

Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name: Antibody to Hepatitis B Surface Antigen (Anti-HBs)

Device Trade Name: AxSYM[®] AUSAB[®] Reagent Pack
AxSYM AUSAB Standard Calibrators
AxSYM AUSAB Controls

Name and Address of Applicant: Abbott Laboratories
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Premarket Approval Application (PMA) Number: P060003

Date of Panel Recommendation: None

Date of Notice of Approval to the Applicant: August 7, 2006

II. Indications for Use

A. AxSYM AUSAB Reagent Pack

AxSYM AUSAB is a microparticle enzyme immunoassay (MEIA) intended for the quantitative determination of antibody to hepatitis B surface antigen (anti-HBs) in adult and pediatric serum (including serum collected in serum separator tubes) or plasma (collected in sodium heparin). The assay is used for the quantitative measurement of antibody response to hepatitis B virus (HBV) vaccination for the determination of HBV immune status, and for the diagnosis of HBV disease associated with HBV infection when used in conjunction with other laboratory results and clinical information.

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B. AxSYM AUSAB Standard Calibrators

The AxSYM[®] AUSAB[®] Standard Calibrators are used for the calibration of the AxSYM System when the system is used for the quantitative determination of antibody to hepatitis B surface antigen (anti-HBs) using the AxSYM AUSAB Reagent Pack. The performance of the AxSYM AUSAB Standard Calibrators has not been established with any other anti-HBs assays.

C. AxSYM AUSAB Controls

The AxSYM[®] AUSAB[®] Controls are used for monitoring the performance of the AxSYM System (reagent, calibrators, and instrument) when used for the quantitative determination of antibody to hepatitis B surface antigen (anti-HBs) when using the AxSYM AUSAB Reagent Pack. The performance of the AxSYM AUSAB Controls has not been established with any other anti-HBs assays.

III. Contraindications: None known.

IV. Warnings and Precautions:

For in vitro diagnostic use only.

AxSYM AUSAB is for in vitro diagnostic use only. Warnings and precautions for the AxSYM AUSAB Reagent Pack, Standard Calibrators, and Controls are stated in the respective product labeling.

IV. Device Description

A. Principle of Device Methodology

AxSYM AUSAB is based on MEIA technology and utilizes the principle of indirect binding between anti-HBs in the sample and recombinant hepatitis B surface antigen (rHBsAg) coated on the microparticles and biotinylated rHBsAg. The antigen-antibody-antigen complex formed is detected by anti-biotin:alkaline phosphatase conjugate. The Matrix Cell is washed with Matrix Cell Wash to remove materials not bound to the microparticles. The substrate, MUP, is added and a fluorescent product is formed. A direct relationship exists between the concentration of anti-

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HBs in the sample and the amount of fluorescent product measured by the MEIA optical assembly on the AxSYM System.

The concentration of anti-HBs in the sample is determined using a previously generated AxSYM AUSAB calibration curve. Samples with anti-HBs concentrations less than 8.0 mIU/mL are considered nonreactive by AxSYM AUSAB. Samples with anti-HBs concentrations greater than 12.0 mIU/mL are considered reactive by AxSYM AUSAB. Samples with anti-HBs concentration values of 8.0 to 12.0 mIU/mL are considered gray zone by AxSYM AUSAB and should be retested in duplicate.

B. Kit Configuration and Components

1. AxSYM AUSAB Reagent Pack

The AxSYM AUSAB Reagent Pack contains the following four reagents:

- 1 Bottle (13.6 mL) Anti-biotin (Rabbit):Alkaline Phosphatase Conjugate in TRIS buffer with protein (0.5% bovine, 2.9% piscine) stabilizers. Minimum concentration: 0.1 µg/mL. Preservative: 0.1% Sodium Azide. (Reagent Bottle 1)
- 1 Bottle (5.3 mL) Hepatitis B Surface Antigen (Recombinant) (Subtypes *ad* and *ay*) Coated Microparticles in TRIS buffer with protein (0.3% bovine) stabilizer. Minimum concentration: 0.125% solids. Preservative: 0.08% Sodium Azide. (Reagent Bottle 2)
- 1 Bottle (13.5 mL) Hepatitis B Surface Antigen (Recombinant) (Subtypes *ad* and *ay*):Biotin Conjugate in TRIS buffer with animal sera (50% bovine, 1% rabbit) and recalcified human plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs. Minimum concentration: 1.25 µg/mL. Preservative: 0.1% Sodium Azide. (Reagent Bottle 3)
- 1 Bottle (31.4 mL) Specimen Diluent. Recalcified human plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs. Preservative: 0.1% Sodium Azide. (Reagent Bottle 4)

2. AxSYM AUSAB Standard Calibrators

The AxSYM AUSAB Standard Calibrators are packaged and sold separately and contain the following:

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- 1 Bottle (4 mL) Standard Calibrator A. Recalcified human plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs. Preservative: 0.1% Sodium Azide.
- 5 Bottles (4 mL each) Standard Calibrators B through F. Recalcified human plasma reactive for anti-HBs, and nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV. Preservative: 0.1% Sodium Azide.

Concentrations are standardized to the World Health Organization (WHO) International Reference Standard Preparation for antibody to HBsAg.

3. AxSYM AUSAB Controls

The AxSYM AUSAB Controls are packaged and sold separately and contain the following:

- 1 Bottle (8 mL) Negative Control. Recalcified human plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs. Preservative: 0.1% Sodium Azide.
- 2 Bottles (8 mL each) Positive Control 1 and Positive Control 2. Recalcified human plasma reactive for anti-HBs, and nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV. Preservative: 0.1% Sodium Azide.

Concentrations are standardized to the World Health Organization (WHO) International Reference Standard Preparation for antibody to HBsAg.

4. AxSYM AUSAB Specimen Diluent

The AxSYM AUSAB Specimen Diluent is packaged and sold separately and contains the following:

- 1 Bottle (100 mL) AxSYM AUSAB Specimen Diluent. Recalcified human plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs. Preservative: 0.1% Sodium Azide.

5. Other Required Components

In addition, the following components are required:

- **AxSYM System** 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.

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- 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.

VI. Alternative Practices and Procedures

Determining the presence of HBV in patients may be achieved by using a variety of commercially available, FDA-approved, serological tests. When these test results are used in combination with a physician's assessment and other laboratory test results, HBV immune status can be identified.

VII. Marketing History

This product, AxSYM AUSAB (List No. 3C74-20), has not been marketed in any other country.

VIII. Potential Adverse Effects of the Device on Health

Anti-HBs reactivity as determined by AxSYM AUSAB should be correlated with patient history and the presence or absence of other hepatitis markers when determining HBV immune status or assessing the laboratory diagnosis of a recovering HBV infection.

Failure of the product to perform as indicated, or human errors in the use of the product, may lead to a false result. A false nonreactive result does not exclude the possibility of exposure to HBV. A nonreactive result may be due to antibody levels below the detection limits of this assay. A nonreactive result cannot be considered a public health concern, as the patient would either unnecessarily receive a vaccine, vaccine booster, hyperimmune globulin, or be considered not to have recovered from an acute HBV infection when she or he have..

A false reactive result may be a patient or public health concern due to the fact that an individual would be considered previously exposed and therefore immune to HBV or that the patient was successfully vaccinated. In this case, the risk is that the patient

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would not receive a vaccine, vaccine booster, hyperimmune globulin, and would be at higher risk of infection if exposed to HBV. Once exposed, the risk of this patient spreading infection to uninfected or non-immune members of the community increases.

IX. Summary of the Nonclinical Laboratory Studies

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

A. Cutoff Rationale and Gray Zone Justification

The assay interpretation cutoff for AxSYM AUSAB (i.e., the value at or above which samples are designated as reactive) was set at 10.0 mIU/mL and standardized to the World Health Organization (WHO) Reference Standard for anti-HBs (First International Reference Preparation for antibody to HBsAg (1977)). A cutoff value of 10.0 mIU/mL was selected, because an anti-HBs concentration ≥ 10 mIU/mL is generally considered protective for hepatitis B virus (HBV) after vaccination.¹

The gray zone for AxSYM AUSAB is set at 8.0 to 12.0 mIU/mL, which is a range equal to $\pm 20\%$ from the cutoff value of 10 mIU/mL. The $\pm 20\%$ range is based on guidance from the Clinical Laboratory Standards Institute (formerly NCCLS) document EP12-A.² The appropriateness of the selected gray zone range was evaluated by calculating the 95% confidence interval (CI) around the cutoff using the results for Precision Panel Member 2 (12.0 mIU/mL) from the Within-Laboratory (20-day) Precision Study to represent worst-case variability near the assay cutoff. The calculated 95% CI around the cutoff was 8.3 to 11.7 mIU/mL, supporting the selected gray zone range for AxSYM AUSAB.

B. Sample Handling and Collection

1. Sample Types (Serum and Plasma)

A study was conducted to evaluate which specimen collection tube types are acceptable for use with the AxSYM AUSAB assay. Sets of specimens

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nonreactive for anti-HBs or from individuals known to have been vaccinated for HBV were collected in the control specimen collection tube type (serum in glass) and the specimen collection tube types selected for evaluation. The specimens nonreactive for anti-HBs were spiked with human plasma positive for anti-HBs to prepare samples throughout the dynamic range of the assay (0.0 to 1,000.0 mIU/mL), and all samples were tested. The results are summarized in Tables 1 and 2 on page 8.

The data support the use of the AxSYM AUSAB assay with serum specimens, specimens collected in serum separator tubes (SST[®]), and plasma specimens collected in tubes containing sodium heparin. The data do not support the use of the AxSYM AUSAB assay with specimens collected in plasma separator tubes or tubes containing potassium EDTA, sodium citrate, or lithium heparin.

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**Table 1: AxSYM AUSAB
Sample Types (Serum and Plasma) Study
%Differences and 95% Confidence Intervals by Sample Type
Control Condition = Serum in Glass**

Evaluation Sample Type	N	%Difference Relative to Control ^a			
		Shapiro-Wilk p-value ^b	Mean	SD	95% Confidence Interval
Serum in plastic	49	0.4878	-6.70	11.09	(-9.88, -3.51)
SST in glass	49	0.3562	-7.24	10.48	(-10.25, -4.23)
SST in plastic	49	0.0928	-7.34	10.80	(-10.44, -4.23)
Sodium Heparin	49	0.0549	-7.14	11.18	(-10.35, -3.93)

^a %Difference = Difference / (mean or median of control tube) x 100%. %Difference was calculated for each donor.

^b The distribution of the percent differences were tested for normality using the Shapiro-Wilk test. If the Shapiro-Wilk p-value is ≤ 0.01 , then normality cannot be assumed and the value displayed is the median, and the confidence interval is for the median.

**Table 2: AxSYM AUSAB
Sample Types (Serum and Plasma) Study
Distribution of %Differences by Sample Type
Control Condition = Serum in Glass**

Evaluation Sample Type	Distribution of %Differences		
	0% to \leq 10%	> 10% to \leq 20%	> 20%
Serum in plastic	59.2% (29/49)	32.7% (16/49)	8.2% (4/49)
SST in glass	59.2% (29/49)	32.7% (16/49)	8.2% (4/49)
SST in plastic	67.3% (33/49)	20.4% (10/49)	12.2% (6/49)
Sodium Heparin	65.3% (32/49)	22.4% (11/49)	12.2% (6/49)

Note: A negative bias was observed for all tube types when compared to serum in glass.

2. Sample Storage Conditions

The Clinical Laboratory Standards Institute (CLSI, formerly NCCLS) document H18-A3³ guidelines provides the following recommendations for storing blood specimens.

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- 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 2-8°C (36-46°F).
- If the assay will not be completed within 48 hours, freeze at or below -20°C (-4°F).

3. Sample Freeze/Thaw

Based on the Clinical Laboratory Standards Institute (formerly NCCLS) document H18-A3³ guidelines for specimen storage samples should not be repeatedly frozen and thawed due to potential analyte deterioration. As stated in the package insert frozen specimens may be thawed only once prior to testing.

C. Interference

1. Analytical Specificity

A study was conducted to evaluate the specificity of the AxSYM AUSAB assay when used to test specimens from individuals with medical conditions unrelated to HBV. Patient samples (210) from the following sub-groups were tested using AxSYM AUSAB and an FDA-licensed anti-HBs reference assay: HAV, HCV, HIV, HTLV, (type not specified), CMV, EBV, HSV (type not specified), rubella, Autoimmune disease (systemic lupus erythematosus, and rheumatoid factor positive), human anti-mouse antibody positive, elevated IgM, influenza vaccine recipients, toxoplasmosis, and nonviral liver disease. Of these 15 sub-groups 137 out of 210 samples were observed nonreactive in the AxSYM AUSAB and the FDA-licensed Anti-HBs reference assay. One out of 210 was determine Gray Zone in the AxSYM AUSAB, and negative with the reference assay. In addition, 64 out of 210 samples were observed reactive with both AxSYM AUSAB and the FDA-licensed Anti-HBs reference assay, whereas, 8 out of 210 samples were determined nonreactive in the AxSYM AUSAB and positive with the reference assay. The results are summarized in Table 3 on page 10.

Table 3
AxSYM AUSAB
Analytical Specificity Study: Specimens From Individuals With Medical
Conditions Unrelated to HBV Infection
Summary of Results

Category ^a	Number of Specimens Tested	FDA-licensed Anti-HBs Reference Assay					
		Positive			Negative		
		AxSYM AUSAB			AxSYM AUSAB		
		Reactive	Gray Zone	Nonreactive	Reactive	Gray Zone	Nonreactive
Hepatitis A Virus	10	5	0	0	0	0	5
Hepatitis C Virus	15	3	0	0	0	1	11
Human Immunodeficiency Virus	15	2	0	0	0	0	13
Human T-Lymphotropic Virus	10	2	0	1	0	0	7
Cytomegalovirus	10	5	0	0	0	0	5
Epstein-Barr Virus	10	7	0	1	0	0	2
Herpes Simplex Virus	15	7	0	3	0	0	5
Rubella	10	2	0	0	0	0	8
Systemic Lupus Erythematosus	15	4	0	0	0	0	11
Rheumatoid Factor Positive	12	2	0	0	0	0	10
Human Anti-mouse Antibody Positive	5	1	0	0	0	0	4
Elevated IgM	9	0	0	0	0	0	9
Influenza Vaccine Recipients	15	4	0	0	0	0	11
Toxoplasmosis	9	4	0	0	0	0	5
Nonviral Liver Disease	50	16	0	3	0	0	31
Total (%)	210	64/210 (30.5%)	0/210 (0.0%)	8/210 (3.8%)	0/210 (0.0%)	1/210 (0.5%)	137/210 (65.2%)

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

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

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

Precision Panel 4 (100 mIU/mL) was diluted with human serum nonreactive for anti-HBs to prepare high negative samples (8.0 mIU/mL target) and low positive samples (12.0 mIU/mL target). A triglyceride test sample was prepared by supplementing the high negative and low positive 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 negative and positive samples with human albumin powder to a minimum concentration of 12 g/dL. A bilirubin test sample was prepared by supplementing the high negative and low positive test samples with unconjugated bilirubin stock solution 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 negative and low positive 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 results for the different interfering substances are listed in Table 4 and 5.

The data support the use of the AxSYM AUSAB 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. It is important to note for the 8 mIU/ml (high negative sample) that while the % bias is greater than 20% for the hemoglobin and total bilirubin samples, the negative samples shifted to a lower negative value when spiked with these interferants. Table 4 and 5 show the testing result summary:

Table 4: AxSYM AUSAB
Evaluation of Potentially Interfering Substances in high negative samples (8.0 mIU/ml)

Potential Interferent	Target Spike Level	Mean Concentration (mIU/mL)			%Bias
		Control (Unspiked)	Spiked	Difference	
Hemoglobin	500 mg/dL	6.7	3.9	-2.8	-41.35 ^a
Total Bilirubin (unconjugated)	20 mg/dL	6.4	4.8	-1.6	-25.32 ^a
Total Protein	12 g/dL	7.5	8.1	0.7	8.95
Triglycerides	3,000 mg/dL	6.3	7.0	0.7	11.36

^a While the % bias is greater than 20% for the hemoglobin and total bilirubin samples, the negative samples shifted to a lower negative value when spiked with these interferents.

Table 5: AxSYM AUSAB
Evaluation of Potentially Interfering Substances in low positive samples (12.0 mIU/ml)

Potential Interferent	Target Spike Level	Mean Concentration (mIU/mL)			%Bias
		Control (Unspiked)	Spiked	Difference	
Hemoglobin	500 mg/dL	11.3	10.5	-0.7	-6.45
Total Bilirubin (unconjugated)	20 mg/dL	10.6	8.8	-1.8	-16.95
Total Protein	12 g/dL	11.5	13.1	1.7	14.44
Triglycerides	3,000 mg/dL	10.5	11.4	0.9	8.08

3. Within- and Between-assay Sample Carryover

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

Carryover events were modeled by testing human plasma nonreactive for anti-HBs 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-HBs, followed again by human plasma nonreactive for

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anti-HBs 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 concentration values was 0.00 mIU/mL, indicating that no within-assay sample carryover was present within the AxSYM AUSAB assay.

For the between-assay carryover study, the difference between the protected negative and unprotected negative mean or median concentration values ranged from 0.00 to 0.40 mIU/mL in the Sampling Center, and the difference between the protected negative and unprotected negative mean or median concentration values was 0.00 mIU/mL in the Processing Center. These results indicate that no between-assay sample carryover was present between the AxSYM AUSAB assay and any of the potential contaminator assays evaluated.

D. Limit of Blank, Limit of Detection, and Limit of Quantitation

A study was conducted based on guidance from the Clinical Laboratory Standards Institute (formerly NCCLS) document EP17-A⁴ to determine the limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) for AxSYM AUSAB.

Testing was performed using a dilution panel prepared at target anti-HBs concentrations of 0, 0.5, 1, 2, 2.5, 3, and 3.5 mIU/mL. The samples were tested in replicates of two using three AxSYM AUSAB Reagent Pack lots for five runs per lot on each of two AxSYM instruments, for a total of 30 runs (n = 60 total replicates per sample).

The AxSYM AUSAB assay demonstrated a LoB of 0.10 mIU/mL, a LoD of 0.30 mIU/mL, and a LoQ of 2.50 mIU/mL.

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E. Dilution Linearity

A study was conducted to evaluate the linearity performance of the AxSYM AUSAB assay using dilutions of the World Health Organization Reference Standard for Anti-HBs (WHO Standard) and using serial dilutions of HBV natural infection specimens (recovered) and HBV vaccinee specimens (vaccinees).

The results from the 0, 10, 50, 100, and 500 mIU/mL WHO Panel members, dilutions of WHO Panel members prepared to concentrations of 250 and 800 mIU/mL, and recovered and vaccinee specimens were evaluated using a linear regression analysis, and by comparing a linear model to the best-fit quadratic or cubic model and determining the degree of deviation from linearity. For the WHO Panel members, the correlation coefficient was 0.99, and, for the 10–500 mIU/mL range, the best-fit cubic model demonstrated less than 20% difference for all dilutions compared to the linear model. For the recovered and vaccinee specimens, the correlation coefficient ranged from 0.98 to 1.00, with a best-fit model of linear or quadratic. The data demonstrate acceptable linearity of the AxSYM AUSAB assay when using dilutions of the WHO Standard in the 10–500 mIU/mL range.

F. Within-Laboratory (20-day) Precision

A within-laboratory (20-day) precision study was conducted based on guidance from Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS) document EP5-A2⁵ to evaluate the precision performance of the AxSYM AUSAB assay.

Testing was performed using two AxSYM AUSAB Reagent Pack and Standard Calibrator lots, one control lot and two AxSYM instruments. Testing included two precision runs per day for each reagent pack lot, on each instrument, on each of 20 days. Each precision run included two replicates of the AxSYM AUSAB Negative Control, Positive Control 1, and Positive Control 2, and each of six members of a precision panel with concentrations of 8, 12, 50, 100, 500, and 800 mIU/mL. Panel members were prepared by adding recalcified human plasma reactive for anti-HBs to nonreactive human serum. The results are summarized in Tables 6 and 7 on pages 15-16.

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Table 6

AxSYM AUSAB Within-Laboratory (20-day) Precision Study

Overall Precision—Two Instruments, Two Reagent Pack/Calibrator Lots

Precision Panel Members/ Controls	Total No. Reps	Target Conc. mIU/mL	Grand Mean Conc. mIU/mL	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	CL	SD	%CV	SD	%CV
Panel Member 1	320	8.0	7.8	0.53	6.7	0.53	6.7	0.59	7.5	8.1	0.61	7.8	0.62	7.9
Panel Member 2	320	12.0	12.5	0.70	5.6	0.77	6.2	0.83	6.7	7.2	0.87	7.0	0.86	6.9
Panel Member 3	320	50.0	47.7	2.69	5.6	2.69	5.6	3.02	6.3	6.8	3.05	6.4	3.02	6.3
Panel Member 4	320	100.0	89.8	4.57	5.1	4.78	5.3	5.30	5.9	6.4	5.53	6.2	5.53	6.2
Panel Member 5	320	500.0	401.7	28.07	7.0	28.07	7.0	30.57	7.6	8.2	42.49	10.6	37.47	9.3
Panel Member 6	320	800.0	610.9	54.10	8.9	55.77	9.1	64.65	10.6	11.4	91.02	14.9	80.56	13.2
NC ^a	320	0.0	0.2	0.06	33.5	0.07	37.1	0.08	40.9	44.1	0.11	58.3	0.08	44.4
PC 1	320	15.0	15.9	0.98	6.2	1.07	6.7	1.13	7.1	7.6	1.17	7.4	1.13	7.1
PC 2	320	80.0	82.1	4.26	5.2	4.86	5.9	5.05	6.2	6.6	5.27	6.4	5.27	6.4

Conc. = Concentration, CL = Upper One-sided 95% Confidence Limit

^a Because the NC concentration values are low (at or approaching zero), relatively small differences in concentration can result in high %CV values.

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Table 7

**AxSYM AUSAB Within-Laboratory (20-day) Precision Study
Individual Component Analysis—Two Instruments, Two Reagent Pack/Calibrator Lots**

Precision Panel Members/ Controls	Total No. Reps	Target Conc. mIU/mL	Grand Mean mIU/mL	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 Member 1	320	8.0	7.8	0.53	6.7	0.00	0.0	0.26	3.3	0.17	2.1	0.19	2.5	0.59	7.5
Panel Member 2	320	12.0	12.5	0.70	5.6	0.33	2.6	0.31	2.5	0.27	2.1	0.23	1.8	0.83	6.7
Panel Member 3	320	50.0	47.7	2.69	5.6	0.00	0.0	1.38	2.9	0.39	0.8	0.00	0.0	3.02	6.3
Panel Member 4	320	100.0	89.8	4.57	5.1	1.40	1.6	2.28	2.5	1.58	1.8	1.58	1.8	5.30	5.9
Panel Member 5	320	500.0	401.7	28.07	7.0	0.00	0.0	12.11	3.0	29.50	7.3	21.66	5.4	30.57	7.6
Panel Member 6	320	800.0	610.9	54.10	8.9	13.54	2.2	32.69	5.4	64.07	10.5	48.07	7.9	64.65	10.6
NC ^b	320	0.0	0.2	0.06	33.5	0.03	15.8	0.03	17.2	0.08	41.6	0.03	17.2	0.08	40.9
PC 1	320	15.0	15.9	0.98	6.2	0.41	2.6	0.37	2.3	0.31	1.9	0.00	0.0	1.13	7.1
PC 2	320	80.0	82.1	4.26	5.2	2.35	2.9	1.37	1.7	1.48	1.8	1.48	1.8	5.05	6.2

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

^b Because the NC concentration values are low (at or approaching zero), relatively small differences in concentration can result in high %CV values.

G. Prozone Evaluation

A two-part study was conducted to evaluate the performance of the AxSYM AUSAB assay when used to test extremely high-titer specimens that may exhibit a prozone (high dose hook) effect.

1. High-titer Anti-HBs

This study was performed to characterize the threshold concentration (hook point concentration) above which a specimen may demonstrate the prozone effect (where the high dose hook effect drops the result below the level of the Standard Calibrator F) in the AxSYM AUSAB assay.

High-titer anti-HBs specimens were diluted to various levels and tested. The hook point concentration was determined by plotting the mean rate of each dilution against the dilution factor and identifying the point at which the mean rate of the specimen dilution dropped below the mean rate of the Standard Calibrator F (1,000 mIU/mL).

The data demonstrated that the prozone effect may occur in the AxSYM AUSAB assay for high-titer anti-HBs specimens with concentrations greater than 130,000 mIU/mL.

2. HBV Vaccines

This study evaluated 211 specimens from HBV vaccine recipients obtained during the AxSYM AUSAB clinical investigation to determine the prevalence of the prozone effect in a potentially high-titer population.

Of the 211 specimens from HBV vaccine recipients, 179 specimens had reported concentration values < 1,000 mIU/mL. These specimens were tested undiluted (neat) and using the AxSYM AUSAB 1:25 auto dilution procedure. All 179 specimens exhibited concentration values < 25,000 mIU/mL when tested in this study using the 1:25 auto dilution procedure; therefore, when taking the 1:25 dilution factor into consideration, none of the 179 samples exhibited the prozone effect.

Summary of Safety and Effectiveness Data

The remaining 32 HBV vaccinee specimens had reported concentration values > 1,000 mIU/mL, ranging from 1,320 to 105,940 mIU/mL. These specimens were not considered to demonstrate a high dose hook effect that would generate falsely underquantitated results, since the undiluted sample result did not drop below the level of the Standard Calibrator F (1,000 mIU/mL).

H. Microbial Challenge

Studies were conducted to establish the level of antimicrobial protection provided by the preservative system used in the components of the AxSYM AUSAB Reagent Pack, Controls, and Standard Calibrators, and to determine the effect of bioburden and/or its by-products on assay performance.

Components of the AxSYM AUSAB Reagent Pack, Controls, and Standard Calibrators were inoculated with the following microorganisms at concentrations between 10^5 to 10^6 colony forming units/mL (CFU/mL): *Bacillus subtilis*, *Candida albicans*, *Aspergillus niger*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Pseudomonas* (fluorescent group). The inoculated materials were evaluated for microbial growth over a period of 15 months.

Components of the AxSYM AUSAB Reagent Pack, Controls, and Standard Calibrators were inoculated with the following microorganisms 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. Assay performance of the inoculated components was acceptable. The data demonstrate that the AxSYM AUSAB Reagent Pack, Controls, and Standard Calibrators are adequately protected by the preservative system used.

I. Stability

1. Recommended Storage Stability – AxSYM AUSAB Reagent Pack, Standard Calibrators, and Controls

A real-time stability study was conducted to demonstrate the shelf-life integrity of the AxSYM AUSAB Reagent Pack, Standard Calibrators, and Controls at the recommended storage condition (2 to 8°C).

Three lots each of AxSYM AUSAB Reagent Packs, Standard Calibrators, and Controls were stored at the recommended storage condition of 2 to 8°C. The AxSYM HBsAg Reagent Packs, Standard Calibrators, and Controls were tested at Month 0, Day 14, and monthly thereafter through Month 19.

The data support a shelf life of 18 months at the recommended storage condition (2 to 8°C) for the AxSYM AUSAB Reagent Pack, Standard Calibrators, and Controls.

2. Onboard Reagent Pack Stability

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

Three lots of AxSYM AUSAB Reagent Packs were stored at 2 to 8°C (recommended storage) and at 31°C (simulated onboard storage) and tested at 24-hour intervals up to a total of 360 hours.

The data support the storage of the AxSYM AUSAB Reagent Pack on board the AxSYM System for 144 hours.

3. Calibration Stability and Control Frequency

An analysis was performed to determine if an AxSYM AUSAB 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).

Summary of Safety and Effectiveness Data

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 AUSAB Reagent Pack lots for 20 days. A calibration was performed on the first day of testing for each instrument and reagent pack lot combination. The AxSYM AUSAB Negative Control, Positive Control 1 and Positive Control 2 were each tested for validity purposes, once per run, twice daily, on each of 20 days, using each instrument and reagent pack lot combination.

The data demonstrate that an AxSYM AUSAB 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 multi-center study was conducted to demonstrate that the AxSYM AUSAB assay performs as intended in a diagnostic population. The study was designed to measure the precision of the AxSYM AUSAB assay, and determine the percent agreement between AxSYM AUSAB and an FDA-approved anti-HBs reference method.

A. System Reproducibility (5-day Precision)

The precision of the AxSYM AUSAB assay was evaluated by testing three AxSYM AUSAB Reagent Pack, Standard Calibrator, 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 AUSAB Negative Control, Positive Control 1, and Positive Control 2. The precision panel was composed of two members, both of which were near the assay cutoff of 10 mIU/mL. Panel members were prepared by adding recalcified human plasma reactive for anti-HBs to nonreactive human serum. The analysis method was based on National Committee for Clinical Laboratory Standard (formerly NCCLS) EP15-A2⁶. The results are presented in Tables 8 and 9 on page 21 .

The AxSYM AUSAB assay demonstrated acceptable precision across three reagent master lots and a range of anti-HBs concentration. In particular, acceptable precision was demonstrated near the assay cutoff.

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**Table 8: AxSYM AUSAB System Reproducibility (5-day Precision): Overall Precision
Three Reagent Master Lots, Three Clinical Testing Sites**

Panel Members/ Controls	Total No. Reps	Target Conc. (mIU/mL)	Grand Mean Conc. (mIU/mL)	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 Components of Site and Lot (Overall)	
				SD	%CV	SD	%CV	SD	%CV	CL	SD	%CV	SD	%CV	SD	%CV
1	360	8.0	8.5	0.52	6.1	0.58	6.8	0.62	7.2	7.8	0.75	8.8	0.82	9.6	0.85	9.9
2	360	12.0	13.5	0.76	5.7	0.80	5.9	0.87	6.5	7.0	1.14	8.5	1.15	8.5	1.25	9.3
NC ^a	360	0.0	0.1	0.05	38.6	0.07	50.4	0.07	51.2	55.7	0.20	143.5	0.08	58.6	0.20	144.0
PC 1	360	15.0	16.4	1.04	6.3	1.16	7.1	1.28	7.8	8.5	1.37	8.3	1.46	8.9	1.46	8.9
PC 2	360	80.0	84.4	4.85	5.7	5.07	6.0	5.97	7.1	7.7	6.45	7.6	7.01	8.3	7.01	8.3

Reps = Replicates; Conc. = Concentration; SD = Standard Deviation; CL = Upper One-sided 95%Confidence Limit

^a Because the NC concentration values are low (at or approaching zero), relatively small differences in concentration can result in high %CV values.

**Table 9: AxSYM AUSAB System Reproducibility (5-day Precision): Individual Component Analysis
Three Reagent Master Lots, Three Clinical Testing Sites**

Panel Members/ Controls	Total No. Reps	Target Conc. (mIU/mL)	Grand Mean Conc. (mIU/mL)	Within-Run		Between-Run		Between-Day		Between-Lot		Between-Site		Total ^a	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	360	8.0	8.5	0.52	6.1	0.24	2.9	0.21	2.5	0.43	5.0	0.53	6.2	0.85	9.9
2	360	12.0	13.5	0.76	5.7	0.24	1.8	0.34	2.6	0.73	5.5	0.75	5.6	1.25	9.3
NC ^b	360	0.0	0.1	0.05	38.6	0.05	32.5	0.01	8.8	0.19	134.0	0.04	28.5	0.20	144.0
PC 1	360	15.0	16.4	1.04	6.3	0.51	3.1	0.53	3.2	0.49	3.0	0.71	4.3	1.46	8.9
PC 2	360	80.0	84.4	4.85	5.7	1.49	1.8	3.15	3.7	2.43	2.9	3.69	4.4	7.01	8.3

Reps = Replicates; Conc. = Concentration; SD = Standard Deviation; CL = Upper One-sided 95%Confidence Limit

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

^b Because the NC concentration values are low (at or approaching zero), relatively small differences in concentration can result in high %CV values.

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B. Percent Agreement

The clinical specimens used in the study were obtained from six specimen collection sites and two specimen vendors. A total of 2,265 linked serum specimens were prospectively collected and tested. In addition, 120 specimens from a surplus pediatric population were obtained.

The specimens included the following categories:

- 1,313 specimens from individuals at increased risk of hepatitis B virus (HBV) infection
- 701 specimens from individuals with signs and symptoms of hepatitis infection
- 211 specimens from hepatitis B vaccine recipients
- 40 matched specimens from 20 hepatitis B vaccine recipients (pre- and post- samples)
- 120 specimens from a pediatric population (This population included specimens from infants > 1 month to 2 years of age, children > 2 to 12 years of age, and adolescents > 12 to 19 years of age.)

Three AxSYM AUSAB Reagent Pack, Standard Calibrator, and Control master lots were used in the percent agreement evaluation. Three clinical testing sites performed the AxSYM AUSAB testing. Specimens were sent to an external reference laboratory for reference method testing, including retesting and dilution where required. Samples that were indeterminate by the reference anti-HBs assay and reactive or nonreactive by AxSYM AUSAB were considered discordant for the percent agreement calculation.

A summary of the percent agreement results for all specimen categories is presented in Table 10 on page 23. The results of the percent agreement evaluation demonstrate that the AxSYM AUSAB assay can be used for the quantitative measurement of antibody response to HBV vaccination for the determination of HBV immune status and, in conjunction with other laboratory results and clinical information, for the diagnosis of HBV disease associated with HBV infection.

Summary of Safety and Effectiveness Data

Table 10
Summary of Percent Agreement Between
AxSYM AUSAB and the Reference Method

Specimen Category	Number of Specimens Tested	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Individuals at Increased Risk of HBV Infection and Individuals With Signs and Symptoms of Hepatitis Infection	2,014	92.11% (689/748)	89.94 – 93.94	96.60% (1,195/1,237)	95.44 – 97.54
Hepatitis B Vaccine Recipients	211	92.31% (144/156)	86.95 – 95.96	88.00% (44/50)	75.69 – 95.47
Hepatitis B Vaccine Recipients (Pre- and Post- Samples)	40	100.00% (18/18)	81.47 – 100.00	100.00% (22/22)	84.56 – 100.00
Pediatric Population	104 ^a	98.51% (66/67)	91.96 – 99.96	100.00% (37/37)	90.51 – 100.00

^a Sixteen specimens were not included in the analysis. No initial reference method results could be obtained for five specimens that had insufficient quantity. Eleven specimens were initially indeterminate by the reference method and could not be retested because of insufficient quantity.

The 2,014 specimens from individuals at increased risk of HBV infection and individuals with signs and symptoms of hepatitis infection 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 Table 11 on page 25. A comparison of AxSYM AUSAB results versus the reference method results by HBV classification category is presented in Table 12 on page 26. The percent agreement between AxSYM AUSAB and the reference method by HBV classification category is summarized in Table 13 on page 27. Samples that were indeterminate by the reference anti-HBs assay and reactive or nonreactive by AxSYM AUSAB were considered discordant for the percent agreement calculation.

Summary of Safety and Effectiveness Data

Specimens were collected from specimen collection sites located in Galveston, TX (39.32%); Dallas, TX (5.81%); Miami, FL (4.42%); St. Petersburg, FL (4.17%); Chicago, IL (8.19%); and Denver, CO (6.11%); or were obtained from a specimen vendor at the following three locations: Colton, CA (5.86%); Plymouth, MA (16.93%); and High Point, NC (9.19%). The population was 52.88% Caucasian, 28.55% African American, 14.65% Hispanic, 1.99% Asian, and 0.45% American Indian/Alaska Native, with the remaining 1.49% represented by other ethnic groups. The population was 52.53% female and 47.47% 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 (39.32%); Clinical Testing Site 2 located in Dallas, TX (40.17%); and Clinical Testing Site 3 located in Raritan, NJ (20.51%).

Summary of Safety and Effectiveness Data

Table 11

**HBV Classification for Individuals at Increased Risk of HBV Infection and
Individuals With Signs and Symptoms of Hepatitis Infection**

Number of Specimens	HBV Reference Markers				HBV Classification
	HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	
2	+	-	-	-	Early Acute
5	+	+	+	-	Acute
1	+	+	+	I	Chronic
2	+	-	+	+	Chronic
35	+	-	+	-	Chronic
1	+	-	-	+	Chronic
2	+	-	+	I	Chronic
1	+	+	+	+	Late Acute/Recovering
4	-	+	+	+	Recovering Acute
3	-	+	+	I	Early Recovery
193	-	-	+	+	Immune Due to Natural Infection
31	-	-	+	I	Distantly Immune/Anti-HBs Unknown
107	-	-	+	-	Distantly Immune/Anti-HBs Not Detected
507	-	-	-	+	Immune Due to HBV Vaccination
66	-	-	-	I	Unknown
1,054	-	-	-	-	Susceptible
2,014					Total

I = Indeterminate

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Summary of Safety and Effectiveness Data

Table 12

Comparison of AxSYM AUSAB Results With Reference Method Results by HBV Classification

HBV Classification	Reference Method Result ^a									Total
	+			I			-			
	+	GZ	-	+	GZ	-	+	GZ	-	
Early Acute	0	0	0	0	0	0	0	0	2	2
Acute	0	0	0	0	0	0	0	0	5	5
Chronic	2	0	1	2	0	1	0	0	35	41
Late Acute/Recovering	0	0	1	0	0	0	0	0	0	1
Recovering Acute	4	0	0	0	0	0	0	0	0	4
Early Recovery	0	0	0	0	0	3	0	0	0	3
Immune Due to Natural Infection	180	4	9	0	0	0	0	0	0	193
Distantly Immune/Anti-HBs Unknown	0	0	0	9	5	17	0	0	0	31
Distantly Immune/Anti-HBs Not Detected	0	0	0	0	0	0	3	0	104	107
Immune Due to HBV Vaccination	503	2	2	0	0	0	0	0	0	507
Unknown	0	0	0	23	24	19	0	0	0	66
Susceptible	0	0	0	0	0	0	2	3	1,049	1,054
Total	689	6	13	34	29	40	5	3	1,195	2,014

I = Indeterminate; GZ = Gray Zone

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

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

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Table 13

**Percent Agreement Between AxSYM AUSAB Results and Reference Method Results
Summarized by HBV Classification**

HBV Classification	Positive Percent Agreement	95% Confidence Interval	Negative Percent Agreement	95% Confidence Interval
Early Acute	NA	NA	2/2 (100.00%)	[15.81%, 100.00%]
Acute	NA	NA	5/5 (100.00%)	[47.82%, 100.00%]
Chronic	2/4 (50.00%)	[6.76%, 93.24%]	35/37 (94.59%)	[81.81%, 99.34%]
Late Acute/Recovering	0/1 (0.00%)	[0.00%, 97.50%]	NA	NA
Recovering Acute	4/4 (100.00%)	[39.76%, 100.00%]	NA	NA
Early Recovery	0/3 (0.00%)	[0.00%, 70.76%]	NA	NA
Immune Due to Natural Infection	180/193 (93.26%)	[88.76%, 96.37%]	NA	NA
Distantly Immune/Anti-HBs Unknown	0/17 (0.00%)	[0.00%, 19.51%]	0/9 (0.00%)	[0.00, 33.63]
Distantly Immune/Anti-HBs Not Detected	NA	NA	104/107 (97.20%)	[92.02%, 99.42%]
Immune Due to HBV Vaccination	503/507 (99.21%)	[97.99%, 99.78%]	NA	NA
Unknown	0/19 (0.00%)	[0.00%, 17.65%]	0/23 (0.00%)	[0.00, 14.82]
Susceptible	NA	NA	1,049/1,054 (99.53%)	[98.90%, 99.85%]
Overall	689/748 (92.11%)	[89.94%, 93.94%]	1,195/1,237 (96.60%)	[95.44%, 97.54%]

NA = Not Applicable

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Summary of Safety and Effectiveness Data

C. Expected Results

Expected results were determined using the AxSYM AUSAB results for individuals at increased risk of HBV infection.

Of the prospective subjects participating in the investigation, 57.97% (1,313/2,265) were from individuals 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	47.60
African American	36.25
Hispanic	12.72
Asian	1.45
American Indian/Alaska Native	0.46
Other	1.52
Gender:	
Female	62.15
Male	37.85

The AxSYM AUSAB assay was reactive in 38.31% 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 AUSAB reactive results observed from each location are presented in Table 14 on page 29. The percent AxSYM AUSAB reactive, gray zone, and nonreactive results by age range and gender is presented in Table 15 on page 29.

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Table 14

AxSYM AUSAB 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 AUSAB Reactive Results Observed From Each Location
Site 1, Galveston, TX	56.51 (742/1,313)	34.23 (254/742)
Site 2, Dallas, TX	4.49 (59/1,313)	25.42 (15/59)
Site 3, Miami, FL	3.96 (52/1,313)	63.46 (33/52)
Site 4, St. Petersburg, FL	4.27 (56/1,313)	25.00 (14/56)
Site 5, Chicago, IL	0.61 (8/1,313)	25.00 (2/8)
Site 6, Denver, CO	2.74 (36/1,313)	63.89 (23/36)
Specimen Vendor Location:		
Colton, CA	5.79 (76/1,313)	43.42 (33/76)
Plymouth, MA	7.54 (99/1,313)	24.24 (24/99)
High Point, NC	14.09 (185/1,313)	56.76 (105/185)

Table 15

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

Age Range	Gender	AxSYM AUSAB Result			Total
		+	GZ	-	
		Number of Specimens (%)	Number of Specimens (%)	Number of Specimens (%)	
10 to 19	Female	10 (71.43)	0 (0.00)	4 (28.57)	14
	Male	7 (63.64)	0 (0.00)	4 (36.36)	11
20 to 29	Female	82 (44.57)	2 (1.09)	100 (54.35)	184
	Male	33 (34.02)	1 (1.03)	63 (64.95)	97
30 to 39	Female	77 (41.85)	5 (2.72)	102 (55.43)	184
	Male	31 (28.97)	0 (0.00)	76 (71.03)	107
40 to 49	Female	103 (41.04)	5 (1.99)	143 (56.97)	251
	Male	47 (29.56)	1 (0.63)	111 (69.81)	159
50 to 59	Female	61 (44.53)	5 (3.65)	71 (51.82)	137
	Male	24 (22.22)	3 (2.78)	81 (75.00)	108
60 to 69	Female	19 (54.29)	2 (5.71)	14 (40.00)	35
	Male	3 (25.00)	0 (0.00)	9 (75.00)	12
70 to 79	Female	3 (37.50)	0 (0.00)	5 (62.50)	8
	Male	2 (66.67)	0 (0.00)	1 (33.33)	3
Unknown ^a	Female	1 (33.33)	0 (0.00)	2 (66.67)	3
Total		503 (38.31)	24 (1.83)	786 (59.86)	1,313

GZ = Gray Zone

^a Age was not provided for three subjects.

XI. Conclusions Drawn From Nonclinical Laboratory Studies and Clinical Investigation

Multi-centered clinical studies were conducted in the US to evaluate the AxSYM AUSAB assay. A method comparison was performed with a commercially available licensed assay to detect anti-HBs in specimens from an intended use diagnostic population.

Hepatitis B virus classification using the prospective population showed 16 unique reference marker patterns. The overall positive percent agreement between the AxSYM AUSAB assay and the reference assay was 92.11% (689/748) in the high risk, and signs and symptoms populations. The overall negative percent agreement between the AxSYM AUSAB assay and the reference assay was 96.60% (1195/1237) in the same population.

In HBV vaccinated individuals, the positive agreement was 92.31% (144/156) and the negative percent agreement was 88.00% (44/50) with the reference method. In Pre- and Post-vaccination HBV vaccine recipients, the positive percent agreement and negative percent agreement with the reference method was 100.00%, 18/18 and 22/22 respectively.

The ability of the AxSYM AUSAB assay to detect anti-HBs was demonstrated in pediatric specimen testing.

Precision and reproducibility of the AxSYM AUSAB was established for within-run ($\leq 8.9\%CV$), within-day ($\leq 9.1\%CV$), within-lab ($\leq 11.4\%CV$), and between instruments ($\leq 7.9\%CV$).

Tube Type Interference study results support the use of human serum specimens, specimens collected in serum separator tubes, and plasma specimens collected in tubes containing sodium heparin in the AxSYM AUSAB assay.

The results from both the non-clinical and clinical studies indicate that the AxSYM AUSAB assay can be used safely and effectively for the qualitative *in vitro* determination of anti-HBs in human serum and plasma. The assay may be used with other HBV serological markers to define the clinical status of patients known to be infected with HBV.

RISK BENEFIT ANALYSIS

As a diagnostic test, the AxSYM AUSAB 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 exposed and or infected individuals

Summary of Safety and Effectiveness Data

tested by the assay 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 the device. 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 AUSAB assay, when used according to the provided directions and in conjunction with other serological and clinical information, should be safe and effective and pose minimal risk to the patient due to false test results.

EFFECTIVENESS

The effectiveness of the AxSYM AUSAB has been demonstrated for use in determining if antibodies to the HBs antigen of the hepatitis B virus are present in an individual's serum or plasma. A reasonable determination of effectiveness of the AxSYM AUSAB assay for aiding in the diagnosis of immunity and status of HBV infection in suspected individuals 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 August 7, 2006.

The applicant's manufacturing facility was inspected on 5/8/06 (N. Chicago), and 5/16/06 (Abbott Park) 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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