

Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name: Antibody to Hepatitis B Virus Core Antigen (anti-HBc)

Device Trade Name: AxSYM CORE™ 2.0

AxSYM CORE 2.0 Controls

Name and Address of Applicant: Abbott Laboratories
Abbott Diagnostics Division
100 Abbott Park Road
Abbott Park, IL 60064-6092

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P060012

Date of Notice of Approval to the Applicant: September 6, 2006

II. Indications for Use

AxSYM CORE 2.0 Reagent Kit

AxSYM CORE 2.0 is a microparticle enzyme immunoassay (MEIA) intended for the qualitative detection of total antibodies (IgG and IgM) to hepatitis B virus core antigen (anti-HBc) in adult and pediatric serum (including serum collected in serum separator tubes) or plasma (collected in potassium EDTA, sodium citrate, sodium heparin, lithium heparin, or plasma separator tubes containing lithium heparin). The assay is used as an aid in the diagnosis of acute, chronic, or resolved hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information.

AxSYM CORE 2.0 Controls

The AxSYM CORE 2.0 Controls are used for monitoring the performance of the AxSYM System (reagent and instrument) when used for the qualitative detection of total antibodies to hepatitis B virus core antigen (anti-HBc) when using the AxSYM CORE 2.0 Reagent Kit. The performance of the AxSYM CORE 2.0 Controls has not been established with any other anti-HBc assays.

III. Contraindications

None known.

IV. Warnings and Precautions

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AxSYM CORE 2.0 is for in vitro diagnostic use only. Warnings and precautions for the AxSYM CORE 2.0 Reagent Kit and Controls are stated in the respective product labeling.

V. Device Description

Kit Configuration and Components

AxSYM CORE 2.0 Reagent Kit

The AxSYM CORE 2.0 Reagent Kit contains one AxSYM CORE 2.0 Reagent Pack and one bottle of Index Calibrator. The AxSYM CORE 2.0 Reagent Pack holds the following three reagents:

- 1 Bottle (3.7 mL) Specimen Diluent. Dithiothreitol in acetate buffer. Minimum concentration: 70 mM. (Reagent Bottle 1)
- 1 Bottle (4.0 mL) Hepatitis B Virus Core Antigen (*E. coli*, Recombinant) Coated Microparticles in TRIS buffer with protein (0.94% bovine) stabilizer. Minimum concentration: 0.03% solids. Preservative: 0.1% Sodium Azide. (Reagent Bottle 2)
- 1 Bottle (11.5 mL) Antibody to Hepatitis B Virus Core Antigen (Human): Alkaline Phosphatase Conjugate in TRIS buffer with protein (0.94% bovine) stabilizer. Minimum concentration: 0.2 µg/mL. Preservatives: 0.1% Sodium Azide and Antimicrobial Agents. (Reagent Bottle 3)

The Index Calibrator is used to determine the cutoff rate of the AxSYM CORE 2.0 assay and contains the following:

- 1 Bottle (8 mL) AxSYM CORE 2.0 Index Calibrator prepared in recalcified human plasma nonreactive for anti-HBc, anti-HBs, HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV. Preservative: 0.1% Sodium Azide. Dye: Green (Acid Yellow No. 23 and Acid Blue No. 9).

AxSYM CORE 2.0 Controls

The AxSYM CORE 2.0 Controls contain the following:

- 1 Bottle (9 mL) Negative Control prepared in recalcified human plasma nonreactive for anti-HBc, anti-HBs, HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV. Preservative: 0.1% Sodium Azide.
- 1 Bottle (9 mL) Positive Control prepared in recalcified human plasma reactive for anti-HBc and anti-HBs, and nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV. Preservatives: 0.1% Sodium Azide and Antimicrobial Agent.

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Other Required Components

In addition, the following are required:

- The AxSYM System is an automated immunoassay analyzer designed for the performance of routine immunoassays and analyte determinations via random access, continuous access, and STAT test processing. The analyzer performs sample and reagent transfers, incubations, optical readings, data processing, and printing of assay reports and screen displays.
- AxSYM Probe Cleaning Solution containing 2% Tetraethylammonium Hydroxide (TEAH).
- Solution 1 (MUP) containing 4-Methylumbelliferyl Phosphate, 1.2 mM, in AMP buffer. Preservative: 0.1% Sodium Azide.
- Solution 3 (Matrix Cell Wash) containing 0.3 M Sodium Chloride in TRIS buffer. Preservatives: 0.1% Sodium Azide and Antimicrobial Agents.
- Solution 4 (Line Diluent) containing 0.1 M Phosphate buffer. Preservatives: 0.1% Sodium Azide and Antimicrobial Agent.

Biological Principles of the Procedure

AxSYM CORE 2.0 is based on MEIA technology and utilizes the principle of two-step competitive/blocking. Anti-HBc in the sample blocks the binding of the anti-HBc (human): alkaline phosphatase conjugate to the rHBcAg coated on the microparticles, and the Specimen Diluent, which contains a reducing agent (dithiothreitol), minimizes nonspecific reactivity. The Matrix Cell is washed with Matrix Cell Wash to remove materials not bound to the microparticles. The substrate (MUP) is added and the fluorescent product is measured by the MEIA optical assembly on the AxSYM System.

The presence or absence of anti-HBc in the sample is determined by comparing the rate of formation of fluorescent product (S) to the cutoff rate (CO), which is calculated from a previous AxSYM CORE 2.0 Index Calibration. Samples with S/CO values of 0.001 to 0.800 are considered reactive by AxSYM CORE 2.0. Samples with S/CO values of 1.200 to 3.000 are considered nonreactive by AxSYM CORE 2.0. Samples with S/CO values of 0.801 to 1.199 are considered gray zone by AxSYM CORE 2.0 and should be retested in duplicate. Samples with S/CO values greater than 3.000 are considered invalid by AxSYM CORE 2.0 and should be retested once using a single sample.

VI. Alternative Practices and Procedures

The patient's medical history and thorough physical examination, including hepatitis serology, determination of liver enzyme levels, and biopsy of the liver, will provide further information on the status of a hepatitis B viral infection.

Alternative procedures for the detection of HBV in human serum and plasma depend on the detection of HBV deoxyribonucleic acid (DNA) by research polymerase chain

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reaction (PCR) assays or nucleic acid testing (NAT), or the detection of HBV antigens and antibodies by commercially-available assays that are licensed or approved in the United States.

VII. Marketing History

This product, AxSYM CORE 2.0 (List No. 8B88), has not been marketed in any other country.

VIII. Potential Adverse Effects of the Device on Health

The main risk involved in the use of the AxSYM CORE 2.0 assay is one associated with any available anti-HBc immunoassay: A nonreactive test result does not exclude the possibility of exposure to or infection with HBV. Levels of anti-HBc may be undetectable in both the early and late stages of infection. For diagnostic purposes, anti-HBc reactivity should be correlated with the overall clinical picture, including the presence or absence of other hepatitis markers.

Other than the circumstances mentioned above, there is no known potential adverse effect on the health of the patient or user if this *in vitro* device is used according to the AxSYM CORE 2.0 package insert instructions.

IX. Summary of the Nonclinical Laboratory Studies

Nonclinical laboratory studies were performed at Abbott Laboratories to evaluate the performance characteristics of the AxSYM CORE 2.0 assay. The studies are summarized below.

Cutoff Rationale

The AxSYM CORE 2.0 assay utilizes a competitive test format. In this type of format, the theoretical cutoff rate is at the midpoint (50% inhibition) between the high signal rate found for negative samples and the low signal rate found for strongly positive samples¹. For an assay in which the rate of a strongly positive sample is considered negligible compared to the rate of a negative sample, or in this case the AxSYM CORE 2.0 Index Calibrator (which contains recalcified human plasma nonreactive for anti-HBc), the cutoff rate at 50% inhibition can be calculated as the Index Calibrator rate divided by 2:

$$\text{Cutoff Rate} = \text{Index Calibrator Mean Rate}/2$$

At the theoretical cutoff rate, the slope of the line from a plot of the log of concentration versus the signal is greatest and maximizes the discrimination between the negative samples and the strongly positive samples. The Seroconversion Detectability study demonstrates that acceptable assay performance is achieved using the theoretical cutoff rate calculation for the AxSYM CORE 2.0 assay.

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The gray zone for AxSYM CORE 2.0 is set at 0.801 to 1.199 S/CO, which is a range approximately equal to $\pm 20\%$ from the cutoff value of 1.00 S/CO. The $\pm 20\%$ range is based on guidance from the Clinical Laboratory Standards Institute (formerly NCCLS) document EP12-A². The appropriateness of the selected gray zone range was evaluated by calculating the 95% confidence interval around the cutoff using the results for Precision Panel Member 1 (0.8 S/CO target) from the 20-day Precision Study to represent worst-case variability near the assay cutoff. The calculated 95% confidence interval around the cutoff was 0.827 to 1.173 S/CO. This falls within 0.801 to 1.199 S/CO; therefore, the selected gray zone range is appropriate for AxSYM CORE 2.0.

Sample Types (Serum and Plasma)

A study was conducted to evaluate which specimen collection tube types are acceptable for use with the AxSYM CORE 2.0 assay. Sets of specimens assumed to be nonreactive for anti-HBc were collected in the control specimen collection tube type (serum in glass) and the specimen collection tube types selected for evaluation. The specimens were spiked with human plasma positive for anti-HBc to prepare high nonreactive samples (1.2 S/CO target) and low reactive samples (0.8 S/CO target), and all samples were tested.

On average, the tube types evaluated showed less than 11% difference when compared to the control tube type (serum in glass). The distribution of the per cent difference values for each tube type is summarized in Table 1.

The data support the use of the AxSYM CORE 2.0 assay with serum specimens, specimens collected in serum separator tubes (SST[®]) or plasma separator tubes (PST) containing lithium heparin, and specimens collected in tubes containing the following anticoagulants:

- potassium ethylenediaminetetraacetic acid (EDTA)
- sodium citrate
- sodium heparin
- lithium heparin

Table 1
AxSYM CORE 2.0
Sample Types (Serum and Plasma) Study
Summary of Results

Evaluation Tube Type	Distribution of %Differences		
	0% to ≤ 10%	> 10% to ≤ 20%	> 20%
Serum in plastic	85.4% (35/41)	14.6% (6/41)	0.0% (0/41)
SST in glass	92.7% (38/41)	7.3% (3/41)	0.0% (0/41)
SST in plastic	90.2% (37/41)	9.8% (4/41)	0.0% (0/41)
PST	87.8% (36/41)	12.2% (5/41)	0.0% (0/41)
Sodium Citrate	80.5% (33/41)	17.1% (7/41)	2.4% (1/41)
Potassium EDTA	70.7% (29/41)	29.3% (12/41)	0.0% (0/41)
Sodium Heparin	90.2% (37/41)	4.9% (2/41)	4.9% (2/41)
Lithium Heparin	92.7% (38/41)	7.3% (3/41)	0.0% (0/41)

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Dilutional Effects of Liquid Anticoagulants

A study was conducted to evaluate the performance of the AxSYM CORE 2.0 assay when used to test specimens collected in tubes containing liquid anticoagulants that have the potential to cause a dilutional effect compared to specimens collected in serum tubes.

Human serum nonreactive for anti-HBc was spiked with human plasma positive for anti-HBc to prepare high nonreactive samples (1.2 S/CO target) and low reactive samples (0.8 S/CO target). The spiked samples were added to the specimen collection tube types selected for evaluation (potassium EDTA and sodium citrate) and the samples were tested.

No adverse dilutional effect on the performance of the AxSYM CORE 2.0 assay was observed when using collection tubes containing liquid anticoagulants.

Sample Storage Conditions

A study was conducted to evaluate the performance of the AxSYM CORE 2.0 assay when used to test specimens that have been stored for a period of time at 2 to 8°C or 20 to 22°C (room temperature) compared to specimens tested within two hours after draw. Testing was performed using specimens before removal from the red blood cells (i.e., “on the cells”). The results were used to support storage conditions for specimens after removal from the red blood cells (i.e., “off the cells”).

Sets of specimens were collected in all recommended specimen collection tube types (serum; and potassium EDTA, sodium citrate, sodium heparin, or lithium heparin plasma). Tubes from each set were spiked with human plasma positive for anti-HBc to prepare high nonreactive samples (1.2 S/CO target). The samples were tested on Day 0 (within two hours of draw), on Days 2 and 7 after being stored at 2 to 8°C, and on Days 1 and 3 after being stored at 20 to 22°C.

The data support the use of the AxSYM CORE 2.0 assay with specimens collected in all recommended collection tubes that have been stored at 2 to 8°C for up to seven days or at 20 to 22°C (room temperature) for up to three days prior to being tested, however, the following sample storage recommendations are included in the package insert:

- Store samples at 22°C (72°F) for no longer than 8 hours.
- If the assay will not be completed within 8 hours, refrigerate the sample at 2 to 8°C (36 to 46°F).
- If the assay will not be completed within 48 hours, freeze at or below –20°C (–4°F).

Sample Freeze/Thaw

A study was conducted to evaluate the performance of the AxSYM CORE 2.0 assay when used to test specimens that have undergone multiple freeze/thaw cycles.

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Sets of specimens from individuals assumed to be nonreactive for anti-HBc were collected in all recommended specimen collection tube types (serum, and potassium EDTA, sodium citrate, sodium heparin, or lithium heparin plasma). Tubes from each set were spiked with human plasma positive for anti-HBc to prepare high nonreactive samples (1.2 S/CO target) and low reactive samples (0.8 S/CO target). The samples were tested on Day 0 (within eight hours of draw) and after being subjected to one, two, or three freeze/thaw cycles.

The data presented support the use of the AxSYM CORE 2.0 assay with specimens collected in all recommended collection tubes that have undergone up to three freeze/thaw cycles.

Analytical Specificity

A study was conducted to characterize the performance of the AxSYM CORE 2.0 assay when used to test specimens from individuals with medical conditions unrelated to HBV infection.

Of the 181 specimens, 133 (73.5%) were nonreactive, 3 (1.7%) were gray zone, and 45 (24.9%) were reactive by AxSYM CORE 2.0. Of the three gray zone specimens, one specimen (from an individual with obstructive jaundice) was negative by an FDA-licensed anti-HBc assay and two specimens (from individuals with antibody to hepatitis A virus) were reactive. Of the 45 reactive specimens, 42 were repeatedly reactive by the FDA-licensed anti-HBc assay, and three specimens (from individuals with rheumatoid arthritis disease) were negative. The results are summarized in Table 2.

Table 2
AxSYM CORE 2.0
Analytical Specificity Study: Specimens from Individuals with Medical Conditions Unrelated to HBV Infection
Summary of Results

Category ^a	Number of Specimens Tested	AxSYM CORE 2.0		
		Nonreactive	Gray Zone	Reactive ^b
Hepatitis A Virus	8	3	2	3
Hepatitis C Virus	10	5	0	5
Human Immunodeficiency Virus	10	4	0	6
Human T-Lymphotropic Virus	9	1	0	8
Cytomegalovirus	10	6	0	4
Epstein-Barr Virus	10	6	0	4
Herpes Simplex Virus	10	8	0	2
Rubella	10	10	0	0
Systemic Lupus Erythematosus	10	9	0	1
Rheumatoid Arthritis Disease	10	5	0	5
Elevated IgG	10	10	0	0
Elevated IgM	10	10	0	0
Influenza Vaccine Recipients	10	9	0	1
HBV Vaccine Recipients	5	5	0	0
Toxoplasmosis	4	3	0	1
Alcoholic Liver Disease	10	10	0	0
Fatty Liver Disease	15	14	0	1
Obstructive Jaundice	15	13	1 ^c	1
Hepatocellular Carcinoma	5	2	0	3
Total (%)	181	133/181 (73.5%)	3/181 (1.7%)	45/181 (24.9%)

NT = Not Tested

^a Information about age and gender of the individuals is not available.

^b With the exception of three Rheumatoid Arthritis Disease specimens, all specimens reactive by AxSYM CORE 2.0 were repeatedly reactive by an FDA-licensed anti-HBc assay.

^c Specimen could not be retested due to insufficient volume. The specimen was negative by an FDA-licensed anti-HBc assay.

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Potentially Interfering Substances – Triglycerides, Total Protein, Bilirubin, and Hemoglobin

Studies were conducted to evaluate the performance of the AxSYM CORE 2.0 assay when used to test specimens containing high levels of triglycerides, total protein, total bilirubin, and hemoglobin.

Human serum nonreactive for anti-HBc was spiked with human plasma positive for anti-HBc to prepare high nonreactive samples (1.2 S/CO target) and low reactive samples (0.8 S/CO target). A triglyceride test sample was prepared by supplementing the high nonreactive and low reactive samples with LIPOSYN® II to a minimum triglyceride concentration of 3,000 mg/dL. A total protein test sample was prepared by supplementing the high nonreactive and low reactive samples with human albumin powder to a minimum concentration of 12 g/dL. A bilirubin (unconjugated) test sample was prepared by supplementing the high nonreactive and low reactive samples with unconjugated bilirubin stock prepared in 0.1 N sodium hydroxide to a minimum concentration of 20 mg/dL. A hemoglobin test sample was prepared by supplementing the high nonreactive and low reactive samples with hemoglobin stock solution to a minimum concentration of 500 mg/dL. Control samples were prepared for each interferent. The controls and samples were tested.

The data support the use of the AxSYM CORE 2.0 assay with specimens that contain up to 3,000 mg/dL of triglycerides, up to 12 g/dL of total protein, up to 20 mg/dL of bilirubin (unconjugated), and up to 500 mg/dL of hemoglobin.

Within- and Between-assay Sample Carryover

Studies were conducted to evaluate the susceptibility of the AxSYM CORE 2.0 assay to sample carryover within the assay or from other AxSYM assays when processing samples containing high concentrations of anti-HBc.

Carryover events were modeled by testing human plasma nonreactive for anti-HBc to mimic a sample that was not exposed to potential sample carryover (protected negative), followed by a human plasma sample containing a high concentration of anti-HBc, followed again by human plasma nonreactive for anti-HBc to mimic a sample exposed to potential sample carryover (unprotected negative).

For the within-assay carryover study, the difference between the protected negative and unprotected negative mean S/CO values was -0.031 , indicating that no within-assay sample carryover was present within the AxSYM CORE 2.0 assay.

For the between-assay carryover study, the difference between the protected negative and unprotected negative mean or median S/CO values ranged from -0.135 to 0.049 in the Sampling Center, and the difference between the protected negative and unprotected negative mean or median S/CO values ranged from -0.099 to 0.183 in the Processing Center. These results indicate that no between-assay sample carryover was present

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between the AxSYM CORE 2.0 assay and any of the potential contaminator assays evaluated.

Seroconversion Detectability

A study was conducted to demonstrate the ability of the AxSYM CORE 2.0 assay to detect anti-HBc in serial bleed specimens from HBV-infected individuals. Six seroconversion panels (a total of 141 serial bleed specimens) from six HBV-infected individuals were obtained from three commercial vendors and tested.

The AxSYM CORE 2.0 results were compared to the assay results supplied by the vendor or generated by Abbott Laboratories using FDA-licensed HBsAg and anti-HBc assays.

Four of the six seroconversion panels demonstrated a change from HBsAg reactive to HBsAg nonreactive. In these four panels, anti-HBc was detected by AxSYM CORE 2.0 concurrent with HBsAg reactivity by an FDA-licensed HBsAg assay, or at a minimum, at the serial bleed following the last serial bleed reported as reactive by the FDA-licensed HBsAg assay. The remaining two seroconversion panels became HBsAg reactive and remained HBsAg reactive for all subsequent serial bleeds. In these two panels, anti-HBc was detected by AxSYM CORE 2.0 concurrent with HBsAg reactivity by the FDA-licensed HBsAg assay.

Anti-HBc was detected by AxSYM CORE 2.0 two days earlier than detection by the FDA-licensed anti-HBc assay in one seroconversion panel, coincident with detection by the FDA-licensed anti-HBc assay in four seroconversion panels, and three days later than detection by the FDA-licensed anti-HBc in one seroconversion panel.

These data demonstrate the ability of the AxSYM CORE 2.0 assay to detect anti-HBc in serial bleed specimens from HBV-infected individuals.

Within-Laboratory (20-day) Precision

A 20-day precision study was conducted based on guidance from Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS) document EP5-A2³ to evaluate the precision performance of the AxSYM CORE 2.0 assay.

Testing was performed using two AxSYM CORE 2.0 Reagent Kit lots and one AxSYM CORE 2.0 Control lot on each of two AxSYM instruments. Testing included two precision runs per day for each reagent kit lot, on each instrument, on each of 20 days. Each precision run included two replicates of the AxSYM CORE 2.0 Index Calibrator (IC), Negative Control (NC), and Positive Control (PC), and each of two members of a precision panel with S/CO values targeted to 0.8 and 1.2. Panel members were prepared by adding anti-HBc positive plasma to anti-HBc negative serum.

The data demonstrated the acceptable precision of the AxSYM CORE 2.0 assay. The results are summarized in Tables 3 and 4.

Table 3
AxSYM CORE 2.0
Within-Laboratory (20-day) Precision Study
Overall Precision—Two Instruments, Two Reagent Lots

Panel Members/ Controls	Total No. Reps	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)			Precision With Additional Component of Between-Lot		Precision With Additional Component of Between- Instrument	
			SD	%CV	SD	%CV	SD	%CV	%CV CL	SD	%CV	SD	%CV
Panel 1	320	0.783	0.0219	2.8	0.0283	3.6	0.0324	4.1	4.5	0.1477	18.9	0.0534	6.8
Panel 2	320	1.216	0.0365	3.0	0.0400	3.3	0.0503	4.1	4.5	0.1520	12.5	0.0881	7.2
NC	320	1.873	0.0556	3.0	0.0611	3.3	0.0714	3.8	4.1	0.1177	6.3	0.1311	7.0
PC	320	0.326	0.0120	3.7	0.0137	4.2	0.0159	4.9	5.3	0.0469	14.4	0.0248	7.6

Index Calibrator	Total No. Reps	Grand Mean Rate	Within-Run		Within-Day		Within-Laboratory Precision (Total)			Precision With Additional Component of Between-Lot		Precision With Additional Component of Between- Instrument	
			SD	%CV	SD	%CV	SD	%CV	%CV CL	SD	%CV	SD	%CV
IC	320	827.51	24.399	2.9	25.220	3.0	30.265	3.7	4.0	35.167	4.2	57.668	7.0

Reps = Replicates, SD = Standard Deviation, CV = Coefficient of Variation, CL = Upper One-sided 95% Confidence Limit

Table 4
AxSYM CORE 2.0
Within-Laboratory (20-day) Precision Study
Individual Component Analysis—Two Instruments, Two Reagent Lots

Panel Members/ Controls	Total No. Reps	Grand Mean S/CO	Within-Run		Between-Run		Between-Day		Between-Lot		Between- Instrument		Total ^a	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Panel 1	320	0.783	0.0219	2.8	0.0179	2.3	0.0159	2.0	0.1441	18.4	0.0424	5.4	0.0324	4.1
Panel 2	320	1.216	0.0365	3.0	0.0165	1.4	0.0305	2.5	0.1434	11.8	0.0723	5.9	0.0503	4.1
NC	320	1.873	0.0556	3.0	0.0252	1.3	0.0370	2.0	0.0936	5.0	0.1099	5.9	0.0714	3.8
PC	320	0.326	0.0120	3.7	0.0066	2.0	0.0080	2.4	0.0442	13.6	0.0191	5.9	0.0159	4.9

Index Calibrator	Total No. Reps	Grand Mean Rate	Within-Run		Between-Run		Between-Day		Between-Lot		Between- Instrument		Total ^a	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
IC	320	827.51	24.399	2.9	6.381	0.8	16.732	2.0	17.908	2.2	49.087	5.9	30.2655	3.7

^a Total variability contains within-run, between-run, and between-day variance components.

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Control Justification

A study was conducted to evaluate whether the plasma-based AxSYM CORE 2.0 Controls are predictive of the performance of both serum and plasma specimens throughout the shelf life of the AxSYM CORE 2.0 Reagent Kit or after inappropriate handling of the reagent kit.

AxSYM CORE 2.0 Kits were stored at the recommended storage condition of 2 to 8°C (untreated). Additional reagent kits were stored for 2 to 4 hours at 56 to 60°C (heat-treated). The reagents were heat-treated to simulate reagents that have been compromised due to storage past expiration or inappropriate handling.

Sets of specimens were collected in all recommended specimen collection tube types (serum, and potassium EDTA, sodium citrate, sodium heparin or lithium heparin plasma) from five donors assumed to be nonreactive for anti-HBc. A portion of each sample was spiked with human plasma positive for anti-HBc to a target S/CO value equivalent to the Positive Control. A portion of each sample remained unspiked to represent a nonreactive sample. Unspiked and spiked samples and the AxSYM CORE 2.0 Negative Control (NC) and Positive Control (PC) were tested using both untreated and heat-treated AxSYM CORE 2.0 Reagent Kits.

For the unspiked samples, all individual donor replicate results were greater than or equal to 1.200 S/CO for the untreated reagent kit and less than 1.500 S/CO for the heat-treated reagent kit. The negative control replicate result for the heat-treated reagent kit was also less than 1.500 S/CO. For the spiked samples, all individual donor replicate results were 0.005 to 0.800 S/CO for the untreated reagent kit and less than or equal to 0.800 S/CO for the heat-treated reagent kit. The positive control replicate result for the heat-treated reagent kit was also less than 0.800 S/CO.

The data showed that under the conditions tested, AxSYM CORE 2.0 Controls are predictive of the performance of both serum and plasma (potassium EDTA, sodium citrate, sodium heparin or lithium heparin) specimens throughout the shelf life of the AxSYM CORE 2.0 Reagent Kit or after inappropriate handling of the reagent kit. However, it is suggested in the labeling that the Controls provided are in serum (recalcified plasma) and the user should provide alternate control material for plasma when necessary.

Justification for Use of Specimens Subjected to Long-term Frozen Storage

The stability of anti-HBc was evaluated by comparing historical test results to recently generated test results for anti-HBc positive specimens subjected to long-term frozen storage.

A commercially-available HBV seroconversion panel was used for this study. The 25-member panel was drawn from a paid plasmapheresis donor over a nine-month period (December 1993 to August 1994). Aliquots had been stored frozen since collection. The

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historical results from an FDA-licensed anti-HBc assay were generated by Abbott Laboratories in January 1997. Testing was performed again in February 2006 by Abbott Laboratories. The results of the January 1997 and February 2006 testing were compared. The time points spanned a period of over nine years of frozen storage.

There was no change in detection of anti-HBc between the two time points, thereby demonstrating the stability of anti-HBc in specimens subjected to long-term frozen storage.

High Dose Hook Effect

A study was conducted to characterize the performance of the AxSYM CORE 2.0 assay when used to test a high-titer anti-HBc specimen that may have the potential to cause a high dose hook effect.

Recalcified human plasma reactive for anti-HBc (titer > 1:65,536) was serially diluted with recalcified human plasma nonreactive for anti-HBc and tested. Results were as expected; the neat sample was reactive (mean S/CO 0.039), and S/CO values increased (trended towards negative) as the samples became more dilute. This indicates that no high dose hook effect occurred in this study.

Microbial Challenge

Studies were conducted to establish the level of antimicrobial protection provided by the preservative system used in the components of the AxSYM CORE 2.0 Reagent Kit (including Index Calibrator) and Controls, and to determine the effect of bioburden and/or its by-products on assay performance.

Components of the AxSYM CORE 2.0 Reagent Kit and Controls were inoculated with the following groups of microorganisms at concentrations between 10^5 to 10^6 colony forming units/mL (CFU/mL): Spore (*Bacillus subtilis*, *Candida albicans*), Mold (*Aspergillus niger*), vegetative (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*), and environmental (*Pseudomonas* [fluorescent group]). In addition, components were also inoculated with *Aspergillus niger* at 10^2 to 10^3 CFU/mL. The inoculated materials were evaluated for microbial growth over a period of 15 months.

Components of the AxSYM CORE 2.0 Reagent Kit and Controls were inoculated with the following microorganisms at concentrations between 10^2 to 10^3 CFU/mL and at concentrations between 10^3 to 10^4 CFU/mL: *Candida albicans*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Pseudomonas* (fluorescent group). The inoculated materials were evaluated for assay performance after a period of 35 days.

No growth of the challenge organisms was observed during the study, with the exception of the microparticles inoculated with the vegetative group, which demonstrated growth between Month 6 and Month 9. However, the bioburden count at Month 9 and for subsequent time points (Months 12 and 15) was below the bioburden count observed at Day 0 by more than one log. Assay performance of the inoculated components was

Summary of Safety and Effectiveness Data

acceptable. The data demonstrate that the AxSYM CORE 2.0 Reagent Kit and Controls are adequately protected by the preservative system used.

Recommended Storage Stability – AxSYM CORE 2.0 Reagent Kit and Controls

Real-time stability studies are being conducted to demonstrate the shelf-life integrity of the AxSYM CORE 2.0 Reagent Kit and Controls at the recommended storage condition (2 to 8°C).

Three lots of AxSYM CORE 2.0 Reagent Kits and Controls were stored at the recommended storage condition of 2 to 8°C. The AxSYM CORE 2.0 Reagent Kits and Controls were tested at Month 0 and monthly thereafter. The stability studies are ongoing and are scheduled to continue for a maximum of 20 months (minimum of seven months). At this time, the data for the first seven months of testing is complete.

The data presented demonstrate that the evaluation criteria were met for both the AxSYM CORE 2.0 Reagent Kits and Controls at the recommended storage condition (2 to 8°C) for seven months.

Transport Simulation – AxSYM CORE 2.0 Reagent Kit and Controls

A study was conducted to evaluate the performance of the AxSYM CORE 2.0 Reagent Kit and Controls following a simulation of ambient shipping conditions (transport simulation).

One lot each of the AxSYM CORE 2.0 Reagent Kit and Controls was tested after being subjected to a series of storage temperatures simulating transport stress.

The data support ambient shipment of the AxSYM CORE 2.0 Reagent Kit and Controls.

Onboard Reagent Pack Stability

A study was conducted to determine how long the AxSYM CORE 2.0 Reagent Pack can be stored on board the AxSYM System.

Testing was performed using three lots of AxSYM CORE 2.0 Reagent Packs that were stored continuously at 2 to 8°C (recommended storage) and at 31°C (simulated onboard storage) for 24, 48, 72, 96, 120, 144, 168, 192, 216, 264, 312, or 360 hours. The AxSYM CORE 2.0 Index Calibrator was not evaluated for onboard stability because this component is not left on board the AxSYM System.

The data support the storage of the AxSYM CORE 2.0 Reagent Pack on board the AxSYM System for up to 360 hours.

Calibration Stability and Control Frequency

Summary of Safety and Effectiveness Data

An analysis was performed to determine if an AxSYM CORE 2.0 calibration that is stored on the AxSYM System for a minimum of 14 days can be used to generate valid results (calibration stability), and to support a minimum control requirement to test controls once every 24 hours (control frequency).

The validity data generated in the Within-Laboratory (20-day) Precision Study were used for this analysis. The study was conducted using two AxSYM instruments and two AxSYM CORE 2.0 Reagent Kit lots for 20 days. A calibration was performed on the first day of testing for each instrument and reagent kit lot combination. The AxSYM CORE 2.0 Negative Control and Positive Control were each tested for validity purposes, once per run, twice daily, on each of 20 days, using each instrument and reagent kit lot combination.

The data demonstrated that an AxSYM CORE 2.0 calibration may be stored on the AxSYM System and used to generate valid results for a minimum of 14 days. These data also support the testing of controls once every 24 hours.

X. Summary of the Clinical Investigation

A multicenter study was conducted to demonstrate that the AxSYM CORE 2.0 assay performs as intended in a diagnostic population. The study was designed to measure the precision of the AxSYM CORE 2.0 assay and determine the percent agreement between AxSYM CORE 2.0 and an FDA-approved anti-HBc test method.

System Reproducibility (5-day Precision)

The precision of the AxSYM CORE 2.0 assay was evaluated by testing three AxSYM CORE 2.0 Reagent Kit and Control master lots at three clinical testing sites for five days. Testing included two precision runs per day (a minimum of two hours apart) for each of three reagent master lots, on each of five days. Each precision run included four replicates of each precision panel member and four replicates each of AxSYM CORE 2.0 Index Calibrator, Negative Control, and Positive Control. Panel members were prepared by adding anti-HBc positive plasma to anti-HBc negative serum. The analysis method was based on Clinical and Laboratory Standards Institute (formerly NCCLS) document EP15-A2⁴. The results are presented in Tables 5 and 6.

The AxSYM CORE 2.0 assay showed acceptable precision across three reagent master lots and a range of anti-HBc reactivity. In particular, acceptable precision was demonstrated near the assay cutoff.

Table 5

**AxSYM CORE 2.0 System Reproducibility: Overall Precision
Three Reagent Master Lots, Three Clinical Testing Sites**

Panel Members/ Controls	Total No. Reps	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)			Precision With Additional Component of Between-Lot		Precision With Additional Component of Between-Site		Precision With Additional Component of Site and Lot (Overall)	
			SD	%CV	SD	%CV	SD	%CV	CL	SD	%CV	SD	%CV	SD	%CV
Panel 1	360	0.728	0.0282	3.9	0.0378	5.2	0.0386	5.3	5.8	0.1515	20.8	0.0402	5.5	0.1519	20.9
Panel 2	360	1.217	0.0431	3.5	0.0516	4.2	0.0556	4.6	5.0	0.1114	9.2	0.0592	4.9	0.1132	9.3
NC	360	1.918	0.0736	3.8	0.0830	4.3	0.0843	4.4	4.7	0.0849	4.4	0.0887	4.6	0.0887	4.6
PC	360	0.296	0.0138	4.6	0.0170	5.7	0.0185	6.3	6.9	0.0894	30.2	0.0217	7.3	0.0901	30.4

Index Calibrator	Total No. Reps	Grand Mean Rate	Within-Run		Within-Day		Within-Laboratory Precision (Total)			Precision With Additional Component of Between-Lot		Precision With Additional Component of Between-Site		Precision With Additional Component of Site and Lot (Overall)	
			SD	%CV	SD	%CV	SD	%CV	CL	SD	%CV	SD	%CV	SD	%CV
IC	360	818.98	29.914	3.7	32.439	4.0	33.936	4.1	4.5	114.309	14.0	50.637	6.2	119.729	14.6

Reps = Replicates; SD = Standard Deviation; CV = Coefficient of Variation; CL = Upper One-sided 95% Confidence Limit

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Table 6

**AxSYM CORE 2.0 System Reproducibility: Individual Component Analysis
Three Reagent Master Lots, Three Clinical Testing Sites**

Panel Members/ Controls	Total No. Reps	Grand Mean S/CO	Within-Run		Between-Run		Between-Day		Between-Lot		Between-Site		Total ^a	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Panel 1	360	0.73	0.028	3.9	0.025	3.5	0.008	1.1	0.147	20.1	0.011	1.6	0.152	20.9
Panel 2	360	1.22	0.043	3.5	0.028	2.3	0.021	1.7	0.097	7.9	0.020	1.7	0.113	9.3
NC	360	1.92	0.074	3.8	0.038	2.0	0.015	0.8	0.010	0.5	0.028	1.4	0.089	4.6
PC	360	0.30	0.014	4.6	0.010	3.3	0.008	2.5	0.087	29.5	0.011	3.8	0.090	30.4

Index Calibrator	Total No. Reps	Grand Mean S/CO	Within-Run		Between-Run		Between-Day		Between-Lot		Between-Site		Total ^a	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
IC	360	818.98	29.914	3.7	12.548	1.5	9.966	1.2	109.16	13.3	37.582	4.6	119.73	14.6

^a Total variability contains within-run, between-run, between-day, between-lot, between-site, and lot-site interaction variance components.

Summary of Safety and Effectiveness Data

Percent Agreement

The clinical specimens used in the study were obtained from six specimen collection sites and two specimen vendors. A total of 2,132 linked serum specimens were prospectively collected and tested. In addition, 100 specimens from a surplus pediatric population were obtained and tested.

The specimens included the following categories:

Specimens Collected From Individuals Living in the United States (US) (Population 1)

- 1,256 specimens from individuals at increased risk of hepatitis B virus (HBV) infection
- 528 specimens from individuals with signs and symptoms of hepatitis infection
- 49 specimens from individuals diagnosed with acute or chronic HBV infection
- 100 specimens from a pediatric population (This population included specimens from children > 2 to 12 years of age and adolescents > 12 to 19 years of age.)

Specimens Collected From Individuals Living in Vietnam (Population 2)

- 100 specimens from individuals at increased risk of HBV infection
- 199 specimens from individuals with signs and symptoms of hepatitis infection

Three AxSYM CORE 2.0 Reagent Kit and Control master lots were used in the percent agreement evaluation. Three clinical testing sites performed AxSYM CORE 2.0 testing. Specimens were sent to an external reference laboratory for reference anti-HBc assay testing.

A summary of the percent agreement results for all specimen categories is presented in Table 7. The results of the clinical investigation demonstrate that the AxSYM CORE 2.0 assay can be used for the qualitative detection of anti-HBc and, in conjunction with other laboratory results and clinical information, as an aid in the diagnosis of acute, chronic, or resolved HBV infection.

Table 7
Summary of Percent Agreement Between
AxSYM CORE 2.0 and the Reference Anti-HBc Assay

Specimen Category	Number of Specimens Tested	Positive Percent Agreement	Negative Percent Agreement
Individuals at Increased Risk of HBV Infection and Individuals With Signs and Symptoms of Hepatitis Infection (US Population)	1,784	99.31% (289/291)	97.45% (1,455/1,493)
Individuals at Increased Risk of HBV Infection and Individuals With Signs and Symptoms of Hepatitis Infection (Vietnam Population)	299	100.00% (216/216)	65.06% (54/83)
Individuals Diagnosed With Acute or Chronic HBV Infection	49	100.00% (49/49)	NA
Pediatric Population	100	66.67% (2/3)	97.94% (95/97)

NA = Not Applicable

Summary of Safety and Effectiveness Data

The 2,083 specimens from individuals at increased risk of HBV infection and individuals with signs and symptoms of hepatitis infection (Populations 1 and 2) were also sent to an external reference laboratory for HBV reference marker testing by FDA-approved reference assays for the detection of HBsAg, anti-HBc IgM, total anti-HBc, and anti-HBs. These specimens were assigned an HBV classification using the results for the four HBV reference markers and the modification of the serological criteria established by the National Center of Infectious Diseases (CDC) for diagnosing HBV infection.

The number of specimens in each HBV classification category is presented in Tables 8 and 9. A comparison of AxSYM CORE 2.0 results versus the reference anti-HBc assay results by HBV classification category is presented in Tables 10 and 11. The percent agreement between AxSYM CORE 2.0 and the reference anti-HBc assay by HBV classification category is summarized in Tables 12 and 13.

One thousand seven hundred eighty-four specimens were prospectively collected in the United States at specimen collection sites located in Galveston, TX (43.55%); Dallas, TX (5.72%); Miami, FL (3.76%); St. Petersburg, FL (2.69%); Chicago, IL (3.64%); and Denver, CO (5.89%); or were obtained from a specimen vendor at the following three locations: Colton, CA (6.45%); Plymouth, MA (17.99%); and High Point, NC (10.31%) (Population 1). Two hundred ninety-nine specimens were also prospectively collected in Vietnam (Population 2) by a specimen vendor.

Population 1 was 53.76% Caucasian, 28.64% African American, 13.62% Hispanic, 2.07% Asian, and 0.39% American Indian/Alaska Native, with the remaining 1.51% represented by other ethnic groups. The population was 54.88% female and 45.12% male and ranged in age from 18 to 83 years. Testing of these specimens occurred at Clinical Testing Site 1 located in Port Jefferson, NY (43.55%); Clinical Testing Site 2 located in Dallas, TX (38.40%); and Clinical Testing Site 3 located in Raritan, NJ (18.05%).

Population 2 was Vietnamese (100.00%). The population was 53.18% female and 46.82% male and ranged in age from 18 to 68 years. Testing of these specimens occurred at a clinical testing site located in Raritan, NJ.

Table 8

**HBV Classification for Individuals at Increased Risk of HBV Infection and
Individuals With Signs and Symptoms of Hepatitis Infection (Population 1)**

Number of Specimens	HBV Reference Markers				HBV Classification
	HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	
1	+	-	-	-	Early Acute
2	+	+	+	-	Acute
20	+	-	+	-	Chronic
1	+	-	-	+	Chronic
2	+	-	+	I	Chronic
3	-	+	+	+	Recovering Acute
2	-	+	+	I	Early Recovery
158	-	-	+	+	Immune Due to Natural Infection
25	-	-	+	I	Distantly Immune/Anti-HBs Unknown
79	-	-	+	-	Distantly Immune/Anti-HBs Not Detected
474	-	-	-	+	Immune Due to HBV Vaccination
57	-	-	-	I	Unknown
960	-	-	-	-	Susceptible
1,784					Total

I = Indeterminate

Table 9

**HBV Classification for Individuals at Increased Risk of HBV Infection and
Individuals With Signs and Symptoms of Hepatitis Infection (Population 2)**

Number of Specimens	HBV Reference Markers				HBV Classification
	HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	
1	+	-	-	-	Early Acute
3	+	-	+	+	Chronic
119	+	-	+	-	Chronic
2	+	-	-	+	Chronic
3	+	-	+	I	Chronic
71	-	-	+	+	Immune Due to Natural Infection
5	-	-	+	I	Distantly Immune/Anti-HBs Unknown
15	-	-	+	-	Distantly Immune/Anti-HBs Not Detected
41	-	-	-	+	Immune Due to HBV Vaccination
39	-	-	-	-	Susceptible
299					Total

I = Indeterminate

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Table 10

**Comparison of AxSYM CORE 2.0 Results With Reference Anti-HBc Assay Results
by HBV Classification (Population 1)**

HBV Classification	Reference Anti-HBc Assay Result ^a				Total
	+		-		
	AxSYM CORE 2.0 Result ^b				
	+	-	+	-	
Early Acute	0	0	1 ^c	0	1
Acute	2	0	0	0	2
Chronic	22	0	0	1	23
Recovering Acute	3	0	0	0	3
Early Recovery	2	0	0	0	2
Immune Due to Natural Infection	157	1 ^d	0	0	158
Distantly Immune/Anti-HBs Unknown	25	0	0	0	25
Distantly Immune/Anti-HBs Not Detected	78	1 ^c	0	0	79
Immune Due to HBV Vaccination	0	0	18 ^f	456	474
Unknown	0	0	1	56	57
Susceptible	0	0	18 ^e	942	960
Grand Total	289	2	38	1,455	1,784

^a Includes retesting performed according to the package insert, if required.

^b Includes retesting performed according to the clinical brochure, if required.

^c This specimen was tested and determined to be positive for HBV DNA and anti-HBc by a second FDA-approved anti-HBc assay.

^d This specimen was tested and determined to be positive for anti-HBc by a second FDA-approved anti-HBc assay.

^e This specimen was tested and determined to be negative for HBeAg, anti-HBe, HBV DNA, and anti-HBc by a second FDA-approved anti-HBc assay.

^f One specimen was tested and determined to be positive for anti-HBe; one specimen was equivocal for anti-HBe; one specimen was positive for HBV DNA; one specimen was positive for anti-HBc by a second FDA-approved anti-HBc assay.

^g Two specimens were tested and determined to be positive for anti-HBc by a second FDA-approved anti-HBc assay; one specimen was positive for HBV DNA and anti-HBc by a second FDA-approved anti-HBc assay.

Note: Thirty-six (36) specimens with an initial grayzone result were retested in duplicate.

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Table 11
Comparison of AxSYM CORE 2.0 Results With Reference Anti-HBc Assay Results
by HBV Classification (Population 2)

HBV Classification	Reference Anti-HBc Assay Result ^a				Total
	+		-		
	AxSYM CORE 2.0 Result ^b				
	+	-	+	-	
Early Acute	0	0	0	1	1
Chronic	125	0	2 ^c	0	127
Immune Due to Natural Infection	71	0	0	0	71
Distantly Immune/Anti-HBs Unknown	5	0	0	0	5
Distantly Immune/Anti-HBs Not Detected	15	0	0	0	15
Immune Due to HBV Vaccination	0	0	23 ^d	18	41
Susceptible	0	0	4 ^e	35	39
Total	216	0	29	54	299

^a Includes retesting performed according to the package insert, if required.

^b Includes retesting performed according to the clinical brochure, if required.

^c Both specimens were tested and determined to be positive for HBeAg and HBV DNA.

^d Five specimens were tested and determined to be positive for anti-HBe; one specimen was equivocal for anti-HBe.

^e One specimen was tested and determined to be positive for anti-HBe; one specimen was positive for anti-HBe and anti-HBc by a second FDA-approved anti-HBc assay.

Note: Ten (10) specimens with an initial grayzone result were retested in duplicate.

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Table 12
Percent Agreement Between AxSYM CORE 2.0 Results and Reference Anti-HBc Assay Results
Summarized by HBV Classification (Population 1)

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Early Acute	NA	NA	0/1 (0.00%)	[0.00%, 97.50%]
Acute	2/2 (100.00%)	[15.81%, 100.00%]	NA	NA
Chronic	22/22 (100.00%)	[84.56%, 100.00%]	1/1 (100.00%)	[2.50%, 100.00%]
Recovering Acute	3/3 (100.00%)	[29.24%, 100.00%]	NA	NA
Early Recovery	2/2 (100.00%)	[15.81%, 100.00%]	NA	NA
Immune Due to Natural Infection	157/158 (99.37%)	[96.52%, 99.98%]	NA	NA
Distantly Immune/Anti-HBs Unknown	25/25 (100.00%)	[86.28%, 100.00%]	NA	NA
Distantly Immune/Anti-HBs Not Detected	78/79 (98.73%)	[93.15%, 99.97%]	NA	NA
Immune Due to HBV Vaccination	NA	NA	456/474 (96.20%)	[94.06%, 97.73%]
Unknown	NA	NA	56/57 (98.25%)	[90.61%, 99.96%]
Susceptible	NA	NA	942/960 (98.13%)	[97.05%, 98.89%]
Overall	289/291 (99.31%)	[97.54%, 99.92%]	1,455/1,493 (97.45%)	[96.52%, 98.19%]

NA = Not Applicable

Table 13

Percent Agreement Between AxSYM CORE 2.0 Results and Reference Anti-HBc Assay Results Summarized by HBV Classification (Population 2)

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Early Acute	NA	NA	1/1 (100.00%)	[2.50%, 100.00%]
Chronic	125/125 (100.00%)	[97.09%, 100.00%]	0/2 (0.00%)	[0.00%, 84.19%]
Immune Due to Natural Infection	71/71 (100.00%)	[94.94%, 100.00%]	NA	NA
Distantly Immune/Anti-HBs Unknown	5/5 (100.00%)	[47.82%, 100.00%]	NA	NA
Distantly Immune/Anti-HBs Not Detected	15/15 (100.00%)	[78.20%, 100.00%]	NA	NA
Immune Due to HBV Vaccination	NA	NA	18/41 (43.90%)	[28.47, 60.25%]
Susceptible	NA	NA	35/39 (89.74%)	[75.78%, 97.13%]
Overall	216/216 (100.00%)	[98.31%, 100.00%]	54/83 (65.06%)	[53.81%, 75.20%]

NA = Not Applicable

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Expected Results

Expected results were determined using the AxSYM CORE 2.0 results for individuals at increased risk of HBV infection living in the United States.

Of the prospective subjects participating in the clinical investigation, 58.91% (1,256/2,132) were individuals, living in the United States, who were at increased risk of HBV infection. All subjects were at risk of HBV infection due to lifestyle, behavior, occupation, or known exposure event but were asymptomatic and reported no current signs or symptoms of hepatitis. The population ranged in age from 18 to 75 years. A demographic summary of this population is presented in the following table:

	Total Number of Specimens (%)
Ethnicity:	
Caucasian	47.45
African American	36.39
Hispanic	12.82
Asian	1.51
American Indian/Alaska Native	0.32
Other	1.51
Gender:	
Female	63.06
Male	36.94

AxSYM CORE 2.0 was reactive in 15.45% (194/1,256) of the individuals in this population. The percent of individuals at increased risk of HBV infection enrolled at each location and the percent of AxSYM CORE 2.0 reactive results observed from each location are presented in Table 14. The percent AxSYM CORE 2.0 reactive and nonreactive results by age range and gender are presented in Table 15.

Table 14

AxSYM CORE 2.0 Reactive Results by Specimen Collection Site or Specimen Vendor for Individuals at Increased Risk of HBV Infection

Specimen Collection Site/ Specimen Vendor	Percent of Individuals at Increased Risk of HBV Infection Enrolled at Each Location	Percent of AxSYM CORE 2.0 Reactive Results Observed From Each Location
Site 1, Galveston, TX	58.52 (735/1,256)	17.41 (128/735)
Site 2, Dallas, TX	4.22 (53/1,256)	20.75 (11/53)
Site 3, Miami, FL	3.74 (47/1,256)	19.15 (9/47)
Site 4, St. Petersburg, FL	3.03 (38/1,256)	23.68 (9/38)
Site 5, Chicago, IL	0.16 (2/1,256)	50.00 (1/2)
Site 6, Denver, CO	2.39 (30/1,256)	23.33 (7/30)
Specimen Vendor 1 Location:		
Colton, CA	5.97 (75/1,256)	1.33 (1/75)
Plymouth, MA	7.32 (92/1,256)	18.48 (17/92)
High Point, NC	14.65 (184/1,256)	5.98 (11/184)

Table 15

AxSYM CORE 2.0 Results by Age Range and Gender for Individuals at Increased Risk of HBV Infection

Age Range	Gender	AxSYM CORE 2.0 Result		Total
		+ Number of Specimens (%)	- Number of Specimens (%)	
10 to 19	Female	0 (0.00)	13 (100.00)	13
	Male	1 (9.09)	10 (90.91)	11
20 to 29	Female	13 (7.34)	164 (92.66)	177
	Male	3 (3.30)	88 (96.70)	91
30 to 39	Female	20 (10.87)	164 (89.13)	184
	Male	12 (12.12)	87 (87.88)	99
40 to 49	Female	35 (14.58)	205 (85.42)	240
	Male	46 (30.46)	105 (69.54)	151
50 to 59	Female	21 (15.67)	113 (84.33)	134
	Male	34 (34.69)	64 (65.31)	98
60 to 69	Female	2 (5.88)	32 (94.12)	34
	Male	3 (27.27)	8 (72.73)	11
70 to 79	Female	3 (42.86)	4 (57.14)	7
	Male	1 (33.33)	2 (66.67)	3
Unknown ^a	Female	0 (0.00)	3 (100.00)	3
Total		194 (15.45)	1,062 (84.55)	1,256

^a Age was not provided for three subjects.

XI. Conclusions Drawn From Nonclinical and Clinical Investigation

A multicenter study was conducted to demonstrate that the AxSYM CORE 2.0 assay performs as intended in a diagnostic population. A total of 2,132 specimens were prospectively collected and tested. In addition, 100 specimens from pediatric population were tested. The adult specimens were assigned an HBV classification and the AxSYM CORE 2.0 results were compared to the reference anti-HBc results. A method comparison was performed with a commercially available assay.

The overall positive percent agreement between the AxSYM CORE 2.0 assay and the reference assay was 99.31% (289/291) in Individuals with Signs and Symptoms of Hepatitis Infection (US Population). The overall negative percent agreement between the AxSYM CORE 2.0 assay and the reference assay was 97.45% (1,455/1,493) in the same population.

Specimens Collected From Individuals Living in Vietnam With Signs and Symptoms of Hepatitis Infection the positive agreement was 100.00% (216/216) and the negative agreement was 65.06% (54/83).

There was 100% (49/49) agreement with Individuals diagnosed with acute or chronic HBV Infection.

The ability of the AxSYM CORE 2.0 assay to detect HBV infections was demonstrated with 6 seroconversion panel evaluations.

In the pediatric population the positive and negative agreement was 66.67% (2/3) and 97.94% (95/97) respectively.

Precision and reproducibility of the AxSYM CORE 2.0 was established for within-run, within-day, within-lab, and between sites.

Tube Type Interference study results support the use of human serum and plasma (potassium EDTA, sodium citrate, lithium heparin, and sodium heparin) in the AxSYM CORE 2.0 assay.

The results from both the non-clinical and clinical studies indicate that the AxSYM CORE 2.0 assay can be used safely and effectively for the qualitative *in vitro* determination of anti-HBc antibodies in human serum and plasma. The data also support the use of this assay as an aid in the diagnosis of acute, chronic, or resolved hepatitis B virus (HBV) infection in conjunction with other laboratory results and clinical information.

RISK BENEFIT ANALYSIS

As a diagnostic test, the AxSYM CORE 2.0 assay involves removal of blood from an individual for testing purposes. This test presents no more of a safety hazard to an individual than is presented to an individual who is having their blood drawn for any other diagnostic evaluation. The benefits to HBV-infected individuals tested by these assays outweigh any potential adverse event or risk to the patient or user due to assay malfunction or operator error.

The potential risks encountered with this *in vitro* diagnostic test are not unusual in the clinical laboratory setting. Appropriate warnings for these risks are contained in the labeling and package inserts for these devices. Standard good laboratory practices are considered sufficient to mitigate the risks to the end user.

SAFETY

Based on the results of the preclinical and clinical laboratory studies, the AxSYM CORE 2.0 assay, when used according to the provided directions and in conjunction with other serological and clinical information, should be safe and pose minimal risk to the patient due to false test results.

EFFECTIVENESS

The effectiveness of the AxSYM CORE 2.0 has been demonstrated for use in determining if antibodies to the core antigen of the hepatitis B virus are present in an individual's serum or plasma. A reasonable determination of effectiveness of the AxSYM CORE 2.0 assay for aiding in the diagnosis of acute and chronic HBV infection has been demonstrated.

XII. Panel Recommendations

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Microbiology Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH Decision

FDA issued an approval order on September 6, 2006.

The applicant's manufacturing facility was inspected on 5/16/06 (Abbott Park), 5/8/06 (N. Chicago), & 5/19/06 (Puerto Rico) and found to be in compliance with the Quality Systems Regulation (21 CFR 820).

XIV. Approval Specifications

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.

XV. Bibliography

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