interval of 98.82% to 99.83%.

Table VI
Reactivity of the ABBOTT PRISM HBcore Assay
in Selected Populations with HBV Infection
and at Increased Risk for HBV Infection

Category	Number Tested	Number Positive By Additional Testing/Pedigree	Number Repeatedly Reactive (% of Positive by Additional Testing/Pedigree)
Preselected Total anti-HBc Positive	251	251 ^a	250 ^b (99.60)
Preselected IgM anti-HBc Positive	250	250 ^a	250 ^b (100.00)
Acute HBV Infection	99	99	97 (97.98)
Chronic HBV Infection	100	100	99 (99.00)
Recovered HBV Infection	46	46	45 (97.83)
Increased Risk for HBV Infection ^c	416	236	236 ^d (100.00)
TOTAL	1,162	982	977 (99.49)

^a Preselected Total and IgM anti-HBc Positive specimens were previously identified as reactive by approved assays.

^b Specimens from the preselected Total anti-HBc and IgM anti-HBc Positive categories were only tested once unless they were initially nonreactive or discordant.

^c Individuals at increased risk for HBV infection included the following categories: intravenous drug users (206), hemodialysis patients (50), hemophilia patients (50), and STD clinic patients (110).

^d The 236 repeatedly reactive specimens included the following: intravenous drug users (101), hemodialysis patients (37), hemophilia patients (33), and STD clinic patients (65).

ASSAY ANALYTICAL SENSITIVITY

In studies performed with three ABBOTT PRISM HBcore reagent lots at three sites and Abbott Laboratories using an anti-HBc dilution panel standardized against reference serum from the Paul Ehrlich Institute (PEI), the ABBOTT PRISM HBcore assay sensitivity was less than 0.8 PEI Units/mL.

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