ABBOTT PRISM® HBcore
Summary Basis for Approval

Product Trade Name	ABBOTT PRISM® HBcore
Proper Name	Hepatitis B Virus Core Antigen (*E. coli*, Recombinant)
Applicant	Abbott Laboratories Dept. 49C, Bldg. AP6C 100 Abbott Park Road Abbott Park, IL 60064
Submission Tracking Number(s)	BL 103785 (Prior Ref. No. PLA# 98-0297 and ELA# 98-0365)
Report Date	October 2005

I. Intended Use

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

II. Brief Description of Test

A. Description of the Test

The ABBOTT PRISM HBcore assay utilizes microparticles coated with recombinant HBc antigen (rHBcAg) as the solid phase. The coated microparticles are incubated with sample (either plasma, serum, calibrator or control) and a Cysteine Solution. The anti-HBc present in the sample binds to the rHBcAg on the microparticles. Acridinium-labeled human anti-HBc conjugate is added and incubated with the microparticles. The conjugate binds to rHBcAg that has not been blocked by human anti-HBc in the sample. A chemiluminescent signal is generated by addition of an alkaline hydrogen peroxide solution. The amount of light emitted is inversely proportional to the amount of anti-HBc in the sample.

B. Reagents

1. The ABBOTT PRISM HBcore Assay Kit (No. 6E66-68) contains the following components:

   a. 1 Bottle (340 mL) Hepatitis B Virus Core Antigen (*E. coli*, Recombinant) Coated Microparticles in TRIS buffered saline with bovine serum albumin and protein stabilizers. Minimum concentration: 0.003% solids.
   Preservative: 0.1% sodium azide. (Symbol: ●)

   b. 1 Bottle (335 mL) Antibody to Hepatitis B Virus Core Antigen (Human): Acridinium Conjugate in phosphate buffered saline with calf serum and recalcified, inactivated human plasma, nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV and anti-HIV-1/HIV-2. Minimum concentration: 0.025 µg/mL. Preservative: 0.1% sodium azide. (Symbol: ⑦)

   c. 3 Bottles (10.4 mL each) Negative Calibrator (Human). Recalcified plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, anti-HIV-1/HIV-2, anti-HBc and anti-HBs. Preservative: 0.1% sodium azide. (Symbol: **NC**)

   d. 3 Bottles (10.4 mL each) Positive Calibrator (Human). Recalcified plasma reactive for anti-HBc and anti-HBs, nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV and anti-HIV-1/HIV-2. Minimum concentration: 40 PEI* Units/mL. Preservative: 0.1% sodium azide. (Symbol: **PC**)

   e. 1 Bottle (9.5 g) Cysteine Powder. (Symbol: **X**)

   f. 1 Bottle (354 mL) Cysteine Diluent containing 10 mM EDTA.

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

C. Other Reagents Required

Note: Any lot of ABBOTT PRISM HBcore Wash Kit, ABBOTT PRISM Activator Concentrate, ABBOTT PRISM Activator Diluent and Control from any lot of ABBOTT PRISM Run Control Kit or ABBOTT PRISM Positive Run Control Kit may be used with any lot of ABBOTT PRISM HBcore Assay Kit.

1. The ABBOTT PRISM HBcore Wash Kit (No. 6E66-58) contains the following components:

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

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

   * ProClin is a registered trademark of Rohm & Haas.

2. The ABBOTT PRISM Activator Concentrate (No. 1A75-02) contains the following component:

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

3. The ABBOTT PRISM Activator Diluent (No. 1A75-01) contains the following component:

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

4. The ABBOTT PRISM Run Control Kit (No. 3E60-10) contains the following components:

   a. 2 Bottles (10 mL each) Positive Control (Human). Purified anti-HBc IgG (Concentration: 0.9 - 2.6 PEI* Units/mL) and recalcified, inactivated plasma reactive for HBsAg (Concentration: 0.10 - 0.40 ng/mL), anti-HCV, anti-HIV-1 and anti-HTLV-I. Plasma is also tested for HIV-1 by either HIV-1 Ag and is nonreactive, or by HIV-1 NAT, and may be reactive. Positive Control may be cross-reactive with antibody to HTLV-II. Preservative: 0.1% sodium azide. (Symbol: **POS**)

   b. 1 Bottle (10 mL) Supplemental Positive Control (Human). Recalcified, inactivated plasma reactive for anti-HIV-2 and anti-HTLV-II, nonreactive for HBsAg, anti-HCV and HIV-1 Ag or HIV-1 NAT. Supplemental Positive Control may be cross-reactive with antibody to HTLV-I. Preservative: 0.1% sodium azide. (Symbol: **SUP**)

   c. 2 Bottles (10 mL each) Negative Control (Human). Recalcified plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, anti-HIV-1/HIV-2, anti-HBc, anti-HBs and anti-HTLV-I/HTLV-II. Preservative: 0.1% sodium azide. (Symbol: **NEG**)

5. The ABBOTT PRISM Positive Run Control Kit (No. 3E60-11) contains the following component:

   a. 6 Bottles (10 mL each) Positive Control (Human). Purified anti-HBc IgG (Concentration: 0.9 - 2.6 PEI* Units/mL) and recalcified, inactivated plasma reactive for HBsAg (Concentration: 0.10 - 0.40 ng/mL), anti-HCV, anti-HIV-1 and anti-HTLV-I. Plasma is also tested for HIV-1 by either HIV-1 Ag and is nonreactive, or by HIV-1 NAT, and may be reactive. Positive Control may be cross-reactive with antibody to HTLV-II. Preservative: 0.1% sodium azide. (Symbol: **POS**)

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

Note: Either the ABBOTT PRISM Run Control Kit **or** the ABBOTT PRISM Positive Run Control Kit may be used.

III. Manufacturing and Controls

A. Manufacturing and Controls

The ABBOTT PRISM HBcore assay is manufactured by Abbott Laboratories and prepared under U.S. License Number 43.

Recombinant HBc antigen is used in the ABBOTT PRISM HBcore assay. The recombinant antigen, HBc101, encompasses the coding region of the HBV core gene. The antigen is from an *Escherichia coli* (*E. coli*) codon optimized synthetic gene and is expressed in *E. coli*. The resulting clone and its sequence was confirmed by DNA sequencing. The plasmid is then transformed into *E. coli* cells to give the final clone for manufacturing of recombinant HBc antigen.

The human plasma reactive for HBcore used in the manufacture of the ABBOTT PRISM HBcore Positive Calibrator is positive for anti-HBc and anti-HBs, nonreactive for HBsAg, and negative for anti-HCV, anti-HIV-1/HIV-2 and HIV-1 Ag. This plasma does not require heat inactivation.

The plasma used in the manufacture of ABBOTT PRISM Positive Control is heat inactivated. After purification, the IgG anti-HBc is tested to ensure that it is nonreactive for HBsAg. This purified IgG does not require heat inactivation.

Raw materials intended for use in the product are subjected to quality control evaluations before they are accepted for use in manufacturing. All components have established acceptance criteria and performance specifications. Final components are subjected to performance testing and assembled into kits. The final ABBOTT PRISM HBcore Assay Kit is then further subjected to final performance testing.

Each lot of the ABBOTT PRISM HBcore Assay Kit is tested with in-house panels of samples with varying levels of anti-HBc reactivity, as well as the CBER anti-HBc Reference Panel, and must meet the performance requirements of both panels.

B. Stability Studies

Components of the ABBOTT PRISM HBcore Assay Kit, ABBOTT PRISM Run Control Kit, ABBOTT PRISM Positive Run Control Kit, ABBOTT PRISM HBcore Wash Kit, as well as the ABBOTT PRISM Activator Concentrate and ABBOTT PRISM Activator Diluent were entered into a stability program to establish the recommended storage conditions and the expiration dating. Three different lots of each component were manufactured, tested, assembled into kits and evaluated during storage. The studies support a 14 month dating period for the Wash Kit components and a 12 month dating period for the components of the Assay Kit, both Run Control Kits, the Activator Concentrate and Activator Diluent. The expiration date of the kit lot is the same as that of the shortest dated kit component.

C. Methods of Validation

Production of components is monitored by in-process testing. Product potency is assured through evaluation of product appearance, sterility or bioburden testing and performance testing. Product consistency is assured through lot uniformity testing of components. Product performance is assessed through laboratory evaluations of each test kit lot against in-house panels and the CBER anti-HBc Reference Panel. Each lot of product and protocols summarizing pertinent product testing are submitted for evaluation and approval by FDA prior to release for distribution.

D. Labeling

The product labeling, including immediate container, package labels, and package insert (directions for use), are in compliance with 21 CFR 610.60, 610.61, 610.62, 801 and 809.10. The product trade name, ABBOTT PRISM HBcore, is not known to conflict with any other biologic or device trade name.

E. Establishment Inspection

A pre-licensing inspection of the areas where product is manufactured, tested, stored and shipped was most recently conducted in August 2005. Facilities and procedures for this product were found to be in substantial conformity with the Quality System Regulation and current good manufacturing procedures.

F. Environmental Impact Analysis Report (EIAR)

Abbott Laboratories has filed a detailed EIAR. This product has no significant environmental impact.

IV. Biological Principles of the Procedure

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

- Microparticles coated with recombinant HBc antigen (rHBcAg) are incubated with sample (either plasma, serum, calibrator, or control) and Cysteine Solution in the incubation well of the reaction tray. During incubation, anti-HBc present in the sample binds to the rHBcAg on the Microparticles.

- After this first incubation is complete, the reaction mixture is transferred to the glass fiber matrix (matrix) of the reaction tray using the Transfer Wash. The Microparticles are captured by the matrix while the remaining mixture flows through to the absorbent blotter.

- The Acridinium-Labeled Human Anti-HBc Conjugate is added to the Microparticles on the matrix and incubated. The conjugate will bind to rHBcAg that has not been blocked by human anti-HBc in the sample. After this second incubation, the unbound Conjugate is washed into the blotter with the Conjugate Wash.

- The chemiluminescent signal is generated by addition of an alkaline hydrogen peroxide solution. The resultant photons are counted.

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

V. Performance Characteristics

A. Summary of Non-Clinical Studies

The following studies were performed: 1) specimen collection (including anticoagulant studies, segment vs. tubes and matched serum and plasma evaluation), 2) specimen handling (including off the blood cell, on the blood cell and on the clot storage conditions, heat inactivation, microbial contamination and specimen freeze-thaw effects), 3) effects of potentially interfering substances (including triglycerides, bilirubin, hemoglobin, protein and red blood cells), 4) assay detectability studies (including end point serial dilution sensitivity and fresh serum vs. plasma specimens) and 5) reagent studies (including microbial challenge of kit components, cysteine concentration guardband comparison, ABBOTT PRISM Positive Control analyte cross-reactivity and evaluation of within-run variability and validation of batch size).

1. Specimen Collection

Results of in-house studies showed that the following specimen collection containers and anticoagulants are suitable for use in the ABBOTT PRISM HBcore assay: serum, serum separator tubes, segmented tubing, EDTA, sodium citrate, CPD, CPDA-1, CP2D, potassium oxalate, sodium heparin, ACD-A, ACD-B and lithium heparin. Since the ABBOTT PRISM System pipettes samples simultaneously for all assays and due to the anticoagulant testing limitations of the ABBOTT PRISM HCV assay, the ABBOTT PRISM HBcore package insert states: "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."

No qualitative differences in results were observed between the serum control specimens and those collected in sodium citrate plasma tubes or those obtained from segmented tubing of sodium citrate plasma units.

No qualitative differences in results were observed between matched donor serum and EDTA plasma specimens.

2. Specimen Handling

The results of in-house studies showed no significant differences when using anti-HBc nonreactive or reactive specimens that have been stored on and off the red blood cells/clot for up to 21 days at 2 to 8°C. However, as a precautionary measure, the package insert states: "Specimens may be stored for up to 14 days at 2 - 8°C."

Results from heat inactivation studies indicated that anti-HBc nonreactive and reactive serum or plasma specimens showed no qualitative differences in results after heat treatment. However, as a precautionary measure, the package insert states "Do not use heat-inactivated specimens."

Studies were conducted to evaluate the effect of microbial contamination of specimens on assay performance in ABBOTT PRISM HBcore. These studies showed that no significant assay performance differences were observed when anti-HBc nonreactive and reactive specimens were inoculated with elevated levels of *B. subtilis*, *C. albicans, A. niger, E. coli, P. aeruginosa,* and *S. aureus,* and *P. aeruginosa* (environmental isolate). However, as a precautionary measure, the package insert states: "Do not use specimens with obvious microbial contamination."

Results from the freeze-thaw studies showed that specimens could be frozen and thawed up to six times with no qualitative performance differences. However, as a precautionary measure, the package insert states: "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."

3. Potentially Interfering Substances

No qualitative performance differences were observed for the ABBOTT PRISM HBcore assay in controlled studies using anti-HBc nonreactive and reactive specimens when testing the following potentially interfering substances at the specified levels: triglycerides (≤ 3,000 mg/dL), bilirubin (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), protein (≤ 12 g/dL), and red blood cells (≤ 0.4% v/v).

4. Detectability Studies

Endpoint serial dilution studies were performed on 48 IgM anti-HBc and eight total HBc (IgG anti-HBc) positive specimens serially diluted in recalcified human plasma nonreactive for anti-HBc. ABBOTT PRISM HBcore provided better endpoint serial dilution sensitivity vs. an FDA licensed assay for six of the 48 IgM anti-HBc specimens tested. An FDA licensed assay provided better endpoint serial dilution sensitivity than ABBOTT PRISM HBcore for one of the 48 IgM anti-HBc specimens tested.

Equivalent endpoint serial dilution sensitivity was obtained with 41 of the 48 IgM anti-HBc specimens tested by both ABBOTT PRISM HBcore and an FDA licensed assay. An FDA licensed assay provided better endpoint serial dilution sensitivity than ABBOTT PRISM HBcore for one of the eight IgG anti-HBc specimens tested. Equivalent endpoint serial dilution sensitivity was obtained with seven of the eight IgG anti-HBc specimens tested by both ABBOTT PRISM HBcore and an FDA licensed assay.

In order to evaluate whether the ABBOTT PRISM HBcore assay is susceptible to the fresh serum effects observed in some assays, freshly collected serum and EDTA plasma specimens were spiked with anti-HBc reactive plasma and analyzed over seven days at various temperatures. There were no significant differences observed between the fresh vs. stored serum, or between fresh serum vs. plasma specimens.

5. Reagent Studies

The data presented on the microbial challenge of kit components indicate that the preservatives used in the ABBOTT PRISM HBcore assay (sodium azide and ProClin) are effective in preventing microbial growth of *B. subtilis*, *C. albicans, A. niger, E. coli, P. aeruginosa* and *S. aureus* and *P. aeruginosa* (environmental isolate).

In the cysteine concentration guardband comparison, samples containing purified IgM anti-HBc were tested using three lots of ABBOTT PRISM HBcore (at nominal and upper guardband cysteine concentrations) and two lots of an FDA licensed assay. The ABBOTT PRISM HBcore assay demonstrated significantly improved IgM and anti-HBc sensitivity with detection of samples at a minimum concentration range of 10 to 40 IgM anti-HBc Units/mL compared to 40 to greater than 100 IgM anti-HBc Units/mL for an FDA licensed assay.

A study was performed to demonstrate the absence of cross reactivity between analytes (HBsAg, anti-HCV, anti-HIV-1, anti-HTLV-I, and anti-HBc) used in the multiconstituent ABBOTT PRISM Positive Control. No significant differences were observed between single analyte and multi-analyte solutions indicating that a reactive result with each of the five ABBOTT PRISM assays is due to the corresponding assay specific analyte.

No significant within-run variability in the S/CO of the ABBOTT PRISM Positive Run Control was observed during in-house investigations. There is minimal variation in the ABBOTT PRISM Positive Run Control S/CO with time over the duration of an 8.5-hour ABBOTT PRISM batch.

B. Summary of Clinical Studies

1. Assay Reproducibility

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

2. 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 II). Two sites tested a total of 8,234 serum specimens with initial and repeat reactive rates of 0.50% (41/8,234) and 0.45% (37/8,234), respectively. Two sites tested a total of 8,144 plasma specimens with initial and repeat reactive rates of 0.58% (47/8,144). There were a total of 84 repeatedly reactive donor specimens. Based on additional testing, 65 specimens were positive (Table III) and 19 specimens were indeterminate.

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

One site evaluated 318 serum or plasma specimens collected from 318 individuals with medical conditions unrelated to HBV infection or containing potentially interfering substances (Table II). Seventy-two of the 318 specimens (22.64%) were initially and repeatedly reactive. Sixty-four of the 72 specimens (88.89%) were positive by additional testing.

Eight of the remaining 254 specimens were indeterminate by additional testing. The eight specimens included one anti-HCV positive (12 tested), one anti-HIV-1 positive (12 tested), one anti-HIV-2 positive (5 tested), one anti-nuclear antibody positive (12 tested), two influenza vaccine recipients (52 tested) and two patients with non-viral liver diseases (43 tested). The estimated specificity in this population was 96.85% (246/254) and was lower than that observed in the low risk volunteer whole blood donor population (99.88%).

3. Assay Sensitivity

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

4. Assay Analytical Sensitivity

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

VI. Package Insert

A copy of the ABBOTT PRISM HBcore package insert (directions for use) is attached.

TABLE I

ABBOTT PRISM HBcore 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	319[b]	0.24	0.010	4.0	0.012	4.7
2	320	0.50	0.018	3.7	0.020	3.9
3	320	1.15	0.039	3.4	0.039	3.4
4	319[c]	1.66	0.049	3.0	0.056	3.4
Negative Control	320	1.64	0.050	3.1	0.055	3.3
Positive Control	320	0.53	0.024	4.5	0.034	6.5

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

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

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

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

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

TABLE II

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

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

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

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

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

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

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

TABLE III

PRISM HBcore Positives by Additional Testing[a]

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

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

[b] Two specimens considered gray-zone reactive by the criteria of the assay.

TABLE IV

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

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

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

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

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

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