ABBOTT PRISM®
HBsAg
List No. 6D19
34-4212/R8

Antibody to Hepatitis B Surface Antigen (Mouse Monoclonal IgM)

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
2°C–8°C	Store at 2-8°C	ACTIVATOR CONCENTRATE	Activator Concentrate
		EC REP	Authorized Representative
15°C–30°C	Store at 15-30°C	CE ABBOTT LABORATORIES Abbott Park, IL 60064 USA	Legal Manufacturer

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ABBOTT LABORATORIES
Diagnostics Division
Abbott Park, IL 60064

List No. 6D19
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NAME AND INTENDED USE

The ABBOTT PRISM HBsAg assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the qualitative detection of hepatitis B surface antigen (HBsAg) in human serum and plasma specimens. The ABBOTT PRISM HBsAg (ChLIA) is intended to screen individual human donors, including volunteer donors of whole blood and blood components, and other living donors for the presence of HBsAg. 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, and in testing blood specimens to screen cadaveric (non-heart-beating) donors. It is not intended for use on cord blood specimens.

SUMMARY AND EXPLANATION OF THE TEST

Hepatitis B virus (HBV) is a small, partially double stranded, DNA virus and a member of the Hepadna virus family. The HBV genome contains four overlapping reading frames representing the core, polymerase, surface, and X genes. This virus is responsible for infecting approximately one third of the global population. Approximately 350 million individuals, world wide, are chronic carriers of HBV.[1] HBV is primarily transmitted through sexual, parenteral, and perinatal routes. Premature mortality from chronic liver disease occurs in 15-25% of the chronically infected HBV patients.[2] HBsAg, hepatitis B surface antigen, is the first viral antigen to circulate in the infected individual.

HBV, unlike other DNA viruses, replicates through reverse transcription. The reverse transcription process lacks proofreading capability; therefore, HBV is subject to a mutation rate 10 times higher than the mutation rate of other DNA viruses.[1] Some of these mutations may cause changes in the antigenic structure of HBsAg, resulting in epitopes that are no longer recognized by anti-HBs.[3-10]

Sensitive immunoassays for the detection of HBsAg were first described in the early 1970s[11-16] and were subsequently used to screen blood and blood products for the presence of HBsAg to prevent transmission of HBV infection to recipients of blood or blood products.[17,18] In addition, assays for HBsAg are routinely used to diagnose suspected HBV infection and to monitor the status of infected individuals, *i.e.*, whether the patient has resolved infection or has become a chronic carrier of the virus.[19-21] The Centers for Disease Control and Prevention have recommended the prenatal screening of all pregnant women so that newborns from HBV carrier mothers may obtain prophylactic treatment. Prenatal transmission of HBV infection from mother to neonate is a major mode of transmission in an HBV endemic population.[22]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ABBOTT PRISM HBsAg assay is a two-step sandwich ChLIA. The reactions occur within the ABBOTT PRISM System in the following sequence:

- Microparticles coated with mouse monoclonal anti-HBs are incubated with sample (either plasma, serum, calibrator, or control) in the incubation well of the reaction tray. During incubation, HBsAg present in the sample binds to the antibody 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 Goat Polyclonal Anti-HBs Conjugate is added to the Microparticles on the matrix and incubated. 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 proportional to the amount of HBsAg in the sample. The presence or absence of HBsAg 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 less than the cutoff value, the sample is considered nonreactive for HBsAg by the criteria of the ABBOTT PRISM HBsAg assay. These specimens need not be further tested. If the number of photons collected from a test sample is greater than or equal to the cutoff value, the sample is considered reactive for HBsAg by the criteria of the ABBOTT PRISM HBsAg 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. A specimen that is repeatedly reactive must be confirmed by the ABBOTT PRISM HBsAg Confirmatory assay, a licensed neutralizing confirmatory test. Only the specimens that are confirmed by specific neutralization with anti-HBs are considered positive for HBsAg.

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 HBsAg Assay Kit (No. 6D19-68)

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

- 1 Bottle (333 mL) Antibody to Hepatitis B Surface Antigen (Mouse Monoclonal IgM) Coated Microparticles in phosphate buffered saline with bovine serum albumin, Tween®* 20, and protein stabilizers. Minimum concentration: 0.03% solids. Preservative: 0.1% sodium azide. (Symbol: ●)
- 1 Bottle (328 mL) Antibody to Hepatitis B Surface Antigen (Goat Polyclonal): Acridinium Conjugate in phosphate buffered saline with calf serum and recalcified, 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, and anti-HIV-1/HIV-2. Preservative: 0.1% sodium azide. (Symbol: NC)
- 3 Bottles (10.4 mL each) Positive Calibrator (Human). Recalcified, inactivated plasma reactive for HBsAg and nonreactive for HIV-1 Ag or HIV-1 NAT, anti-HCV, and anti-HIV-1/HIV-2. HBsAg concentration: 0.25-0.65 ng/mL. Preservative: 0.1% sodium azide. (Symbol: PC)

Other Reagents Required

ABBOTT PRISM HBsAg Wash Kit (No. 6D19-58)

- 1 Bottle (3393 mL) Transfer Wash. Phosphate buffered saline. Preservative: 0.1% sodium azide. (Symbol: ~)
- 1 Bottle (2811 mL) Conjugate Wash. Borate buffered saline. Preservative: 0.1% sodium azide. (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.

*Tween is a registered trademark of ICI Americas.

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 HBsAg 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 HBsAg, 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.[23] Biosafety Level 2[24] or other appropriate biosafety practices[25,26] 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.[26,27,28]
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.[29,30]

- 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.

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 HBsAg 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 HBsAg Assay Kits.
- Any lot of ABBOTT PRISM HBsAg Wash Kit can be used with any lot of ABBOTT PRISM HBsAg 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 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 (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 HBsAg 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 HBsAg 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 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 3.11 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

- 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 HBsAg 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 cadaveric plasma 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.

- Failure to follow the specified centrifugation procedure on specimens tested with the ABBOTT PRISM HBsAg assay may cause a reduction in Sample Net Counts and in S/CO (Sample Net Counts/Cutoff Value).
- 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).
- For cadaveric specimens, follow general standards and/or regulations for collection, storage and handling. Cadaveric specimens may be stored frozen (-20°C or colder) or stored for up to 2 days at 2 - 8°C. If storage periods greater than 2 days at 2 - 8°C are anticipated, the serum should be removed from the clot to avoid hemolysis and stored frozen.
- 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 18 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 HBsAg assay is unknown.
- Performance has not been established using 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 HBsAg 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 HBsAg assay requires 100 µL sample dispense. For ABBOTT PRISM Sample Cups, the minimum specimen volume required for one ABBOTT PRISM HBsAg 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

- No. 6D19-68 ABBOTT PRISM HBsAg Assay Kit

Materials Required but not Provided

- No. 6D19-58 ABBOTT PRISM HBsAg 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
- Protective Disposable Gloves
- Disinfectant
- Purified Water-rinsed or Clean Disposable Measuring Equipment

Additional Materials Available

- No. 7B36-01 ABBOTT PRISM Sample Cups

ABBOTT PRISM HBsAg 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).

  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 HBsAg 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 HBsAg assay is a two-step ChLIA procedure.

QUALITY CONTROL PROCEDURES

Calibration

The ABBOTT PRISM HBsAg 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 HBsAg 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 HBsAg assay cutoff value using the following formula:

Cutoff Value = Mean Negative Calibrator (NC) Net Counts + (0.19 × Mean Positive Calibrator [PC] Net Counts)

Example: Mean NC Net Counts = 100
Mean PC Net Counts = 1,000
100 + (0.19 × 1,000) = 290
Cutoff Value = 290

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

S/CO = Sample Net Counts ÷ Cutoff Value

Example: Sample Net Counts = 580
Cutoff Value = 290
580 ÷ 290 = 2.00
S/CO = 2.00

Interpretation of Results

- In the ABBOTT PRISM HBsAg assay, specimens with Net Counts less than the cutoff value are nonreactive and need not be tested further. Nonreactive specimens are considered negative for HBsAg by the criteria of ABBOTT PRISM HBsAg.
- Specimens with Net Counts greater than or equal to the cutoff value are considered initially reactive by the criteria of the ABBOTT PRISM HBsAg 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 HBsAg Assay Kit.

  NOTE: Specimens retested within 24 hours of initial centrifugation do not require recentrifugation.
- If the sample Net Counts for both retests are less than the cutoff value, the specimen is nonreactive. Nonreactive specimens are considered negative for HBsAg by the criteria of ABBOTT PRISM HBsAg.
- If the sample Net Counts for either duplicate retest are greater than or equal to the cutoff value, the specimen is considered repeatedly reactive.
- Repeatedly reactive specimens must be tested by the ABBOTT PRISM HBsAg Confirmatory assay, a licensed neutralizing confirmatory test. Only the specimens which are confirmed by specific neutralization with anti-HBs are considered positive for HBsAg.
- 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 HBsAg is strong, it is recognized that presently available methods for HBsAg detection are not sensitive enough to detect all potentially infectious units of blood, 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 HBsAg assay, specimens with S/CO values of less than 1.00 are considered nonreactive. Specimens with an S/CO value of greater than or equal to 1.00 are considered reactive.

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.
- An increased occurrence of drain time errors may be observed for cadaveric specimens.
- Do not use cadaveric plasma specimens.
- Performance has not been established using 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 HBsAg assay.
- Do not use heat-inactivated specimens.
- Do not use specimens with obvious microbial contamination, gross lipemia or gross hemolysis.

SPECIFIC PERFORMANCE CHARACTERISTICS

ASSAY REPRODUCIBILITY

Assay reproducibility was determined by testing a seven-member panel consisting of three diluted specimens reactive for HBsAg *ad* subtype (panel members 1, 2, and 3), three diluted specimens reactive for HBsAg *ay* subtype (panel members 4, 5, and 6) and one specimen nonreactive for HBsAg (panel member 7). Panel members were prepared in recalcified human plasma. Each panel member was tested in replicates of four in five runs over five days with each of three reagent lots at six 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 of the six sites. The Negative and Positive Controls were tested once at the beginning and end of each run on each subchannel. The 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[31] for a mixed model[32] (Table III).

TABLE III
ABBOTT PRISM HBsAg Assay Reproducibility

Panel Member or Control	Number of Replicates	Mean S/CO*	Intra-assay SD	Intra-assay %CV	Inter-assay[a] SD	Inter-assay[a] %CV
1	440	6.98	0.283	4.1	0.390	5.6
2	440	4.06	0.160	3.9	0.222	5.5
3	440	1.39	0.068	4.9	0.077	5.6
4	439[b]	8.86	0.513	5.8	0.596	6.7
5	438[c]	4.62	0.162	3.5	0.244	5.3
6	439[b]	1.37	0.078	5.7	0.083	6.1
7	440	0.34	0.036	10.6	0.039	11.6
Negative Control	439[b]	0.26	0.038	14.6	0.041	15.6
Positive Control	440	2.63	0.138	5.2	0.204	7.8

* Cutoff Value = Mean Negative Calibrator Net Counts + (0.19 x Mean Positive Calibrator Net Counts)

Calibrator	Number of Replicates	Mean Net Counts	Intra-assay SD	Intra-assay %CV	Inter-assay SD	Inter-assay %CV
Negative	660	89	9.6	10.8	13.1	14.7
Positive	660	1299	73.3	5.6	73.3	5.6

[a] Inter-assay variability contains intra-assay variability.

[b] One replicate was invalid due to instrument detection of sample drain time error.

[c] Two replicates were invalid due to instrument detection of sample dispense errors.

ASSAY SPECIFICITY

A total of 25,238 fresh serum and plasma specimens from volunteer whole blood donors and plasmapheresis donors were collected and tested at six geographically distinct blood centers (Table IV). Two sites tested a total of 8,246 serum specimens with initial and repeat reactive rates of 0.06% (5/8,246) and 0.04% (3/8,246), respectively. Three sites tested a total of 13,911 plasma specimens with initial and repeat reactive rates of 0.06% (8/13,911) and 0.04% (5/13,911), respectively. One site tested a total of 3,081 plasmapheresis donor specimens with initial and repeat reactive rates of 0.03% (1/3,081) and 0.00% (0/3,081), respectively. A total of eight specimens were repeatedly reactive. In six of the eight specimens (75.00%), the presence of HBsAg was confirmed by specific neutralization with anti-HBs. Two of the eight specimens were not confirmed as positive.

Specificity based on assumed zero prevalence of HBsAg in whole blood and plasmapheresis donors was estimated in these studies to be 99.99% (25,230/25,232) with a 95% confidence interval (CI) of 99.97% to 100.00%. The six repeatedly reactive specimens that confirmed positive for HBsAg were excluded from these calculations.

Three sites evaluated 870 serum and plasma specimens either collected from individuals with medical conditions unrelated to HBV infection or containing potentially interfering substances (Table IV). Fifty-nine of the 870 specimens (6.78%) were initially reactive, and 50 of the 870 specimens (5.75%) were repeatedly reactive. Forty of the 50 specimens (80.00%) confirmed positive for HBsAg, and ten specimens did not confirm by specific antibody neutralization. The ten specimens included one anti-EBV positive (12 tested), one anti-HSV positive (12 tested), one rubella antibody positive (12 tested), one anti-nuclear antibody positive (12 tested), one elevated triglycerides (10 tested), and five pregnant females (555 tested). The estimated specificity in this population was 98.80% (820/830).

TABLE IV
Reactivity of the ABBOTT PRISM HBsAg Assay in Whole Blood and Plasmapheresis 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 Confirmed Positive[a] (% of RR)
Volunteer Blood Donors				
Serum	8,246	5 (0.06) (0.02 - 0.14)	3 (0.04) (0.01 - 0.11)	2 (66.67)
Plasma	13,911	8 (0.06) (0.02 - 0.11)	5 (0.04) (0.01 - 0.08)	4 (80.00)
Plasmapheresis Donors	3,081	1 (0.03) (0.00 - 0.18)	0 (0.00) (0.00 - 0.12)	
Total Donors	25,238	14 (0.06) (0.03 - 0.09)	8 (0.03) (0.01 - 0.06)	6 (75.00)
Medical Conditions Unrelated to HBV Infection and Potentially Interfering Substances[b]	870	59 (6.78)	50[c] (5.75)	40[d] (80.00)

IR = Initial Reactive; RR = Repeat Reactive; CI = Confidence Interval

[a] A specimen was confirmed positive for HBsAg if the non-neutralized specimen (with ABBOTT PRISM HBsAg Confirmatory assay Reagent B added) exhibited a net count greater than or equal to the ABBOTT PRISM HBsAg Confirmatory assay cutoff value and if the neutralization with anti-HBs (Reagent A) was 50% or greater.

[b] Specimens from individuals with medical conditions unrelated to HBV infection and specimens containing potentially interfering substances included the following categories: anti-CMV positive (11), anti-EBV positive (12), anti-HSV positive (12), anti-HAV positive (12), anti-HCV positive (12), anti-HIV-1 positive (12), anti-HIV-2 positive (5),

anti-HTLV-I positive (12), anti-HTLV-II positive (12), non-viral liver diseases (42), rubella antibody positive (12), toxoplasma antibody positive (11), *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 (10), elevated bilirubin (12), elevated hemoglobin (11), and pregnant females (555).

[c] The 50 repeatedly reactive specimens included the following: anti-EBV positive (1), anti-HSV positive (1), anti-HCV positive (1), anti-HIV-1 positive (5), anti-HIV-2 positive (1), non-viral liver diseases (5), rubella antibody positive (1), anti-nuclear antibody positive (1), influenza vaccine recipients (1), elevated triglycerides (1), and pregnant females (32).

[d] The following 40 specimens confirmed positive for HBsAg: anti-HCV positive (1), anti-HIV-1 positive (5), anti-HIV-2 positive (1), non-viral liver diseases (5), influenza vaccine recipients (1), and pregnant females (27).

ASSAY SENSITIVITY

A total of 1,212 serum and plasma specimens from 514 individuals known to be positive for HBsAg, 98 individuals with acute HBV infection, 101 individuals with chronic HBV infection, 47 individuals who have recovered from HBV infection, and 452 individuals at increased risk for HBV infection were tested with the ABBOTT PRISM HBsAg assay. A total of 767 specimens (63.28%) were repeatedly reactive, of which 754 (98.31%) were confirmed positive by specific antibody neutralization (Table V). The overall sensitivity was estimated in these studies to be 100.00% (754/754) with a 95% CI of 99.51% to 100.00%.

TABLE V
Reactivity of the ABBOTT PRISM HBsAg Assay in Selected Populations with HBV Infection and at Increased Risk for HBV Infection

Category	Number Tested	Number Repeatedly Reactive (% of Total)	Number Confirmed Positive (% of Repeatedly Reactive)
Preselected HBsAg Positive	514	514[a] (100.00)	514[b] (100.00)
Acute HBV Infection	98	98 (100.00)	98 (100.00)
Chronic HBV Infection	101	101 (100.00)	101 (100.00)
Recovered HBV Infection	47	0 (0.00)	
Increased Risk for HBV Infection[c]	452	54[d] (11.95)	41[e] (75.93)
Total	1,212	767 (63.28)	754 (98.31)

[a] Specimens from the preselected HBsAg positive category were tested only once.

[b] Preselected HBsAg positive specimens were previously confirmed positive by specific antibody neutralization.

[c] Individuals at increased risk for HBV infection included the following categories: intravenous drug users (204), hemodialysis patients (50), hemophilia patients (50), and STD clinic patients (148).

[d] The 54 repeatedly reactive specimens included the following: intravenous drug users (25), hemodialysis patients (6), hemophilia patients (4), and STD clinic patients (19).

[e] The 41 specimens that confirmed positive for HBsAg included the following: intravenous drug users (15), hemodialysis patients (5), hemophilia patients (3), and STD clinic patients (18). Of these 41 specimens, 32 were confirmed positive by a licensed reference HBsAg test. The PRISM assay confirmed an additional 9 specimens. In addition, there were no specimens in this category (452 specimens) that were confirmed positive by the licensed reference HBsAg test that were not confirmed positive by the PRISM assay.

The sensitivity of the ABBOTT PRISM HBsAg assay was evaluated using a seven-member panel comprised of specimens from an Abbott Laboratories HBsAg Sensitivity Panel. Panel members were prepared in recalcified human plasma. Three panel members were reactive for HBsAg *ad* subtype, three members were reactive for HBsAg *ay* subtype, and one member was nonreactive for HBsAg. The panel was tested as described in the **ASSAY REPRODUCIBILITY** section of this package insert. The detection of HBsAg *ad* and *ay* subtypes is presented in Tables VI and VII, respectively.

TABLE VI
Detection of Purified HBsAg *ad* by the ABBOTT PRISM HBsAg Assay

HBsAg Concentration (ng/mL)	Mean S/CO Value	Result
0.917	6.98	+
0.525	4.06	+
0.124	1.39	+
0.000	0.34	-

TABLE VII
Detection of Purified HBsAg *ay* by the ABBOTT PRISM HBsAg Assay

HBsAg Concentration (ng/mL)	Mean S/CO Value	Result
1.002	8.86	+
0.485	4.62	+
0.131	1.37	+
0.000	0.34	-

The ability of the ABBOTT PRISM HBsAg assay to detect HBsAg was evaluated by testing 12 HBV seroconversion panels from blood and plasmapheresis donors who seroconverted over the course of their donation history. All specimens were also tested by a FDA licensed assay. The ABBOTT PRISM HBsAg assay detected HBsAg three to 13 days (one to three bleeds) earlier in ten of the 12 panels and five to 48 days (one to three bleeds) longer in four of the 12 panels when compared to the licensed assay. Both assays detected HBsAg in the first available bleed for two of the 12 panels.

PERFORMANCE CHARACTERISTICS OF CADAVERIC SERUM TESTING

Reproducibility

Inter-assay reproducibility of PRISM HBsAg was assessed using 10 postmortem donor sera. These sera specimens were spiked with human plasma positive for HBsAg to create low-level reactive specimens. Each of the specimens was tested in triplicate on three different days on each of three lots of PRISM HBsAg at one site for a total of 270 replicates. Three replicates generated dispense errors and 16 replicates generated drain time errors and were excluded from the analysis. For intra-assay reproducibility, the %CV ranged from 2.9 to 5.5 for the low level reactive specimens. For inter-assay reproducibility over all lots, the percent coefficient of variation (%CV) ranged from 4.4 to 8.7 for the low-level reactive specimens. The total reproducibility ranged from 5.3 to 9.7 for the low level reactive specimens. Note: Inter-assay reproducibility includes intra-assay and inter-assay variation. Total reproducibility includes intra-assay, inter-assay and inter-lot variations.

Specificity

Specificity was evaluated using 51 postmortem donor specimens and 54 normal donor specimens. Each of the specimens was tested once on each of three lots of PRISM HBsAg. The mean sample to cutoff (S/CO) ratio for the 136 nonreactive postmortem replicates (51 specimens with three reagent lots; see Table VIII, footnotes a and b) was 0.35, and the mean S/CO for 162 normal donor replicates (54 specimens with three reagent lots) was 0.24. Results are presented in Table VIII.

Table VIII
Reactivity with PRISM HBsAg

Population	No. of Specimens	No. of Replicates	Mean S/CO	Nonreactive	Initial Reactive
Postmortem	51	137[a]	0.35	136 (99.27%)	1[b] (0.73%)
Normal Donor	54	162	0.24	162 (100.0%)	0 (0.0%)

[a] No results were obtained for 15 specimens on one lot due to drain time errors and one specimen on one lot due to an invalid result.

[b] Specimen was not retested due to insufficient specimen volume.

Assuming the specimen with the initial reactive result would have a reactive result upon retest, the PRISM HBsAg assay has an estimated specificity of 99.27% (136/137)(binomial confidence interval = [96.00%, 99.98%]) in these studies of postmortem serum specimens collected up to 16.1 hours after death.

Sensitivity

Sensitivity was evaluated using 51 postmortem specimens and 54 normal donor specimens that were pre-screened for anti-HBs and HBsAg and found to be negative. The 105 specimens were spiked with human plasma positive for HBsAg to create low-level reactive specimens. Each of the specimens was tested once on each of three lots of PRISM HBsAg. The mean sample to cutoff (S/CO) for the 142 postmortem replicates (51 specimens, with three reagent lots; see Table IX, footnote a) was 2.05, and the mean S/CO ratio for the 162 normal donor replicates (54 specimens, with three reagent lots) was 2.07. Results are presented in Table IX.

Table IX
Reactivity with PRISM HBsAg

Population	No. of Specimens	No. of Replicates	Mean S/CO	Nonreactive	Initial Reactive
Postmortem	51	142[a]	2.05	0 (0.0%)	142 (100.0%)
Normal Donor	54	162	2.07	0 (0.0%)	162 (100.0%)

[a] No results were obtained for 7 unique specimens, and 2 specimens using 2 reagent lots due to drain time errors.

The PRISM HBsAg assay has an estimated sensitivity of 100.00% (142/142)(binomial confidence interval = [97.44%, 100.00%]) in these studies of postmortem serum specimens collected up to 16.1 hours after death.

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U.S. Patent No. 4,380,580, licensed under patent rights of Bayer Corp., Tarrytown, New York, USA, relates to this product.

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