

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

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

Device Trade Name: ARCHITECT® CORE Reagent Kit
ARCHITECT® CORE Calibrator
ARCHITECT® CORE Controls

Applicant's Name and Address: Abbott Laboratories
Abbott Diagnostics Division
100 Abbott Park Road
Abbott Park, IL 60064-3500

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P080023

Date of FDA Notice of Approval: April, 10 2009

Expedited: Not Applicable

II. INDICATIONS FOR USE

ARCHITECT CORE Reagent Kit

The ARCHITECT CORE assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, sodium heparin) and neonatal serum. It is intended 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.

ARCHITECT CORE Calibrator

The ARCHITECT CORE Calibrator is used for the calibration of the ARCHITECT *i* System when the system is used for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) with the ARCHITECT CORE Reagent Kit. The performance of the ARCHITECT CORE Calibrator has not been established with any other anti-HBc assays.

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ARCHITECT CORE Controls

The ARCHITECT CORE Controls are used for monitoring the performance of the ARCHITECT *i* System when used for the qualitative detection of IgG and IgM antibodies to hepatitis B core antigen (anti-HBc) with the ARCHITECT CORE Reagent Kit. The performance of the ARCHITECT CORE Controls has not been established with any other anti-HBc assays.

III. **CONTRAINDICATIONS**

None known.

IV. **WARNINGS AND PRECAUTIONS**

Not intended for use in screening blood, plasma, or tissue donors. The effectiveness of ARCHITECT CORE for use in screening blood, plasma, or tissue donors has not been established.

For *in vitro* diagnostic use only. Warnings and precautions for the ARCHITECT CORE Reagent Kit, ARCHITECT CORE Calibrator, and ARCHITECT CORE Controls are stated in their respective product labeling.

V. **DEVICE DESCRIPTION**

Kit Configurations and Components

The ARCHITECT CORE Reagent Kit (6L22) for detection of IgG and IgM antibodies to hepatitis B core antigen is composed of the following four components:

- ARCHITECT CORE Microparticles: 1 or 4 Bottle(s) (6.60 mL/27.00 mL) hepatitis B core (*E. coli*, recombinant) antigen coated microparticles in TRIS buffer. Minimum concentration: 0.08% solids. Preservatives: ProClin® 950 and sodium azide.
- ARCHITECT CORE Conjugate: 1 or 4 Bottle(s) (11.00 mL/28.82 mL) anti-human (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein stabilizers (bovine). Minimum concentration: 0.048 µg/mL. Preservatives: sodium alkyl paraben and sodium azide.
- ARCHITECT CORE Assay Diluent: 1 or 4 Bottle(s) (5.36 mL/23.72 mL) assay diluent containing protein stabilizers (mouse) in MOPSO buffer. Preservatives: ProClin® 950 and sodium azide.
- ARCHITECT CORE Specimen Diluent: 1 or 4 Bottle(s) (5.36 mL/ 23.72 mL) specimen diluent containing reductant in MOPSO buffer.

In addition, the following components are required for the ARCHITECT CORE Reagent Kit:

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- ARCHITECT i System is an analyzer designed to perform automated immunoassay tests based on the use of CMIA detection technology.
- ARCHITECT CORE Calibrator 1 for the calibration of the instrument.
- ARCHITECT CORE Controls (or other control material), which consist of a negative control and a positive control.
- ARCHITECT i Pre-Trigger Solution, containing 1.32% (w/v) hydrogen peroxide.
- ARCHITECT i Trigger Solution, containing 0.35N sodium hydroxide.
- ARCHITECT i Wash Buffer, containing phosphate buffered saline solution with preservative.

The ARCHITECT CORE Calibrator contains:

- 1 Bottle (4 mL) of Calibrator 1, which is anti-HBc positive human plasma in recalcified anti-HBc negative human plasma. Calibrator 1 contains yellow and blue dyes. Preservatives: ProClin® 950 and sodium azide.

The ARCHITECT CORE Controls contain:

- 1 Bottle (8 mL) Negative Control, which is recalcified anti-HBc negative human plasma. Preservatives: ProClin® 950 and sodium azide.
- 1 Bottle (8 mL) Positive Control, which is anti-HBc positive human plasma in recalcified anti-HBc negative human plasma. The positive control contains blue dye. Preservatives: ProClin® 950 and sodium azide.

Assay Principle and Format

The ARCHITECT CORE assay is a two-step immunoassay for the qualitative determination of anti-HBc antibodies in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. In the first step, sample, assay diluent, specimen diluent, and rHBcAg coated paramagnetic microparticles are combined. Human anti-HBc antibodies present in the sample bind to the rHBcAg coated microparticles and the reaction mixture is washed. In the second step, anti-human IgG and IgM acridinium-labeled conjugate is added. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A relationship exists between the presence of anti-HBc antibodies in the sample and the RLUs detected by the ARCHITECT i optics. The presence or absence of anti-HBc antibodies in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active ARCHITECT CORE calibration.

This assay is designed for use on the ARCHITECT i Systems (i 2000 and i 2000_{SR}).

Calculation of the results

The ARCHITECT i System calculates the cutoff RLU from the mean RLU of three replicates of Calibrator 1 and stores the result. The cutoff RLU is determined by multiplying the ARCHITECT CORE Calibrator 1 mean RLU by 1.0.

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The ARCHITECT *i* System calculates the S/CO result for each specimen and control as follows: S/CO = Sample RLU/Cutoff RLU.

Interpretation of Results

The assay's final outcome is either "Reactive" or "Nonreactive", following the process described below:

Initial ARCHITECT CORE Results			
Initial Result (S/CO)	Instrument Flag	Interpretation	Retest Procedure
< 0.80	NONREACTIVE	Nonreactive	No retest required.
0.80 to < 1.21	GRAYZONE	Grayzone	Retest same specimen in duplicate.
≥ 1.21	REACTIVE	Reactive	Retest same specimen in duplicate.

Final ARCHITECT CORE Interpretation		
Initial Interpretation	Results with Retest	Final Interpretation
Nonreactive	No retest required.	Nonreactive
Grayzone	If two of the three results are < 1.00 S/CO	Nonreactive
	If two of the three results are ≥ 1.00 S/CO	Reactive
Reactive	If both retest results are < 1.00 S/CO	Nonreactive
	If two of the three results are ≥ 1.00 S/CO	Reactive

- A nonreactive final interpretation indicates that anti-HBc antibodies were not detected in the sample; it is possible that the individual is not infected with HBV.
- A reactive final interpretation indicates presumptive evidence of anti-HBV; anti-HBc antibodies were detected in the sample which suggests either on-going or previous HBV infection.

For additional information on system procedures and assay technology, refer to the ARCHITECT System Operations Manual

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Patient medical history and thorough physical examinations, including hepatitis serology, determination of liver enzyme levels, and liver biopsy evaluation, will provide further information regarding the status of HBV infection.

Alternate procedures for the detection of HBV in human serum and plasma depend on the detection of HBV deoxyribonucleic acid (DNA) by polymerase chain reaction (PCR) assays or nucleic acid testing (NAT), or the detection of HBV antibodies or antigens by commercially available assays that are licensed or approved in the United States.

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VII. MARKETING HISTORY

The ARCHITECT CORE, list No. 6L22, has not been marketed in the United States or any other country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Since the ARCHITECT CORE Reagent Kit together with Calibrators and Quality Control materials are for *in vitro* diagnostic use, there is no direct adverse effect on the health of the patient. However, failure of the product to perform as intended or errors in the use of the product may lead to a false result. This assay, used as an aid in the diagnosis of individuals with acute, chronic, or resolved HBV infection, must be interpreted within the context of all relevant clinical history and laboratory findings and in conjunction with other HBV serological markers for the laboratory diagnosis of HBV disease associated with HBV infection. This assay can also be used as an aid in the differential diagnosis in individuals displaying signs and symptoms of hepatitis in whom etiology is unknown.

A false nonreactive result does not exclude the possibility of exposure to HBV. Levels of anti-HBc antibodies may be undetectable in both, the early and late stages of infection. A nonreactive result may be due to antibody levels below the detection limits of this assay. Since this assay is used in combination with other HBV assays, a false nonreactive result is not considered a public health risk, as the individual would be tested with other methodologies if signs and symptoms are indicative of HBV infection.

A false reactive result is also not considered a public health risk, since the immune status of the patient should be evaluated in conjunction with results from other hepatitis B virus marker assays, related risk factors, and clinical picture.

IX. SUMMARY OF PRECLINICAL STUDIES

Nonclinical studies were performed at Abbott Laboratories to evaluate the performance characteristics of the ARCHITECT CORE assay. All of them correspond to laboratory studies and are described below.

Assay Cutoff Determination

The presence or absence of antibody to the hepatitis B virus core antigen (anti-HBc) in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff RLU determined from an active ARCHITECT CORE calibration. The ARCHITECT CORE assay results are expressed as the ratio of the sample RLU to the cutoff RLU (S/CO). The S/CO is calculated using the equation:

$S/CO = \text{Sample RLU} / \text{Cutoff RLU}$, where

$\text{Cutoff RLU} = \text{Calibrator 1 Mean RLU} \times \text{Cutoff Multiplier}$

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To select the appropriate cutoff RLU for ARCHITECT CORE, the assay performance in detecting 2,125 specimens (1,984 normal specimens, 32 specimens from true anti-HBc positive hospitalized patients, and 109 anti-HBc positive seroconversion samples) was evaluated by varying the cutoff multiplier value between 0.8 and 1.1. Receiver operating characteristic (ROC) analysis was employed in this evaluation. The following cutoff RLU equation and assay cutoff were selected for ARCHITECT CORE:

$$\text{Cutoff RLU} = \text{Calibrator 1 Mean RLU} \times 1.0$$

The value 1.00 S/CO was selected to be the ARCHITECT CORE assay cutoff.

The seroconversion detection sensitivity of the ARCHITECT CORE assay was verified utilizing the assay cutoff value of 1.00 S/CO and found to be acceptable when compared to an FDA-approved anti-HBc assay.

A clinical investigation was performed for the ARCHITECT CORE assay, list No. 6L22. The percent agreement between the ARCHITECT CORE assay and the comparator anti-HBc assay was evaluated and the data support the selected assay cutoff for the ARCHITECT CORE assay.

Tube Type Interference

A study was conducted to evaluate which anticoagulants (blood collection tube types) are acceptable for use with the ARCHITECT CORE assay. Sample sets of human specimens were collected in the control tube type (plastic serum) and the blood collection tube types selected for evaluation. The blood collection tubes for the sample sets were supplemented with anti-HBc positive plasma to prepare high negative samples (targeted to 0.80 S/CO) and low positive samples (targeted to 1.20 S/CO) and were tested.

The data support the use of the following blood collection tube types in the ARCHITECT CORE assay:

Glass tubes

- Serum

Plastic tubes

- Serum
- Serum separator
- Dipotassium EDTA
- Sodium heparin
- Lithium heparin plasma separator

On average, the tube types evaluated showed less than a 10% difference when compared to the control tube type (plastic serum). The distribution of the percent differences per tube type is listed in Table 1 below.

Table 1. ARCHITECT CORE Tube Type Interference

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Distribution of Absolute % Difference

Evaluation Tube Type	Distribution of Absolute Percent Difference ^a	
	≤ 10%	> 10% to ≤ 20%
Glass Serum	98.0% (50/51)	2.0% (1/51)
Plastic Serum Separator	98.0% (50/51)	2.0% (1/51)
Plastic Dipotassium EDTA	98.0% (50/51)	2.0% (1/51)
Plastic Sodium Heparin	96.1% (49/51)	3.9% (2/51)
Plastic Lithium Heparin Plasma Separator	100.0% (51/51)	0.0% (0/51)

^a There were no absolute % difference values in the >20% to ≤30% or > 30% ranges, therefore, these columns were omitted from the table.

Sample Stability of Serum and Plasma

A study was conducted to evaluate the sample storage temperature and number of freeze/thaw cycles for each blood collection tube type acceptable for use with the ARCHITECT CORE assay. Sample sets of human specimens were collected in each of the blood collection tube types and supplemented with anti-HBc positive stock (targeted at 1.1 S/CO). The samples were tested at baseline (time point 1) and after being stored at 2 to 8°C for ≥ 7 days, at 23 to 30°C for ≥ 3 days, or after being subjected to three freeze/thaw cycles. Specimens that were stored at the 23 to 30°C condition and 2 to 8°C condition were tested from the blood collection tubes, as on the clot represents worst-case condition (*i.e.* specimen contact with the red blood cells). The specimens that were subjected to the freeze/thaw conditions were tested off the clot.

The data demonstrate that human serum (collected in glass or plastic tubes, or plastic serum separator tubes) or plasma collected in dipotassium EDTA, lithium heparin plasma separator, or sodium heparin tubes may be used with the ARCHITECT CORE assay when:

- stored at 2 to 8°C for up to 7 days
- stored at 23 to 30°C (room temperature) for up to 3 days
- subjected to up to 3 freeze/thaw cycles

Sample On Board Stability

A study was conducted to evaluate samples when stored on the ARCHITECT *i* System (on board storage) and tested using the ARCHITECT CORE assay. High negative samples (targeted to 0.80 S/CO) and low positive samples (targeted to 1.20 S/CO) were tested using one lot of reagents, one lot of calibrator, and one lot of controls on two instruments (one *i* 2000 and one *i* 2000_{SR}). Time point 1 consisted of testing the two analyte levels immediately after pipetting the samples. Time point 2 consisted of testing the two analyte levels after being stored on board the instrument for at least 3 hours.

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The data support sample storage of up to 3 hours on board the ARCHITECT *i* System when tested using the ARCHITECT CORE assay.

Within-Laboratory Precision (20-day Precision)

A 20-day precision study was conducted to evaluate the precision performance of the ARCHITECT CORE assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP5-A2 and to confirm that the ARCHITECT CORE assay can be used on the ARCHITECT *i* 2000 and *i* 2000_{SR}. Testing was performed using three ARCHITECT CORE reagent lots, three calibrator lots, and one control lot on two instruments (one *i*2000 and one *i*2000_{SR}). The ARCHITECT CORE Negative Control (NC) and Positive Control (PC), high negative panel (targeted to 0.80 S/CO) and low positive panel (targeted to 1.20 S/CO) were assayed in a minimum of two replicates at two separate times of the day for 20 time points over 25 days.

The ARCHITECT CORE assay demonstrated acceptable precision. The data confirm that the ARCHITECT CORE assay can be used on the ARCHITECT *i*2000 and *i*2000_{SR}. The results are summarized in Table 2 below.

Table 2. ARCHITECT CORE Precision (20-Day)

Overall Precision – Three Reagent Lots

Instrument	Sample	n	Mean S/CO	Within-Run		Within-Laboratory Precision (Total)	
				SD	%CV	SD	%CV
1	Positive Control	359	2.86	0.068	2.4	0.104	3.6
	Low positive panel	359	1.14	0.029	2.6	0.044	3.8
	High negative panel	360	0.78	0.022	2.8	0.030	3.8
	Negative Control	358	0.14	0.016	N/A	0.018	N/A
2	Positive Control	360	2.93	0.071	2.4	0.107	3.6
	Low positive panel	359	1.19	0.028	2.4	0.040	3.3
	High negative panel	360	0.82	0.021	2.6	0.032	4.0
	Negative Control	360	0.15	0.014	N/A	0.015	N/A

N/A = not applicable

Analytical Specificity

A study was conducted to evaluate the ARCHITECT CORE assay for potential cross-reactivity with specimens from individuals with medical conditions unrelated to HBV infection. Specimens with various medical conditions were tested using the ARCHITECT CORE assay and the comparator anti-HBc assay. The final interpretations for each of the specimens were compared between the two assays.

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For the medical conditions evaluated, the ARCHITECT CORE assay demonstrated no cross-reactivity with specimens from individuals with medical conditions unrelated to HBV. The data are summarized in Table 3 below.

Table 3. ARCHITECT CORE versus Comparator Anti-HBc Assay Final Results by Category

Category	n ^a	Comparator Anti-HBc			
		Negative		Reactive	
		ARCHITECT CORE	ARCHITECT CORE	ARCHITECT CORE	ARCHITECT CORE
		NR ^a	R ^a	NR ^a	R ^a
Anti-Cytomegalovirus (Anti-CMV positive)	10	8	0	1 ^b	1
Anti- <i>Escherichia coli</i> (anti- <i>E.coli</i>)	2	0	0	0	2
Anti-Nuclear Antibody (ANA)	7	7	0	0	0
Epstein-Barr Virus (anti-EBV positive)	6	3	0	0	3
Hepatitis A Virus (anti-HAV IgM positive)	8	6	0	0	2
Hepatitis C Virus (anti-HCV positive)	10	9	0	0	1
Herpes Simplex Virus (HSV) positive	10	9	0	1 ^b	0
Human anti-mouse antibodies (HAMA) positive	5	5	0	0	0
Human Immunodeficiency Virus (anti-HIV-1 positive)	8	2	0	0	6
Influenza vaccine recipient	9	9	0	0	0
Mumps Virus positive	10	10	0	0	0
Non-viral liver disease	5	3	0	0	2
Rheumatoid factor positive	10	7	0	0	3
Rubella Virus positive	10	7	0	0	3
Rubeola Virus (Measles) positive	9	9	0	0	0
Syphilis	9	9	0	0	0
Systemic Lupus Erythematosus (SLE)	4	4	0	0	0
Toxoplasmosis IgG positive	2	2	0	0	0
Varicella Zoster (anti-VZV positive)	10	8	0	0	2
Yeast Infection	9	8	0	0	1
Total	153	125	0	2	26

^a n = Number of specimens tested per category. NR = Nonreactive. R = Reactive

^b These specimens were tested and determined to be nonreactive for HBsAg; nonreactive for anti-HBs; and nonreactive for IgM anti-HBc. A second FDA-approved total anti-HBc assay was performed and the specimens were determined to be nonreactive

Analytical Sensitivity

A study was conducted to determine the analytical sensitivity of the ARCHITECT CORE assay. The analytical sensitivity of the ARCHITECT CORE assay was determined using

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four Paul Erlich Institute (PEI) standard member panels prepared at 0.25 PEI units/mL, 0.50 PEI units/mL, 1.0 PEI units/mL, and 2.5 PEI units/mL.

Testing was performed with the standard panel members on one instrument using three lots of reagents, three lots of calibrator, and one lot of controls.

The mean analytical sensitivity of the ARCHITECT CORE assay was 0.5 PEI units/mL, with a 95% confidence interval of 0.4 PEI units/mL to 0.5 PEI units/mL across the three reagent lots (see table 4 below). Therefore, the ARCHITECT CORE assay demonstrated acceptable analytical sensitivity.

Table 4. Analytical Sensitivity Summary

Reagent Lot	Calibrator Lot	Intercept	Slope	Analytical Sensitivity ^a
61015ST00	1	0.3	1.56	0.5
	2	0.3	1.53	0.5
	3	0.3	1.54	0.5
61181ST00	1	0.3	1.58	0.4
	2	0.3	1.54	0.4
	3	0.3	1.50	0.5
61190ST00	1	0.2	1.76	0.4
	2	0.2	1.65	0.5
	3	0.2	1.66	0.5

^a Analytical Sensitivity = (1.0 - Intercept) / Slope

Interferences – Bilirubin, Hemoglobin, Total Protein, and Triglycerides

A study was conducted to evaluate the susceptibility of the ARCHITECT CORE assay to potentially interfering substances based on guidance from the CLSI document EP7-A2.

A bilirubin test sample was prepared by adding bilirubin (conjugated and unconjugated) at > 20 mg/dL (targeted to 22 mg/dL) to nonreactive serum and supplementing with anti-HBc positive stock to yield two test samples with different analyte levels (0.80 and 1.20 S/CO). A hemoglobin test sample was prepared by adding hemolysate at > 500 mg/dL (targeted to 550 mg/dL) to nonreactive serum and supplementing with anti-HBc positive stock to yield two test samples with different analyte levels (0.80 and 1.20 S/CO). A high protein test sample (> 12 g/dL [targeted to 13.2 g/dL]) was prepared by dissolving 2 g of BSA into 25.00 mL of a nonreactive serum specimen and supplementing with anti-HBc positive stock to yield two test samples with different analyte levels (0.80 and 1.20 S/CO). A triglyceride test sample was prepared by supplementing the high negative and low positive samples with Liposyn[®] III at > 3000 mg/dL (targeted to 3300 mg/dL). Reference samples were prepared for each test sample at each analyte level. The reference and test samples were tested.

At the concentrations listed below, bilirubin, hemoglobin, total protein, and triglycerides showed less than 10% interference in the ARCHITECT CORE assay for high negative samples targeted to 0.80 S/CO (S/CO range: 0.60 to 0.99) and low positive samples targeted to 1.20 S/CO (S/CO range: 1.00 to 1.40):

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- Bilirubin (≤ 20 mg/dL)
- Hemoglobin (≤ 500 mg/dL)
- Total Protein (≤ 12 g/dL)
- Triglycerides (≤ 3000 mg/dL)

Seroconversion Panels

A study was conducted to evaluate the seroconversion detection of the ARCHITECT CORE assay when compared to the comparator anti-HBc assay. Seven anti-HBc patient seroconversion panel sets were obtained from two commercial vendors. The panel sets were tested using the ARCHITECT CORE assay and the comparator anti-HBc assay.

When compared to the results of the comparator anti-HBc assay, the first reactive time point for the ARCHITECT CORE assay occurred earlier in two panels, at the same time in four panels, and later in one panel for all three reagent lots, demonstrating acceptable seroconversion detection.

Table 5. Seroconversion summary for all three reagent lots

Panel ID	Days to Anti-HBc First Reactive Result		Difference in Days to Anti-HBc First Reactive Result (ARCHITECT-Comparator)
	ARCHITECT CORE Assay	Comparator Anti-HBc Assay	
RP009	30	30	0
RP016	57	57	0
26982/14399	25	25	0
43527/3453	35	42	-7
1672/3471	50	39	11
13867/3482	42	64	-22
1807/3463	64	64	0

Neonate Serum

A study was conducted to determine the performance characteristics of the ARCHITECT CORE assay when testing neonatal serum (cord blood) specimens. Twenty-two matched sets of maternal serum (adult) and neonatal serum (cord blood) specimens were supplemented with anti-HBc positive plasma to represent high negative samples (targeted to 0.80 S/CO) and low positive samples (targeted to 1.20 S/CO). The samples were tested using the ARCHITECT CORE assay.

The data generated provided performance characteristics of the ARCHITECT CORE assay when testing neonatal serum (cord blood) specimens. The data are summarized in Table 6 below.

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**Table 6. ARCHITECT CORE Neonate Serum
Distribution of Absolute Percent Differences**

Analyte Level S/CO	Distribution of Absolute % Differences		
	< 10%	≥ 10% to < 20%	≥ 20% to < 30%
0.80	59.1% (13/22)	31.8% (7/22)	9.1% (2/22)
1.20	86.4% (19/22)	13.6% (3/22)	0.0% (0/22)

High Dose Hook Effect

A study was conducted to characterize the performance of the ARCHITECT CORE assay when used to test specimens containing high levels of anti-HBc that have the potential to cause a high dose hook effect. Two unique stocks of anti-HBc positive human plasma were used for the study (S/CO mean values of 10.51 and 10.72), and each stock was serially diluted with recalcified anti-HBc negative human plasma and tested on the ARCHITECT *i* System.

The data demonstrate that the ARCHITECT CORE assay is not susceptible to interference from specimens with high levels of anti-HBc.

Instrument Percent Agreement

A study was conducted to confirm that the ARCHITECT CORE assay can be used on the ARCHITECT *i* 2000 and *i* 2000_{SR} systems. One hundred anti-HBc negative specimens and 50 anti-HBc positive specimens were tested on two instruments (one *i* 2000 and one *i* 2000_{SR}) using one lot of reagents, calibrator, and controls. One replicate of each specimen was tested on both instruments.

The negative percent agreement was 100.0% with a 95% confidence interval of 96.4% to 100.0%. The positive percent agreement was 100.0% with a 95% confidence interval of 92.9 % to 100.0%. The ARCHITECT CORE assay demonstrated acceptable agreement between the ARCHITECT *i* 2000 and *i* 2000_{SR}.

Within-Assay Sample Carryover

A study was conducted to evaluate the susceptibility of within-assay sample carryover within the ARCHITECT CORE assay by comparing the results of a low anti-HBc sample (S/CO value of 0.80) when tested before (protected) and after testing a high (7,763 PEI U/mL) anti-HBc sample (unprotected).

The difference between the protected low sample and the unprotected low sample mean S/CO values was 0.05 S/CO, indicating that no within-assay sample carryover was

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present. Therefore, the ARCHITECT CORE assay is not susceptible to within-assay sample carryover.

Reagent On Board Evaluation

A study was conducted to evaluate the performance of the ARCHITECT CORE reagents when stored on board the ARCHITECT *i* System while the instrument was in continuous running mode (on board evaluation). ARCHITECT CORE 100-test kit reagent lots and ARCHITECT CORE 500-test kit reagent lots were subjected to transport/motion-stress simulation. Test reagent kits were stored on board the instrument for a minimum of 31 days for each reagent lot. Reference reagent kits were stored at 2 to 8°C off of the instrument for each reagent lot. The test and reference reagent kits were tested over a minimum of 31 days.

The data support a 30-day reagent storage of the ARCHITECT CORE reagent kit on board the ARCHITECT *i* System while the instrument is in continuous running mode.

Calibration Storage

A study was conducted to evaluate the acceptability of an ARCHITECT CORE calibration stored on the ARCHITECT *i* System for a minimum of 30 days. Testing was performed as an extension of the Reagent On Board Evaluation study described above.

The data support the storage of an ARCHITECT CORE calibration on the ARCHITECT *i* System for a minimum of 30 days.

Reagent, Calibrator, and Control Developmental Stability

The developmental stability is an on-going study to establish the stability (shelf-life integrity) of the ARCHITECT CORE Reagents, Calibrator, and Controls at the intended storage condition of 2 to 8°C and during on board storage (for reagents only). In addition, the developmental stability includes the in-use and freeze/thaw conditions. The in-use condition for the reagents, calibrator, and controls simulates customer use over time. The freeze/thaw condition for the reagents, calibrator, and controls supports the transport simulation studies described below. Stability testing is performed on three lots of reagents, calibrator, and controls.

The developmental stability is scheduled to continue for a maximum of 15 months (with a minimum of 6 months). To date, the data support 9 months of expiration dating for the ARCHITECT CORE Reagents and 8 months of expiration dating for the ARCHITECT Calibrator and Controls.

Reagent Transport Stability

A study was conducted to support the stability of the ARCHITECT CORE Reagents following simulated transport stress conditions. One 100-test kit lot and one 500-test kit

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lot of the ARCHITECT CORE Reagents was tested after being subjected to simulated transport stress.

The data support the stability of the ARCHITECT CORE Reagents following transport at ambient temperatures.

Calibrator and Control Transport Stability

A study was conducted to support the stability of the ARCHITECT CORE Calibrator and Controls following simulated transport stress conditions. One lot each of the ARCHITECT CORE Calibrator and Controls was tested after being subjected to simulated transport stress.

The data support the stability of the ARCHITECT CORE Calibrator and Controls following transport at ambient temperatures.

Microbial Challenge Characterization

A Microbial Challenge Characterization (MCC) evaluation was performed for the ARCHITECT CORE Reagents, Calibrator, and Controls, which consisted of an Antimicrobial Effectiveness Testing (AET) evaluation and a Microbial Interference Characterization (MIC) evaluation. The MCC evaluation integrated the results from both AET and MIC, which determined that the product is adequately protected.

X. SUMMARY OF CLINICAL STUDIES

A multi-center study was conducted to evaluate the efficacy of the ARCHITECT CORE assay for the qualitative detection of anti-HBc in human serum and plasma as measured by precision and method comparison.

System Reproducibility (5-day Precision)

A study was conducted to validate the precision performance of the ARCHITECT CORE assay based on guidance from the CLSI document EP15-A2. Three lots of ARCHITECT CORE Reagents, Calibrator, and Controls were tested per site. The ARCHITECT CORE Negative Control and Positive Control, and a high negative panel member (Panel 1) (targeted to 0.80 S/CO) and low positive panel member (Panel 2) (targeted to 1.20 S/CO) were assayed in replicates of four at two separate times per day for five days. The data are summarized in Table 7 and Table 8 below.

**Table 7. ARCHITECT CORE System Reproducibility (5-Day Precision)
All Sites, All Reagent Lots. Individual Variance Components**

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Sample	n	Grand Mean S/CO	Within-Run		Between-Run		Between-Day		Total ^a			Between-Lot		Between-Site		Overall ^b	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	%CV Upper CL ^c	SD	%CV	SD	%CV	SD	%CV
Panel 1	360	0.80	0.030	3.7	0.006	0.7	0.009	1.1	0.032	4.0	4.2	0.015	1.9	0.020	2.5	0.039	4.8
Panel 2	360	1.17	0.040	3.4	0.016	1.4	0.000	0.0	0.043	3.7	3.9	0.027	2.3	0.031	2.6	0.055	4.7
Negative Control	360	0.20	0.014	7.2	0.006	2.9	0.000	0.0	0.015	7.7	8.2	0.036	18.5	0.013	6.7	0.041	20.7
Positive Control	360	2.98	0.075	2.5	0.024	0.8	0.027	0.9	0.083	2.8	3.0	0.069	2.3	0.096	3.2	0.136	4.6

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

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

^c One-sided upper 95% confidence limit for % CV with degrees of freedom calculated by Satterthwaite's method
n = number of replicates tested

**Table 8. ARCHITECT CORE System Reproducibility (5-Day Precision)
All Sites, All Reagent Lots. Cumulative Variance Components**

Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)		Precision with Additional Component of Between-Site ^a		Precision with Additional Component of Between-Lot ^a		Precision with Additional Components of Site and Lot (Overall) ^a	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	360	2.98	0.075	2.5	0.079	2.6	0.083	2.8	0.127	4.3	0.108	3.6	0.136	4.6
Low Positive Panel	360	1.17	0.040	3.4	0.043	3.7	0.043	3.7	0.053	4.5	0.050	4.3	0.055	4.7
High Negative Panel	360	0.80	0.030	3.7	0.030	3.8	0.032	4.0	0.037	4.7	0.035	4.4	0.039	4.8
Negative Control	360	0.20	0.014	N/A	0.015	N/A	0.015	N/A	0.020	N/A	0.039	N/A	0.041	N/A

N/A = not applicable; ^a Includes site-lot interaction variance component; n = number of replicates tested

Method Comparison

Study Overview and Subject Population

A prospective multi-center study was conducted to evaluate the ability of the ARCHITECT CORE assay to detect IgM and IgG anti-HBc antibodies in specimens from an intended use diagnostic population.

Of the 2,259 specimens tested and analyzed in the ARCHITECT CORE clinical study, 1,254 specimens were from individuals at increased risk of HBV infection due to lifestyle, behavior, occupation, disease state, or known exposure event and 625 specimens were from individuals exhibiting signs and symptoms of hepatitis infection living in the United States (Population 1); 97 specimens were from individuals at increased risk of HBV infection due to lifestyle, behavior, occupation, disease state, or

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known exposure event and 127 specimens were from individuals exhibiting signs and symptoms of hepatitis infection living in Vietnam (Population 2); six specimens were from individuals diagnosed with acute HBV infection; 50 specimens were from individuals diagnosed with chronic HBV infection; and 100 surplus specimens were from a pediatric population.

The 2,259 specimens were collected from specimen collection sites or were purchased from specimen vendors. Each specimen was tested using the ARCHITECT CORE assay at one of the three clinical testing sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

Each specimen was also tested with the comparator anti-HBc assay at an external laboratory. Specimens from Population 1, Population 2, and the acute population were also tested with three HBV reference assays. The comparator and reference assays were from a single manufacturer and during the clinical study, all comparator and reference testing was performed according to manufacturer's instructions.

HBV classification was then determined using the results from the HBV reference markers and a modification of the serological criteria established by the National Center of Infectious Disease (CDC) for diagnosing HBV infection, which is presented in Table 9 below. Eighteen unique reference marker patterns are represented.

Table 9. HBV Classification

HBV Reference Markers				HBV Classification
HBsAg/ HBsAg Confirmatory	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	
+	-	-	-	Early Acute
+	+	+	-	Acute
+	+	+	I	Chronic [†]
+	-	+	+	Chronic
+	-	+	-	Chronic
+	-	-	+	Chronic
+	-	+	I	Chronic*
-	+	+	I	Early Recovery*
-	+	+	+	Recovering Acute
-	+	+	-	Recovering Acute/Undetectable HBsAg
-	+	-	+	Recovering Acute [†]
-	+	-	-	Possible Recovering Acute/Undetectable HBsAg [†]
-	-	+	+	Immune Due to Natural Infection
-	-	+	I	Distantly Immune/Anti-HBs Unknown
-	-	+	-	Distantly Immune/ Anti-HBs Not Detected
-	-	-	+	Immune Due to HBV Vaccination
-	-	-	I	Unknown
-	-	-	-	Susceptible

+ = Positive/Reactive; - = Nonreactive/Negative; I = Indeterminate

[†] Three serological marker patterns were not observed during the clinical evaluation.

* Two additional serological marker patterns were observed during the clinical evaluation.

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The ARCHITECT CORE results were compared to the comparator anti-HBc results. For specimens that were discordant between the ARCHITECT CORE assay and the comparator anti-HBc assay, supplemental testing was performed to better characterize the specimens. Supplemental testing was performed on different specimen aliquots at external reference laboratories.

Results by Specimen Classification

Following testing with the comparator anti-HBc assay and the three reference HBV assays, specimens from Population 1, Population 2, and the acute population were assigned an HBV classification using the reactive (+) and nonreactive (-) patterns.

The 15 unique reference marker patterns observed in the ARCHITECT CORE clinical study for Population 1 are presented in Table 10 below. The 10 unique reference marker patterns observed in the ARCHITECT CORE clinical study for Population 2 are presented in the following table, Table 11.

Acute status was determined for all of the specimens in the acute population.

Table 10. HBV Classification for Increased Risk and Signs and Symptoms Population (Population 1)

HBV Classification	HBV Reference Markers				
	HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	n
Early Acute	+	-	-	-	14
Acute	+	+	+	-	11
Chronic	+	-	+	+	4
Chronic	+	-	+	-	73
Chronic	+	-	-	+	2
Recovering Acute	-	+	+	+	6
Recovering Acute/Undetectable HBsAg	-	+	+	-	4
Immune Due to Natural Infection	-	-	+	+	219
Distantly Immune/Anti-HBs Unknown	-	-	+	I	37
Distantly Immune/Anti-HBs Not Detected	-	-	+	-	107
Immune Due to HBV Vaccination	-	-	-	+	341
Susceptible	-	-	-	-	1004
Chronic	+	-	+	I	4
Early Recovery	-	+	+	I	1
Unknown	-	-	-	I	52
Total					1879

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I = Indeterminate

Table 11. HBV Classification for Increased Risk and Signs and Symptoms Population (Population 2)

HBV Classification	HBV Reference Markers				
	HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	n
Early Acute	+	-	-	-	1
Chronic	+	-	+	+	2
Chronic	+	-	+	-	65
Chronic	+	-	-	+	1
Immune Due to Natural Infection	-	-	+	+	61
Distantly Immune/Anti-HBs Unknown	-	-	+	I	5
Distantly Immune/Anti-HBs Not Detected	-	-	+	-	16
Immune Due to HBV Vaccination	-	-	-	+	40
Susceptible	-	-	-	-	31
Chronic	+	-	+	I	2
Total					224

I = Indeterminate

Comparison of Results

The ARCHITECT CORE assay results were compared to the comparator anti-HBc assay results for Population 1 and Population 2. The data are presented in Table 12 below for Population 1 and in the following table, Table 13, for Population 2.

Table 12. ARCHITECT CORE Results versus Comparator Anti-HBc Results. Comparison for Increased Risk and Signs and Symptoms Population (Population 1) by HBV Classification

HBV Classification	Comparator Anti-HBc								Total	
	Reactive				Negative					
	ARCHITECT CORE				ARCHITECT CORE					
	Reactive		Nonreactive		Reactive		Nonreactive			
	n	%	n	%	n	%	n	%	n	%
Early Acute	0	0.00	0	0.00	4 ^a	0.21	10	0.53	14	0.75
Acute	11	0.59	0	0.00	0	0.00	0	0.00	11	0.59
Chronic	81	4.31	0	0.00	0	0.00	2	0.11	83	4.42
Recovering Acute	6	0.32	0	0.00	0	0.00	0	0.00	6	0.32
Recovering Acute/Undetectable HBsAg	4	0.21	0	0.00	0	0.00	0	0.00	4	0.21
Immune Due to Natural Infection	213	11.34	6 ^b	0.32	0	0.00	0	0.00	219	11.66

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HBV Classification	Comparator Anti-HBc								Total	
	Reactive				Negative					
	ARCHITECT CORE				ARCHITECT CORE					
	Reactive		Nonreactive		Reactive		Nonreactive			
	n	%	n	%	n	%	n	%	n	%
Distantly Immune/Anti-HBs Unknown	37	1.97	0	0.00	0	0.00	0	0.00	37	1.97
Distantly Immune/Anti-HBs Not Detected	102	5.43	5 ^c	0.27	0	0.00	0	0.00	107	5.69
Immune Due to HBV Vaccination	0	0.00	0	0.00	17 ^d	0.90	324	17.24	341 ^e	18.15
Susceptible	0	0.00	0	0.00	7 ^f	0.37	997	53.06	1004	53.43
Early Recovery	1	0.05	0	0.00	0	0.00	0	0.00	1	0.05
Unknown	0	0.00	0	0.00	2 ^g	0.11	50	2.66	52	2.77
Total	455	24.22	11	0.59	30	1.60	1383	73.60	1879	100.00

^a Two specimens were tested and determined to be negative for HBeAg and anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and anti-HBe; positive for HBV DNA; and reactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be positive for HBeAg; negative for anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay.

^b Three specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. Two specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and reactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay.

^c These specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay.

^d Eight specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. Three specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and reactive by a second FDA-approved total anti-HBc assay. Two specimens were tested and determined to be negative for HBeAg and HBV DNA; positive for anti-HBe; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and anti-HBe; not tested for HBV DNA due to insufficient sample volume; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg; positive for anti-HBe and HBV DNA; and reactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg; equivocal for anti-HBe; and nonreactive by a second FDA-approved total anti-HBc assay.

^e Although serological HBV classification indicates immune due to HBV vaccination, 142 were recorded as vaccinated, 113 were recorded as unknown, and 86 were recorded as not vaccinated.

^f Three specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. Two specimens were tested and determined to be negative for HBeAg and anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and HBV DNA; positive for anti-HBe; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg; positive for anti-HBe; not tested for HBV DNA due to insufficient sample volume; and nonreactive by a second FDA-approved total anti-HBc assay.

^g These specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay.

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Table 13. ARCHITECT CORE Results versus Comparator Anti-HBc Results Comparison for Increased Risk and Signs and Symptoms Population (Population 2) by HBV Classification

HBV Classification	Comparator Anti-HBc								Total	
	Reactive				Negative					
	ARCHITECT CORE				ARCHITECT CORE					
	Reactive		Nonreactive		Reactive		Nonreactive			
	n	%	n	%	n	%	n	%	n	%
Early Acute	0	0.00	0	0.00	0	0.00	1	0.45	1	0.45
Chronic	69	30.80	0	0.00	1 ^a	0.45	0	0.00	70	31.25
Immune Due to Natural Infection	61	27.23	0	0.00	0	0.00	0	0.00	61	27.23
Distantly Immune/Anti-HBs Unknown	5	2.23	0	0.00	0	0.00	0	0.00	5	2.23
Distantly Immune/Anti-HBs Not Detected	16	7.14	0	0.00	0	0.00	0	0.00	16	7.14
Immune Due to HBV Vaccination	0	0.00	0	0.00	19 ^b	8.48	21	9.38	40 ^c	17.86
Susceptible	0	0.00	0	0.00	3 ^d	1.34	28	12.50	31	13.84
Total	151	67.41	0	0.00	23	10.27	50	22.32	224	100.00

^a One specimen was tested and determined to be positive for HBeAg; negative for anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay.

^b Nine specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. Four specimens were tested and determined to be negative for HBeAg and anti-HBe; not tested for HBV DNA due to insufficient sample volume; and nonreactive by a second FDA-approved total anti-HBc assay. Three specimens were tested and determined to be negative for HBeAg and HBV DNA; positive for anti-HBe; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and reactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and anti-HBe; positive for HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg and HBV DNA; equivocal for anti-HBe; and nonreactive by a second FDA-approved total anti-HBc assay.

^c Although serological HBV classification indicates immune due to HBV vaccination, all 40 were recorded as not vaccinated.

^d Two specimens were tested and determined to be negative for HBeAg, anti-HBe, and HBV DNA; and nonreactive by a second FDA-approved total anti-HBc assay. One specimen was tested and determined to be negative for HBeAg; positive for anti-HBe; not tested for HBV DNA due to insufficient sample volume; and reactive by a second FDA-approved total anti-HBc assay.

Percent Agreement

The negative percent agreement and positive percent agreement between the ARCHITECT CORE assay and the comparator anti-HBc assay and their corresponding 95% exact confidence intervals were calculated for Population 1, Population 2, and the acute and chronic populations.

The percent agreement between ARCHITECT CORE and the comparator anti-HBc assay for Population 1 by HBV classification is presented in Table 14 below. The percent

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agreement between ARCHITECT CORE and the comparator anti-HBc assay for Population 2 by HBV classification is presented in the following table, Table 15.

For the acute population, the positive percent agreement was 100.00% (6/6) with a 95% confidence interval of 54.07% to 100.00%. For the chronic population, the positive percent agreement was 100.00% (50/50) with a 95% confidence interval of 92.89% to 100.00%.

Table 14. ARCHITECT CORE Results versus Comparator Anti-HBc Results. Percent Agreement for Increased Risk and Signs and Symptoms Population (Population 1) by HBV Classification

HBV Classification	Positive Percent Agreement (%)	95% Confidence Interval	Negative Percent Agreement (%)	95% Confidence Interval
Early Acute	N/A	N/A	71.43 (10/14)	41.90-91.61
Acute	100.00 (11/11)	71.51-100.00	N/A	N/A
Chronic	100.00 (81/81)	95.55-100.00	100.00 (2/2)	15.81-100.00
Recovering Acute	100.00 (6/6)	54.07-100.00	N/A	N/A
Recovering Acute/Undetectable HBsAg	100.00 (4/4)	39.76-100.00	N/A	N/A
Immune Due to Natural Infection	97.26 (213/219)	94.13-98.99	N/A	N/A
Distantly Immune/Anti-HBs Unknown	100.00 (37/37)	90.51-100.00	N/A	N/A
Distantly Immune/Anti-HBs Not Detected	95.33 (102/107)	89.43-98.47	N/A	N/A
Immune Due to HBV Vaccination	N/A	N/A	95.01 (324/341)	92.14-97.07
Susceptible	N/A	N/A	99.30 (997/1004)	98.57-99.72
Early Recovery	100.00 (1/1)	2.50-100.00	N/A	N/A
Unknown	N/A	N/A	96.15 (50/52)	86.79-99.53
Total	97.64 (455/466)	95.82-98.82	97.88 (1383/1413)	96.98-98.56

N/A = not applicable

Positive % agreement=

$$\frac{[\text{No. of ARCHITECT CORE reactive results in agreement with the comparator anti-HBc reactive results}]}{[\text{Total number of comparator anti-HBc reactive results}]} \times 100$$

Negative % agreement=

$$\frac{[\text{No. of ARCHITECT CORE nonreactive results in agreement with the comparator anti-HBc negative results}]}{[\text{Total number of comparator anti-HBc negative}]} \times 100$$

Table 15. ARCHITECT CORE Results versus Comparator Anti-HBc Results. Percent Agreement for Increased Risk and Signs and Symptoms Population (Population 2) by HBV Classification

HBV Classification	Positive Percent Agreement (%)	95% Confidence Interval	Negative Percent Agreement (%)	95% Confidence Interval
Early Acute	N/A	N/A	100.00 (1/1)	2.50-100.00
Chronic	100.00 (69/69)	94.79-100.00	0.00 (0/1)	0.00-97.50
Immune Due to Natural Infection	100.00 (61/61)	94.13-100.00	N/A	N/A
Distantly Immune/Anti-HBs Unknown	100.00 (5/5)	47.82-100.00	N/A	N/A
Distantly Immune/Anti-HBs Not Detected	100.00 (16/16)	79.41-100.00	N/A	N/A
Immune Due to HBV Vaccination	N/A	N/A	52.50 (21/40)	36.13-68.49
Susceptible	N/A	N/A	90.32 (28/31)	74.25-97.96

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Total	100.00 (151/151)	97.59-100.00	68.49 (50/73)	56.56-78.87
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N/A = not applicable

Positive % agreement=

$$\frac{[\text{No. of ARCHITECT CORE reactive results in agreement with the comparator anti-HBc reactive results}]}{[\text{Total number of comparator anti-HBc reactive results}]} \times 100$$

Negative % agreement=

$$\frac{[\text{No. of ARCHITECT CORE nonreactive results in agreement with the comparator anti-HBc negative results}]}{[\text{Total number of comparator anti-HBc negative}]} \times 100$$

Percent of Positive Specimens

The percent of positive ARCHITECT CORE specimens for individuals diagnosed with acute HBV infection was 100.00% (6/6, with a 95% confidence interval of 54.07% to 100.00%). The percent of positive ARCHITECT CORE specimens for individuals diagnosed with chronic HBV infection was 100.00% (50/50, with a 95% confidence interval of 92.89% to 100.00%).

Clinical Performance in a Pediatric Population

The performance of the ARCHITECT CORE assay in a pediatric population was evaluated by testing 100 surplus specimens from a pediatric population collected in Fall River, MA by a specimen vendor, and from the 112 prospectively-collected pediatric specimens from Population 1, Population 2, and the chronic population. The negative and positive percent agreement between ARCHITECT CORE results and the comparator anti-HBc results for the surplus and prospective pediatric populations was calculated.

For the surplus pediatric specimens, the negative percent agreement was 98.99% (98/99) with a 95% confidence interval of 94.50% to 99.97%. The positive percent agreement was 100.00% (1/1) with a 95% confidence interval of 2.50% to 100.00%.

For the prospectively-collected pediatric specimens, the negative percent agreement was 96.63% (86/89) with a 95% confidence interval of 90.46% to 99.30%. Positive percent agreement was 100.00% (23/23) with a 95% confidence interval of 85.18% to 100.00%.

The distribution of the ARCHITECT CORE reactive and nonreactive results for the surplus pediatric population and prospectively-collected pediatric population is presented below in Table 16 and Table 17, respectively.

Table 16. ARCHITECT CORE Results by Age Range and Gender for the Surplus Pediatric Population

Age Range	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
2 to 12 Years	F	0 (0.00)	17 (100.00)	17
	M	0 (0.00)	33 (100.00)	33
>12 to 18 Years	F	0 (0.00)	22 (100.00)	22
	M	2 (18.18)	9 (81.82)	11

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Age Range	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
>18 to 21 Years	F	0 (0.00)	12 (100.00)	12
	M	0 (0.00)	5 (100.00)	5
Total		2 (2.00)	98 (98.00)	100

Table 17. ARCHITECT CORE Results by Age Range and Gender for the Prospective Pediatric Population

Age Range	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
>12 to 18 Years	F	1 (25.00)	3 (75.00)	4
	M	2 (50.00)	2 (50.00)	4
>18 to 21 Years	F	17 (28.81)	42 (71.19)	59
	M	6 (13.33)	39 (86.67)	45
Total		26 (23.21)	86 (76.79)	112

Expected Results

Of the 2,159 prospectively-collected specimens tested and analyzed in the ARCHITECT CORE clinical study, 1,254 were from individuals living in the United States with increased risk of HBV infection. All 1,254 were at risk for HBV due to lifestyle, behavior, occupation, or a known exposure event but were asymptomatic and reported no current signs or symptoms of hepatitis.

The 1,254 increased risk specimens from Population 1 were collected from specimen collection sites or were purchased from specimen vendors. Testing of these specimens was performed at three clinical sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

A demographic summary of the increased risk population in Population 1 by race/ethnic group is provided in Table 18 below.

Table 18. Demographic Summary of Increased Risk Population by Race/Ethnic Group (Population 1)

Race/Ethnic Group	n	Percent (%)
African American	385	30.70
American Indian/Alaska Native	2	0.16
Asian	28	2.23
Caucasian	635	50.64
Hispanic	177	14.11

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Race/Ethnic Group	n	Percent (%)
Other	25	1.99
Unknown	2	0.16
Total	1254	100.00

Of the 1,254 increased risk subjects in Population 1, 590 (47.05%) were female and 664 (52.95%) were male. The age was not reported for two subjects. Of the remaining 1,252 subjects, the mean age was 39 years (age range: 17 to 82 years).

The ARCHITECT CORE assay was reactive in 231 (18.42%) of the individuals in the increased risk population. The number and percent of ARCHITECT CORE reactive results observed at each collection location are presented in Table 19 below.

Table 19. Number and Percent of Reactive Results by Clinical Testing Site for Increased Risk Population (Population 1)

Specimen Collection Site/ Vendor Location	Percent of Specimens Enrolled at Each Site	Percent of Reactive Results at Each Site
Specimen Collection Site 1: Galveston, TX	19.94 (250/1254)	11.20 (28/250)
Specimen Collection Site 2: Dallas, TX	13.00 (163/1254)	17.79 (29/163)
Specimen Collection Site 3: Miami FL	9.65 (121/1254)	28.10 (34/121)
Specimen Collection Site 4: St. Petersburg, FL	31.82 (399/1254)	16.79 (67/399)
Specimen Collection Site 5: Chicago, IL	7.50 (94/1254)	40.43 (38/94)
Specimen Collection Site 6: Denver CO	3.91 (49/1254)	26.53 (13/49)
Specimen Vendor 1: Diagnostic Support Services, Inc., Site Location 1: High Point, NC	2.71 (34/1254)	0.00 (0/34)
Specimen Vendor 1: Diagnostic Support Services, Inc., Site Location 2: Colton, CA	2.63 (33/1254)	9.09 (3/33)
Specimen Vendor 1: Diagnostic Support Services, Inc., Site Location 3: Plymouth, MA	8.85 (111/1254)	17.12 (19/111)

The distribution of ARCHITECT CORE reactive and nonreactive results among the increased risk population by age range and gender is presented in Table 20 below.

Table 20. Results by Age Range and Gender for Individuals at Increased Risk Population (Population 1)

Age Range	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
10 to 19	F	1 (7.69)	12 (92.31)	13
	M	1 (12.50)	7 (87.50)	8
20 to 29	F	13 (7.22)	167 (92.78)	180
	M	6 (4.41)	130 (95.59)	136
30 to 39	F	8 (6.72)	111 (93.28)	119

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

Age Range	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
40 to 49	M	26 (14.53)	153 (85.47)	179
	F	37 (25.00)	111 (75.00)	148
50 to 59	M	51 (24.29)	159 (75.71)	210
	F	18 (20.93)	68 (79.07)	86
60 to 69	M	37 (36.63)	64 (63.37)	101
	F	14 (40.00)	21 (60.00)	35
70 to 79	M	9 (45.00)	11 (55.00)	20
	F	3 (60.00)	2 (40.00)	5
80 to 89	M	6 (66.67)	3 (33.33)	9
	F	1 (33.33)	2 (66.67)	3
Unknown	F	0 (0.00)	1 (100.00)	1
	M	0 (0.00)	1 (100.00)	1
Total		231 (18.42)	1023 (81.58)	1254

XI. PANEL RECOMMENDATION

Pursuant to Section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Microbiology Devices Advisory Panel meeting because the information in the PMA substantially duplicated information previously reviewed by this Panel.

XII. CDRH DECISION

CDRH issued an approval order on April 10, 2009.

The final conditions of approval cited in the approval order are described below.

The applicant's manufacturing facilities were inspected on 12/11/08 (Abbott Park, IL) and 12/1/08 (Barceloneta, PR) and found to be in compliance with the Quality Systems Regulations (21 CFR 820).

XIII. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

XIV. REFERENCES - NONE