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

Customer Service: Contact your local representative or find country specific contact information on www.abbottdiagnostics.com

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to Symbols

<table>
<thead>
<tr>
<th>LOT</th>
<th>Lot Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>REF</td>
<td>List Number</td>
</tr>
<tr>
<td>IVD</td>
<td>In Vitro Diagnostic Medical Device</td>
</tr>
<tr>
<td>Caution</td>
<td>Consult instructions for use</td>
</tr>
<tr>
<td>Storage</td>
<td>Store at 2-8°C</td>
</tr>
<tr>
<td>Storage</td>
<td>Store at 15-30°C</td>
</tr>
<tr>
<td>Expiration Date</td>
<td>Authorized Representative in the European Community</td>
</tr>
<tr>
<td>Manufacturer</td>
<td></td>
</tr>
<tr>
<td>Activator Line Treatment</td>
<td></td>
</tr>
<tr>
<td>ASSAY KIT CARD</td>
<td>Assay Kit Card</td>
</tr>
<tr>
<td>CALIBRATORS</td>
<td>Calibrators</td>
</tr>
<tr>
<td>CONTAINS: AZIDE</td>
<td>Contains Sodium Azide. Contact with acids liberates very toxic gas.</td>
</tr>
<tr>
<td>DISTRIBUTED BY</td>
<td>Distributed by</td>
</tr>
<tr>
<td>LINE CLEANER</td>
<td>Line Cleaner</td>
</tr>
<tr>
<td>MASTER LOT</td>
<td>Master Lot</td>
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<tr>
<td>PIPETTE TIPS</td>
<td>Pipette Tips</td>
</tr>
<tr>
<td>PRIME/PURGE ACCESSORIES</td>
<td>Prime/Purge Accessories</td>
</tr>
<tr>
<td>PRODUCED FOR ABBOTT BY</td>
<td>Produced for Abbott by</td>
</tr>
<tr>
<td>PRODUCT OF USA</td>
<td>Product of USA</td>
</tr>
<tr>
<td>PURGE CONCENTRATE</td>
<td>Purge Concentrate</td>
</tr>
<tr>
<td>REACTION TRAYS</td>
<td>Reaction Trays</td>
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<tr>
<td>REAGENT COMPONENTS</td>
<td>Reagent Components</td>
</tr>
<tr>
<td>RUN CONTROL ADAPTERS</td>
<td>Run Control Adapters</td>
</tr>
<tr>
<td>SAMPLE CUPS</td>
<td>Sample Cups</td>
</tr>
<tr>
<td>WARNING: INGESTION HAZARD</td>
<td>Warning: Harmful if swallowed.</td>
</tr>
<tr>
<td>WARNING: SENSITIZER</td>
<td>Warning: May cause an allergic reaction.</td>
</tr>
<tr>
<td>WARNING: SEVERE IRRITANT</td>
<td>Warning: Severe Irritant</td>
</tr>
</tbody>
</table>

See REAGENTS section for a full explanation of symbols used in reagent component naming.

U.S. License No. 43

Abbott
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 specimens. The product is intended to screen individual human donors, including volunteer donors of whole blood and blood components, and other living donors to prevent transmission of hepatitis B virus (HBV) from such donors. It is also intended for use in testing blood and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating. It is not intended for use on cord blood specimens.

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 (HBcAg) 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 HBcAg on the Microparticles.
- After the 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 blower.
- The Acridinium-Labeled Human Anti-HBc Conjugate is added to the Microparticles on the matrix and incubated. The Conjugate will bind to HBcAg and conjugate has not been blocked by human anti-HBc in the sample. After this second incubation, the unbound Conjugate is washed into the blower 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 HBcAg 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 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. Customers outside the U.S. must follow their country’s government 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. 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 (REF 6666-68)

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

- **MICROPARTICLES**: 1 Bottle (340 mL) Hepatitis B Virus Core Antigen (E. coli, Recombinant) Coated Microparticles in TRIS buffered salineline with bovine serum albumin and protein stabilizers. Minimum concentration: 0.005 % solids. Preservative: 0.1% sodium azide. (Symbol: Ⓗ)
- **CONJUGATE** 1 Bottle (335 mL) Antibody to Hepatitis B Virus Core Antigen (Human): Acidinium Conjugate in phosphate buffered saline with calf serum and recalcified, inactivated human plasma. Minimum concentration: 0.025 μg/mL. Preservative: 0.1% sodium azide. (Symbol: Ⓓ)
- **CAL** 1 Bottle (10.4 mL each) Negative Calibrator (Human), Recalciﬁed plasma. Preservative: 0.1% sodium azide. (Symbol: NC)
- **CAL** 1 Bottle (10.4 mL each) Positive Calibrator (Human). Recalciﬁed plasma reactive for anti-HBc and anti-HBs. Minimum concentration: 40 IU1 Units/mL. Preservative: 0.1% sodium azide. (Symbol: PD)

**CYSTEINE POWDER**

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)

**CYSTEINE DILUENT**

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 (REF 6666-58)

- **TRANSFER WASH**: 1 Bottle (3422 mL) Transfer Wash. MES [2-(N-morpholino)ethanesulfonic acid] buffered saline. Preservative: 0.1% ProClin 300. (Symbol: ~)
- **CONJUGATE WASH**: 1 Bottle (1757 mL) Conjugate Wash. MES [2-(N-morpholino)ethanesulfonic acid] buffered saline. Preservative: 0.1% ProClin 300. (Symbol: Ⓓ)

**ABBOTT PRISM Activator Concentrate**

1775-02 or 3270-02

- **ACTIVATOR CONCENTRATE**: 4 Bottles (900 mL each) Activator Concentrate. 0.4% hydrogen peroxide/0.08% diethylaminoethylmethylacetic acid.

**ABBOTT PRISM Activator Diluent**

1775-01 or 3270-01

- **ACTIVATOR DILUENT**: 4 Bottles (900 mL each) Activator Diluent. 0.3% sodium hydroxide.

**ABBOTT PRISM Run Control Kit**

REF 3601-10

Or

**ABBOTT PRISM Positive Run Control Kit**

REF 3601-11

NOTE: Each batch MUST end in a release control (ABBOTT PRISM Positive Control). The ABBOTT PRISM Positive Control (Inclued in Kit REF 3601-10 or 3601-11) 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.

WARNINGS AND PRECAUTIONS

- **IVD**

- **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.

- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in the package insert.
Safety Precautions

CAUTION: This product contains human sourced and/or potentially infectious components. 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, Biosafety Level 2 or other appropriate biosafety practices 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 pipet 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.
- Decontaminate and dispose of all specimens, reagents and other potentially contaminated materials in accordance with local, state and federal regulations.

- The human plasma used in the Conjugate is nonreactive for HbsAg, HIV-1 Ag or HIV-1 RNA, anti-HCV, and anti-HIV-1/HIV-2.
- The human plasma used in the Negative Calibrator is nonreactive for HbsAg, HIV-1 Ag or HIV-1 RNA, anti-HCV, anti-HIV-1/HIV-2, anti-Hbc, and anti-Hbs.
- The human plasma used in the Positive Calibrator is reactive for anti-Hbc and anti-Hbs, and nonreactive for HbsAg, HIV-1 Ag or HIV-1 RNA, anti-HCV, and anti-HIV-1/HIV-2.

This product contains sodium azide; for a specific listing, refer to the REAGENTS section. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.

The following warnings and precautions apply to the Cysteine Powder:

WARNING

Prevention
P264 Wash hands thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.

Response
P301-P332 IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell
P330 Rinse Mouth.

Disposal
P501 Dispose of contents/container in accordance with local regulations.

The following warnings and precautions apply to the Purge Concentrate:

WARNING: Contains methylisothiazolones.

Prevention
P261 Avoid breathing mist / vapours / spray.
P272 Contaminated work clothing should not be allowed out of the workplace.
P280 Wear protective gloves / protective clothing / eye protection.

Response
P302+P352 IF ON SKIN: Wash with plenty of water.
P333+P313 If skin irritation or rash occurs: Get medical advice / attention.
P362+P348 Take off contaminated clothing and wash it before reuse.

Disposal
P501 Dispose of contents/container in accordance with local regulations.

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.
- Gently invert calibrators in the calibrator pack several times prior to each use.
- 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 or calibrators 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 [REF 6463-50]. 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
- For the software versions that may be used to perform the assay, refer to the ABBOTT PRISM Assay / Software Version Matrix located in the Supplemental Information tab of the ABBOTT PRISM Operations Manual.
- 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-hemolysed 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 (≤ 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, sputum, 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

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>RCF (x g)</th>
<th>g-minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>3,000</td>
<td>30,000</td>
</tr>
<tr>
<td>15</td>
<td>2,000 - 3,000</td>
<td>30,000 - 45,000</td>
</tr>
<tr>
<td>20</td>
<td>1,500 - 3,000</td>
<td>30,000 - 60,000</td>
</tr>
<tr>
<td>25</td>
<td>1,300 - 3,000</td>
<td>32,500 - 75,000</td>
</tr>
</tbody>
</table>

Convert rpm to RCF as follows: RCF = 1.12 x rpm/1000

Convert RCF to rpm as follows: rpm = 1000 x \( \frac{RCF}{1.12 \times \text{rpm}} \)

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

NOTE: If custom tube adapters (i.e., adapters not defined by the centrifuge manufacturer) are used, then the radius \( r_{	ext{max}} \) should be manually measured in millimeters and the RCF calculated.

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

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>RCF (x g)</th>
<th>g-minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>12,000</td>
<td>180,000</td>
</tr>
<tr>
<td>20</td>
<td>9,000 - 12,000</td>
<td>180,000 - 240,000</td>
</tr>
<tr>
<td>25</td>
<td>7,200 - 12,000</td>
<td>180,000 - 300,000</td>
</tr>
</tbody>
</table>

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 re centrifugation.
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 µL sample dispense. For ABBOTT PRISM Sample Cups, the minimum specimen volume required for one ABBOTT PRISM Hbcore assay is 400 µL. For either primary or aliquot tubes or additional assay volume requirements, refer to the ABBOTT PRISM Operations Manual, Section 5.

PROCEDURE

Materials Provided

- REF 8666-68 ABBOTT PRISM Hbcore Assay Kit

Materials Required but Not Provided

- REF 8660-58 ABBOTT PRISM Hbcore Wash Kit
- REF 1A75-02 or 3L27-02 ABBOTT PRISM ACTIVATOR CONCENTRATE
- REF 1A75-01 or 3L27-01 ABBOTT PRISM ACTIVATOR DILUENT
- REF 5A07-01 ABBOTT PRISM REACTION TRAYS
- REF 6A07-10 ABBOTT PRISM PIPETTE TIPS
- REF 6A36-00 ABBOTT PRISM Accessory Kit
- REF 8660-10 ABBOTT PRISM Run Control Kit
  or
- REF 8660-11 ABBOTT PRISM Positive Run Control Kit
  or
- REF 6A36-31 ABBOTT PRISM RUN CONTROL ADAPTERS

- Magnetic Stir Plate Plate width ≥ 3 inches
- Disinfectant
- Purified Water-rinsed or Clean Disposable Measuring Equipment

Additional Materials Available

- REF 7A30-01 ABBOTT PRISM SAMPLE CUPS
- REF 1A75-10 or 3L27-10 ABBOTT PRISM ACTIVATOR LINE TREATMENT
- REF 7A03-01 or 3L00-01 ABBOTT PRISM PRIME/PURGE ACCESSORIES
- REF 7A03-30 or 3L00-30 ABBOTT PRISM PURGE CONCENTRATE
- REF 7A03-31 ABBOTT PRISM LINE CLEANER

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 Cystine Solution, if necessary. Refer to the Preparation of Cystine Solution section of this packet insert.

NOTE: Gently invert each component several times prior to loading on the ABBOTT PRISM System to ensure a homogeneous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Gently invert calibrators in the calibrator pack several times prior to each use. 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 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. Gently invert calibrators in the calibrator pack several times. 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 shut down 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 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 the bottle flip-top cap is open, 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:

\[ \text{Cutoff Value} = 0.58 \times \text{Mean Negative Calibrator} + (0.42 \times \text{Mean Positive Calibrator}) \]

Example: Mean NC Net Counts = 38,000
Mean PC Net Counts = 1,500
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:

\[ \text{S/CO} = \frac{\text{Sample Net Counts}}{\text{Cutoff Value}} \]

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

Interpretation of Results

- In the ABBOTT PRISM HBcore assay, specimens with Net Counts lower 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 reneutralization.
- If the sample Net Counts for both retests are greater than the cutoff value, the specimen is considered negative for anti-Hbc by the criteria of ABBOTT PRISM HBcore.
- If the sample Net Counts for either duplicate retest is less than or equal to the cutoff value, the specimen is considered repeatedly reactive. Repeated 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. Customers outside the U.S. must follow their country’s government 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 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 four more 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 analysis to a model (Table III).

Table III

<table>
<thead>
<tr>
<th>ABBOTT PRISM HBcore Assay Reproducibility</th>
<th>Panel Member or Control</th>
<th>Number of Replicates</th>
<th>Mean Net Counts (SD)</th>
<th>Intra-assay SD (%CV)</th>
<th>Inter-assay SD (%CV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>319a</td>
<td>0.24</td>
<td>0.010</td>
<td>4.0</td>
<td>0.012</td>
</tr>
<tr>
<td>2</td>
<td>320</td>
<td>0.50</td>
<td>0.018</td>
<td>3.7</td>
<td>0.020</td>
</tr>
<tr>
<td>3</td>
<td>320</td>
<td>1.15</td>
<td>0.039</td>
<td>3.4</td>
<td>0.039</td>
</tr>
<tr>
<td>4</td>
<td>319b</td>
<td>1.56</td>
<td>0.049</td>
<td>3.0</td>
<td>0.058</td>
</tr>
<tr>
<td>Negative Control</td>
<td>320</td>
<td>1.64</td>
<td>0.050</td>
<td>3.1</td>
<td>0.055</td>
</tr>
<tr>
<td>Positive Control</td>
<td>320</td>
<td>0.53</td>
<td>0.024</td>
<td>4.5</td>
<td>0.034</td>
</tr>
</tbody>
</table>

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

b Inter-assay variability contains intra-assay variability.

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

d 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 0.43% (37/8,234), respectively. Two sites tested a total of 8,144 plasma specimens with initial and repeat reactive rates of 0.56% (47/8,144). The total of 84 repeat 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 99.98% (16,294/16,313) with a 95% confidence interval of 99.92% to 99.99%. Sixty-five repeat 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 repeat 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-HM-1 positive (12 tested), one anti-HIV-2 positive (5 tested), one anti-nucleic-acid 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 98.85% (248/254) and was lower than that observed in the low risk volunteer whole blood donor population (99.88%).

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Number Tested</th>
<th>IR (% of Total) (95% CI)</th>
<th>RR (% of Total) (95% CI)</th>
<th>Number Positive by Additional Testing* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volunteer Blood Donors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>8,234</td>
<td>41 (0.50) (0.46 - 0.45)</td>
<td>32 (0.40) (0.36 - 0.44)</td>
<td>25 (0.31) (0.27 - 0.29)</td>
</tr>
<tr>
<td>Plasma</td>
<td>8,144</td>
<td>47 (0.58) (0.54 - 0.62)</td>
<td>37 (0.46) (0.42 - 0.50)</td>
<td>40 (0.51) (0.47 - 0.55)</td>
</tr>
<tr>
<td>Total Donors</td>
<td>16,378</td>
<td>88 (0.54) (0.51 - 0.66)</td>
<td>84 (0.50) (0.47 - 0.63)</td>
<td>95 (0.77) (0.72 - 0.80)</td>
</tr>
</tbody>
</table>

Medical Conditions Unrelated to HBV Infection and Specimens Containing Potentially Interfering Substances

<table>
<thead>
<tr>
<th>Category</th>
<th>Number Tested</th>
<th>IR (% of Total) (95% CI)</th>
<th>RR (% of Total) (95% CI)</th>
<th>Number Positive by Additional Testing* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimens</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>318</td>
<td>72 (22.64) (22.44 - 22.84)</td>
<td>64 (88.89) (88.68 - 89.09)</td>
<td></td>
</tr>
<tr>
<td>Plasma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Donors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Repeated test results for the following HBV markers were performed to support a PRISM HbcRe reactive test result: HBsAg, anti-Hbc detected by a licensed screening assay, IgM anti-Hbc, anti-Hbs, anti-HBe, and HBV DNA. A PRISM HbcRe 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-HBe 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, and 3) negative for all HbcRe markers tested.

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 46 individuals at increased risk for HBV infection were tested with the ABBOTT PRISM HbcRe 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 HbcRe assay detected 99.49% (977/982) of these specimens with a 95% confidence interval of 98.82% to 99.93%.

Table V
PRISM HbcRe Positives by Additional Testing

<table>
<thead>
<tr>
<th>Result</th>
<th>Licensed anti-Hbc</th>
<th>HBsAg</th>
<th>anti-Hbc</th>
<th>anti-HbV</th>
<th>HBV DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>62</td>
<td>4</td>
<td>21</td>
<td>55</td>
<td>19</td>
</tr>
<tr>
<td>Negative</td>
<td>3</td>
<td>61</td>
<td>62</td>
<td>8</td>
<td>24</td>
</tr>
</tbody>
</table>

a Not all PRISM HbcRe 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 ANALYTICAL SENSITIVITY

In studies performed with three ABBOTT PRISM HbcRe 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 HbcRe assay sensitivity was less than 0.8 PEI Units/mL.

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Number Tested</th>
<th>Number Positive by Additional Testing (95% CI)</th>
<th>Number Reactively Positive by Additional Testing (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescreened Total anti-Hbc Positive</td>
<td>251</td>
<td>250 (99.60)</td>
<td>250 (99.60)</td>
</tr>
<tr>
<td>Prescreened IgM anti-Hbc Positive</td>
<td>250</td>
<td>250 (100.00)</td>
<td>250 (100.00)</td>
</tr>
<tr>
<td>Acute HBV Infection</td>
<td>99</td>
<td>99 (100.00)</td>
<td>99 (100.00)</td>
</tr>
<tr>
<td>Chronic HBV Infection</td>
<td>100</td>
<td>100 (100.00)</td>
<td>100 (100.00)</td>
</tr>
<tr>
<td>Recovered HBV Infection</td>
<td>46</td>
<td>46 (100.00)</td>
<td>46 (100.00)</td>
</tr>
<tr>
<td>Increased Risk for HBV Infection</td>
<td>416</td>
<td>236 (99.60)</td>
<td>236 (99.60)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1,192</td>
<td>977 (99.49)</td>
<td>977 (99.49)</td>
</tr>
</tbody>
</table>

a Prescreened Total and IgM anti-Hbc Positive specimens were previously identified as reactive by approved assays.

b Specimens from the prescreened 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), hemodialysis patients (50), and STD clinic patients (110).

d The 206 repeatedly reactive specimens included the following: intravenous drug users (101), hemodialysis patients (37), hemodialysis patients (33), and STD clinic patients (65).

ASSAY ANALYTICAL SENSITIVITY

In studies performed with three ABBOTT PRISM HbcRe 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 HbcRe assay sensitivity was less than 0.8 PEI Units/mL.
BIBLIOGRAPHY


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