SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Hepatitis B Surface Antigen
Hepatitis B Surface Antigen Confirmatory

Device Trade Name: ARCHITECT HBsAg Qualitative
ARCHITECT HBsAg Qualitative Confirmatory
ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent
ARCHITECT HBsAg Qualitative Calibrators
ARCHITECT HBsAg Qualitative Controls

Applicant's Name and Address:

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Date(s) of Panel Recommendation: Not applicable

Premarket Approval Application (PMA) Number: P110029

Date of FDA Notice of Approval: April 12, 2012

Expedited: Not applicable

II. INDICATIONS FOR USE

1. ARCHITECT HBsAg Qualitative.

The ARCHITECT HBsAg Qualitative assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of hepatitis B surface antigen (HBsAg) in human adult and pediatric serum and plasma and neonate serum. The assay may also be used to screen for HBV infection in pregnant women to identify neonates who are at risk for acquiring hepatitis B during the perinatal period. Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with the hepatitis B virus (HBV) (state of infection or associated disease not determined)

in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis B infection. Not intended for use in screening blood, plasma, or tissue donors.

2. ARCHITECT HBsAg Qualitative Confirmatory

The ARCHITECT HBsAg Qualitative Confirmatory assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative confirmation of the presence of hepatitis B surface antigen (HBsAg) in human adult and pediatric serum and plasma and neonate serum by means of specific antibody neutralization. Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with the hepatitis B virus (HBV) (state of infection or associated disease not determined) in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis B infection. Not intended for use in screening blood, plasma, or tissue donors.

3. ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent

The ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent is used for manually diluting specimens for testing on the ARCHITECT *i* System using the ARCHITECT HBsAg Qualitative Confirmatory reagent kit. The performance of the ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent has not been established with any other HBsAg assays.

4. ARCHITECT HBsAg Qualitative Calibrators

The ARCHITECT HBsAg Qualitative Calibrators are for the calibration of the ARCHITECT *i* System when used for qualitative detection of the presence of hepatitis B surface antigen (HBsAg) using the ARCHITECT HBsAg Qualitative and HBsAg Qualitative Confirmatory reagent kits. The performance of the ARCHITECT HBsAg Qualitative Calibrators has not been established with any other HBsAg assays.

5. ARCHITECT HBsAg Qualitative Controls

The ARCHITECT HBsAg Qualitative Controls are used for monitoring the performance of the ARCHITECT *i* System (reagents, calibrators, and instrument) when used for the qualitative detection of hepatitis B surface antigen (HBsAg) using the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory reagent kits. The performance of the ARCHITECT HBsAg Qualitative Controls has not been established with any other HBsAg assays.

III. CONTRAINDICATIONS

None.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ARCHITECT HBsAg Qualitative, the ARCHITECT HBsAg Qualitative Confirmatory, the ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent, the ARCHITECT HBsAg Qualitative Calibrators and the ARCHITECT HBsAg Qualitative Controls labeling.

V. DEVICE DESCRIPTION

Kit Configurations and Components

The ARCHITECT HBsAg Qualitative reagent kit is comprised of the following three components:

- 1 bottle anti-HBs (mouse, monoclonal, IgM, IgG) coated microparticles in MES buffer with protein (bovine serum albumin) stabilizer.
- 1 bottle anti-HBs (mouse, monoclonal, IgG) and anti-HBs (goat IgG) acridinium-labeled conjugate in phosphate buffer with human plasma and protein (bovine serum albumin, fetal bovine serum, goat IgG, mouse IgG) stabilizers.
- 1 bottle ancillary wash buffer containing MES buffer.
- ProClin 300 and ProClin 950 were added as preservatives to each of the three components.

The ARCHITECT HBsAg Qualitative Confirmatory reagent kit is comprised of the following five components:

- 1 bottle anti-HBs (mouse, monoclonal, IgM, IgG) coated microparticles in MES buffer with protein (bovine serum albumin) stabilizer.
- 1 bottle anti-HBs (mouse, monoclonal, IgG) and anti-HBs (goat, IgG) acridinium-labeled conjugate in phosphate buffer with human plasma and protein (bovine serum albumin, fetal bovine serum, goat IgG, mouse IgG) stabilizers.
- 1 bottle ancillary wash buffer containing MES buffer.
- 1 bottle (2.4 mL) Pre-Treatment 1 containing recalcified human plasma reactive for anti-HBs.
- 1 bottle (2.4 mL) Pre-Treatment 2 containing recalcified human plasma.
- ProClin 300 and ProClin 950 were added as preservatives to each of the three components.

The ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent contains:

- 1 bottle of ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent. The manual diluent contains recalcified human plasma. Preservatives: ProClin 950 and sodium azide.

The ARCHITECT HBsAg Calibrators contain:

- 2 bottles of ARCHITECT HBsAg Qualitative Calibrators. Calibrator 1 contains inactivated purified human HBsAg (subtype ad) in phosphate buffer with human plasma and protein (bovine serum albumin) stabilizers. Preservatives: ProClin 300 and ProClin 950.
- Calibrator 2 contains recalcified human plasma. Preservatives: ProClin 950 and sodium azide.

The ARCHITECT HBsAg Controls contain:

- 2 bottles of ARCHITECT HBsAg Qualitative Controls. The Negative Control contains recalcified human plasma. Preservatives: ProClin 950 and sodium azide.
- The Positive Control contains inactivated purified human HBsAg (subtypes ad/ay) in phosphate buffer with human plasma and protein (bovine serum albumin) stabilizers. The positive control is blue and contains Acid Blue No. 9. Preservatives: ProClin 300 and ProClin 950.

In addition, the following components are required for the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory reagent kits:

- ARCHITECT *i* System is an analyzer designed to perform fully-automated immunoassay tests based on the use of CMIA detection technology.
- ARCHITECT *i* Pre-Trigger Solution contains 1.32% (w/v) hydrogen peroxide.
- ARCHITECT *i* Trigger Solution contains 0.35 N sodium hydroxide.
- ARCHITECT *i* Wash Buffer contains phosphate buffered saline solution. Preservatives: antimicrobial agents.

Assay Principle and Format

ARCHITECT HBsAg Qualitative

The assay is a one-step assay, ancillary wash buffer is added in a second incubation step, so the assay performs a two-step assay protocol. Sample, anti-HBs coated paramagnetic microparticles, and anti-HBs acridinium-labeled conjugate are combined to create a reaction mixture. HBsAg in the sample binds to the anti-HBs coated microparticles and the anti-HBs acridinium labeled conjugate. After washing, ancillary wash buffer is added to the reaction mixture. 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 direct relationship exists between the amount of HBsAg in the sample and the RLUs detected by the ARCHITECT system optics.
The presence or absence of HBsAg in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active calibration. If the chemiluminescent signal in the specimen is greater than or equal to the cutoff signal, the sample is considered reactive for HBsAg.

ARCHITECT HBsAg Qualitative Confirmatory
The assay consists of two single tests that are both one-step pre-treatment immunoassays. Ancillary wash buffer is added in a second incubation step, so the assay performs a two-step assay protocol. Sample and Pre-Treatment 1 reagent are combined in a reaction vessel (RV) and incubated. When HBsAg is present in the sample, it is neutralized by the anti-HBs in Pre Treatment 1. An aliquot of the pretreated sample, anti-HBs coated paramagnetic microparticles, and anti-HBs acridinium-labeled conjugate are combined to create a reaction mixture. Any non-neutralized HBsAg present in the sample binds to the anti-HBs coated microparticles and the anti-HBs acridinium labeled conjugate. The neutralized HBsAg is blocked from forming a sandwich with acridinium labeled anti-HBs conjugate and anti-HBs microparticles. After washing, ancillary wash buffer is added to the RV and incubated. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as RLUs. A direct relationship exists between the amount of HBsAg in the sample and the RLUs detected by the ARCHITECT system optics.
This sequence is repeated for the sample and Pre-Treatment 2 reagent, except Pre Treatment 2 does not contain anti-HBs and will not neutralize HBsAg in the sample. If the signal for the non-neutralized sample (incubated with Pre Treatment 2) result is greater than or equal to the cutoff of 0.70 S/CO and the signal of the neutralized sample (incubated with Pre Treatment 1) is reduced by at least 50% compared to the non-neutralized sample, the sample is considered confirmed positive for HBsAg.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

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

Alternative procedures for the detection of HBV in human adult and pediatric serum and plasma and neonatal serum 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 antigens and antibodies by

commercially available assays that are licensed or approved in the United States (US).

VII. MARKETING HISTORY

The ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory reagent kits, ARCHITECT HBsAg Qualitative Calibrators and Controls have not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

When used according to the instructions in the package insert, there are no known direct adverse effects of this device on the health of the user. Failure of the test to perform as indicated or human error during performance of the test may lead to a false diagnosis and improper patient management. Below is a list of the potential adverse effects associated with the use of the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory reagent kits, ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent, ARCHITECT HBsAg Qualitative Calibrators and Controls:

- Failure of the device to perform as indicated or human error in use of the device may lead to a false result.
- A false positive result using an HBsAg assay is not considered a patient or public health concern as a positive result in a clinical lab setting is usually followed up with supplemental testing. Either additional HBV marker testing is performed or an HBsAg positive result is confirmed by neutralization. An exception to this is using HBsAg tests to screen pregnant women for the presence of HBsAg. This testing helps to determine if a neonate is at high risk of acquiring HBV during the prenatal period.
- Pregnant women are tested during an early prenatal visit. If they are HBsAg nonreactive during this testing, and at high risk for HBV infection, they are re-tested during the third trimester. If the result is positive, it is recommended that hepatitis 3 immune globulin (HBIG) and vaccine be provided to the newborn within 12 hours of birth. If an assay is false positive and the newborn receives HBIG, the newborn would be exposed to the risks of receiving a human source product.
- The risks of a false negative result in a diagnostic setting are highest when testing pregnant women because HBsAg may be the only marker used. If the result is negative then the child is vaccinated within 2 months of birth. If the result is incorrect (false negative), then the neonate is at a higher risk of acute and chronic HBV infection, since HBIG and vaccine would not be provided within 12 hours of birth.

- From time to time false negative results due to gene mutation have been reported for the HBsAg assays produced by a number of different manufacturers. Because of the complexity of the mutations that can occur, no manufacturer can guarantee to detect all patients.
- A false positive result using an HBsAg confirmatory neutralization procedure is not considered a patient or public health concern because in order for a false positive to occur, the control sample (non-neutralized result) and the percent neutralization (in the neutralized tube) would both have to be incorrect for a reported false positive result. If this situation were to occur, the implications would be the same as described for false positive results for HBsAg assays
- A false negative result using an HBsAg confirmatory neutralization procedure could occur if the neutralized sample were incorrect either due to a falsely increased signal with the neutralized sample, or due to some other malfunction, laboratory or technician error when assayed. A falsely increased signal could be interpreted as a failure to neutralize. If this situation were to occur, the implications would be the same as described for false negative results for HBsAg.

IX. SUMMARY OF NONCLINICAL LABORATORY STUDIES

Nonclinical studies were performed at Abbott Laboratories to evaluate the performance characteristics of the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays. The studies are described below.

Assay Cutoff Determination

The presence or absence of HBsAg in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff RLU determined from an active ARCHITECT HBsAg Qualitative or ARCHITECT HBsAg Qualitative Confirmatory calibration. If the sample RLU is greater than or equal to the cutoff RLU, the sample is considered reactive for HBsAg. The ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assay results are expressed as a ratio (S/CO) of the sample RLU to the cutoff RLU. The S/CO is calculated using the equation:

S/CO = Sample RLU / Cutoff RLU.

To select the appropriate cutoff RLU for ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory, negative and known positive specimens were tested to optimize the sensitivity and specificity performance by varying the cutoff negative and positive multiplier factors.

The following cutoff RLU equation and assay cutoff were selected for ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays:

Cutoff RLU = (Cal 1 Mean RLU * 0.0575) + (Cal 2 Mean RLU * 0.8)

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

The value 0.70 S/CO was selected to be the ARCHITECT HBsAg Qualitative Confirmatory assay cutoff. This cutoff value was chosen to ensure the assay will detect a low-level reactive specimen from the ARCHITECT HBsAg Qualitative assay and compensates for the dilution effect of the assay pretreatment reagents on the specimen.

The confirmation of the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory cutoffs of 1.00 S/CO and 0.70 S/CO, respectively, was demonstrated through nonclinical laboratory studies (within-laboratory precision, seroconversion sensitivity, and analytical sensitivity) and the clinical investigation (system reproducibility and method comparison).

Within-Laboratory Precision (20-Day)

A 20-day precision study was conducted to evaluate the precision performance of the ARCHITECT HBsAg Qualitative assay based on guidance from the NCCLS document EP5-A2. Testing was performed on 3 ARCHITECT instruments (2 *i* 2000_{SR} and 1 *i* 2000) using 3 lots of reagents, 3 lots of calibrators, and 1 lot of controls. Each reagent lot was matched with a different lot of calibrator. A single calibration per reagent lot was performed on each instrument by testing the calibrators in replicates of 3. The calibration generated for each reagent lot was stored on each instrument for the duration of the study. The controls and panels were tested with a minimum of 2 replicates 2 times per day (separated by a minimum of 2 hours) for a total of 20 testing days.

The total imprecision across lots and instrument systems for the ARCHITECT HBsAg Qualitative assay was

- 2.1 to 2.9 %CV for the positive control
- 2.3 to 3.3 %CV for the low positive panel
- 2.2 to 2.9 %CV for the moderate positive panel, and
- The SD was 0.025 to 0.033 S/CO for the high negative panel

The results are summarized in the following table.

Table 1: ARCHITECT HBsAg Qualitative Within-Laboratory Precision (20-Day) S/CO Results

					Within-Run		Within-Laboratory Precision (Total)[a]	
Instrument	**Reagent Lot**	**Sample Level**	**n**	**Mean (S/CO)**	**SD**	**%CV**	**SD**	**%CV**
$i2000_{SR}$ (1)	1	Negative Control	118	0.18	0.012	NA	0.030	NA
		Positive Control	119	3.45	0.059	1.7	0.095	2.7
		High Negative Panel	119	0.77	0.022	2.9	0.033	4.3
		Low Positive Panel	119	1.27	0.028	2.2	0.039	3.1
		Moderate Positive Panel	118	3.63	0.071	1.9	0.093	2.6
	2	Negative Control	120	0.17	0.015	NA	0.030	NA
		Positive Control	119	3.44	0.068	2.0	0.099	2.9
		High Negative Panel	119	0.75	0.023	3.1	0.031	4.2
		Low Positive Panel	119	1.25	0.031	2.4	0.040	3.2
		Moderate Positive Panel	120	3.57	0.074	2.1	0.103	2.9
	3	Negative Control	120	0.15	0.012	NA	0.021	NA
		Positive Control	120	3.31	0.063	1.9	0.084	2.5
		High Negative Panel	120	0.72	0.023	3.2	0.031	4.4
		Low Positive Panel	120	1.20	0.032	2.7	0.039	3.3
		Moderate Positive Panel	120	3.40	0.060	1.8	0.088	2.6

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

Table 1(Continued)
ARCHITECT HBsAg Qualitative Within-Laboratory Precision (20-Day)
S/CO Results

					Within-Run		Within-Laboratory Precision (Total)[a]	
Instrument	**Reagent Lot**	**Sample Level**	**n**	**Mean (S/CO)**	**SD**	**%CV**	**SD**	**%CV**
i 2000$_{SR}$ (2)	1	Negative Control	119	0.17	0.012	NA	0.017	NA
		Positive Control	120	3.43	0.063	1.8	0.088	2.5
		High Negative Panel	120	0.75	0.023	3.0	0.025	3.3
		Low Positive Panel	120	1.26	0.026	2.1	0.029	2.3
		Moderate Positive Panel	119	3.61	0.066	1.8	0.082	2.3
	2	Negative Control	120	0.16	0.012	NA	0.016	NA
		Positive Control	120	3.43	0.059	1.7	0.086	2.5
		High Negative Panel	119	0.73	0.024	3.2	0.025	3.4
		Low Positive Panel	119	1.23	0.029	2.4	0.033	2.7
		Moderate Positive Panel	120	3.54	0.070	2.0	0.087	2.5
	3	Negative Control	119	0.15	0.012	NA	0.014	NA
		Positive Control	120	3.38	0.056	1.7	0.072	2.1
		High Negative Panel	120	0.72	0.021	2.9	0.027	3.7
		Low Positive Panel	119	1.22	0.032	2.7	0.038	3.1
		Moderate Positive Panel	120	3.47	0.063	1.8	0.075	2.2
i 2000	1	Negative Control	120	0.17	0.014	NA	0.025	NA
		Positive Control	120	3.28	0.073	2.2	0.077	2.3
		High Negative Panel	120	0.73	0.022	3.1	0.029	3.9
		Low Positive Panel	120	1.21	0.030	2.5	0.035	2.9
		Moderate Positive Panel	120	3.42	0.082	2.4	0.098	2.9

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

Seroconversion Sensitivity

A study was conducted to evaluate the seroconversion detection of the ARCHITECT HBsAg Qualitative assay and confirmation by the ARCHITECT HBsAg Qualitative Confirmatory assay. Thirty-eight (38) seroconversion panel sets of serial bleed panel members were tested using the ARCHITECT HBsAg Qualitative assay and confirmed (as warranted) using the ARCHITECT HBsAg Qualitative Confirmatory assay. The results were compared to the comparator HBsAg and HBsAg confirmatory results.

HBsAg was first detected by the ARCHITECT HBsAg Qualitative assay and confirmed by the ARCHITECT HBsAg Qualitative Confirmatory assay 2 to 15 days earlier than it was first detected by the comparator HBsAg assay in 17 seroconversion panel sets and coincident with the first day detected by the comparator HBsAg assay in 21 seroconversion panel sets.

A comparison of the number of days to reactive result for the ARCHITECT HBsAg Qualitative assay to the comparator HBsAg assay is presented in the following Table.

Table 2: Seroconversion Sensitivity
Days to First HBsAg Reactive Result
ARCHITECT HBsAg Qualitative and Confirmatory and
Comparator HBsAg and Confirmatory

Panel ID	Days to HBsAg Reactive Result from Initial Draw Date		Difference in Days to HBsAg Reactive Result (Comparator – ARCHITECT)
	Comparator HBsAg	ARCHITECT HBsAg Qualitative	
PHM909	9	9	0
PHM917	43	36	7
PHM925	8	4	4
PHM926	13	9	4
PHM927	4	4	0
PHM928	9	7	2
PHM929	18	14	4
PHM930	3	3	0
PHM933	7	7	0
PHM934	0	0	0
PHM935B	128	128	0
PHM935A(M2)	21	21	0
26982/14399	3	3	0
13867/3482	19	19	0
1807/3463	11	11	0

26022/14518	12	12	0
0994/3457	11	4	7
43527/3453	13	13	0
6271	7	7	0
6272	101	94	7
6273	25	25	0
6274	4	0	4
6275	22	7	15
11000	26	21	5
11001	44	44	0
11002	9	7	2
11003	142	142	0
11005	142	142	0
11006	51	42	9
11007	43	34	9
11008	72	69	3
11009	86	79	7
11011	110	103	7
11012	18	18	0
11013	252	247	5
11014	51	51	0
11016	27	27	0
11017	42	42	0

Analytical Sensitivity (Detectable Concentration at the Assay Cutoff)

The ARCHITECT HBsAg Qualitative assay is designed to have a mean analytical sensitivity value of less than or equal to 0.20 ng/mL (0.036 IU/mL). Analytical sensitivity was evaluated using serial dilutions of the WHO 2nd International HBsAg Standard (subtype *adw2*, genotype A, NIBSC Code 00/588).

The dilutions ranged from 0.01 to 0.50 IU/mL. HBsAg negative normal human serum or plasma was used as the diluent and represented the 0.00 IU/mL sample. The dilutions were tested across 3 reagent lots on 3 ARCHITECT instruments (2 *i* 2000_{SR} and 1 *i* 2000). The analytical sensitivity for ARCHITECT HBsAg Qualitative ranged from 0.017 to 0.022 IU/mL across the instruments.

In the analytical sensitivity study, the observed limit of detection (LoD), calculated per NCCLS document EP17-A, was less than or equal to 0.002 IU/mL across the instruments.

Genotype Detection

A study was performed to evaluate the ability of the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays to detect and confirm HBV genotypes A through H by testing a total of 19 genotype panel members.

HBV genotypes A through H were reactive by the ARCHITECT HBsAg Qualitative assay and confirmed positive by the ARCHITECT HBsAg Qualitative Confirmatory assay.

Mutant Detection

A study was performed to evaluate the ability of the ARCHITECT HBsAg Qualitative assay to detect HBsAg mutants. Each member of a panel of 9 HBsAg recombinant proteins containing defined mutations between amino acid positions 122 and 145 was diluted with recalcified negative human plasma to an S/CO of 2.0 ± 0.5. The panel was tested using the ARCHITECT HBsAg Qualitative assay.

All nine mutant samples were repeatedly reactive by ARCHITECT HBsAg Qualitative. The ARCHITECT HBsAg Qualitative assay demonstrated the ability to detect (as reactive) the HBsAg mutant Thr-123-Ala and to have the ability to detect (as reactive) other HBsAg mutants (including Gly-145-Arg) when compared to the comparator HBsAg assay.

Neonate Serum Evaluation

A study was conducted to characterize the performance of the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays with neonate serum. Cord blood serum was used as a surrogate for neonate serum. A minimum of 20 cord blood specimens and matched maternal serum specimens that were negative for HBsAg and anti-HBs activity were obtained. Each specimen was divided into two aliquots. A high negative sample (target: 0.80 S/CO) was prepared for one aliquot; a low positive sample (target: 1.20 S/CO) was prepared from the other aliquot. The high negative and low positive samples were tested using the ARCHITECT HBsAg Qualitative assay. The low positive samples were tested using the ARCHITECT HBsAg Qualitative Confirmatory assay.

For the ARCHITECT HBsAg Qualitative assay, each cord blood sample was compared to the corresponding maternal sample. For the high negative sample, the mean difference between the cord blood sample and the matched maternal sample was 0.04 S/CO with an upper one-sided 95% confidence limit of 0.05 S/CO. For the low positive sample, the mean percent difference between the cord blood sample and the matched maternal sample, was 3.1% with a lower one-sided 95% confidence limit of 1.5%.

All low positive samples were confirmed positive by the ARCHITECT HBsAg Qualitative Confirmatory assay.

This study supports the use of ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays with neonate serum.

Interferences – Bilirubin, Hemoglobin, Total Protein, and Triglycerides

A study was conducted to evaluate the susceptibility of the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays to potentially interfering substances based on guidance from the CLSI document EP7-A2.

At the concentrations listed below, the upper 95% confidence limits for the interferences from unconjugated bilirubin, conjugated bilirubin, hemoglobin, total protein, and triglycerides in the ARCHITECT HBsAg Qualitative assay were less than or equal to 0.15 S/CO shift for high negative samples and the lower 95% confidence limits were greater than or equal to -15% for low positive samples:

- Unconjugated bilirubin up to and including 20 mg/dL
- Conjugated bilirubin up to and including 20 mg/dL
- Hemoglobin up to and including 500 mg/dL
- Protein up to and including 12 g/dL
- Triglycerides up to and including 3000 mg/dL

Analytical Specificity – Medical Conditions and Other Disease States

The ARCHITECT HBsAg Qualitative assay was evaluated for potential cross-reactivity for specimens from individuals with other medical conditions. A list of the potential cross reactants tested and the results of the testing is presented in the following table.

Table 3: Cross Reactivity Study for the ARCHITECT HBsAg Qualitative and Confirmatory and Comparator HBsAg and Confirmatory

Category	N	Comparator HBsAg Assay			
		Negative/Not Confirmed		Positive [a]	
		ARCHITECT HBsAg Qualitative		ARCHITECT HBsAg Qualitative	
		Nonreactive	Reactive	Nonreactive	Reactive
Anti-nuclear antibodies (ANA)	10	10	0	0	0
Auto-immune hepatitis	10	10	0	0	0
C. trachomatis	7	7	0	0	0
Cytomegalovirus (CMV)	10	10	0	0	0
Epstein-Barr virus (EBV)	10	10	0	0	0
Fatty liver disease	10	10	0	0	0
Hemodialysis patient	10	10	0	0	0
Hepatitis A virus (HAV)	10	10	0	0	0
Hepatitis C virus (HCV)	10	10	0	0	0
Hepatocellular carcinoma	10	10	0	0	0
Herpes simplex virus (HSV)	10	10	0	0	0
HIV-1	10	10	0	0	0
HIV-2	17	14	0	0	3
Human anti-mouse antibodies (HAMA) positive	15	15	0	0	0
Human T-lymphotropic virus (HTLV-1/2)	9	9	0	0	0
IgG monoclonal gammopathy	10	10	0	0	0
IgM monoclonal gammopathy	10	10	0	0	0
Influenza vaccine recipients	10	10	0	0	0
Multiparous pregnancies	10	10	0	0	0
Multiple myeloma	10	10	0	0	0
Multiple transfusion recipients	10	10	0	0	0
N. gonorrhea	9	9	0	0	0

Pregnancy 1st trimester	15	15	0	0	0
Pregnancy 2nd trimester	14	14	0	0	0
Pregnancy 3rd trimester	15	15	0	0	0
Rheumatoid arthritis (RF)	10	10	0	0	0
T. cruzi	10	10	0	0	0
T. pallidum	10	10	0	0	0

All specimens were observed to be nonreactive with both the ARCHITECT HBsAg Qualitative and comparator HBsAg assays except for three specimens in the HIV-2 category that were HBsAg confirmed positive with the ARCHITECT HBsAg Qualitative and HBsAg positive with the comparator HBsAg assay. No discordant results were observed in this study.

Tube Type Interference

A study was conducted to evaluate which anticoagulants (blood collection tube types) are acceptable for use with the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays. The study was evaluated using samples from a minimum of 25 donors spiked with HBsAg positive stock to reach two analyte levels; high negative sample level of 0.8 S/CO (S/CO range: 0.60-0.99) and a low positive sample level of 1.2 S/CO (S/CO range 1.00- 1.40)

The data support the use of serum (including serum collected in serum separator tubes) and plasma collected in lithium heparin (including separator tubes), dipotassium EDTA, tripotassium EDTA, or sodium heparin in the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays. For all of these tube types the differences between the control tube type for the low positive samples was <15% and less than 0.15 S/CO for the high negative samples.

Sample Stability of Serum and Plasma

A study was conducted to evaluate the sample storage temperatures and number of freeze/thaw cycles for each blood collection tube type acceptable for use with the ARCHITECT HBsAg assay.

The data demonstrate that human serum (including serum collected in serum separator tubes) or plasma collected in lithium heparin (including separator tubes), potassium EDTA, or sodium heparin tubes may be used with the ARCHITECT HBsAg Qualitative assay when:

- Stored at 2 to 8°C for up to 6 days
- Stored at 15 to 30°C (room temperature) for up to 24 hours
- Subjected to up to 3 freeze/thaw cycles

Lithium heparin tube type may demonstrate higher S/CO values for low positive specimens after freeze/thaw.

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 HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays on one ARCHITECT *i* 2000_{SR} instrument.

The study was evaluated using negative samples spiked with HBsAg positive stock to reach two analyte levels; high negative sample level of 0.8 S/CO and a low positive sample level of 1.2 S/CO.

For the ARCHITECT HBsAg Qualitative Assay, the sample on board stability was acceptable if, when comparing samples stored on-board the instrument for > 3 hours to samples tested immediately upon loading on the instrument,

• the difference for the high negative sample was less than or equal to 0.15 S/CO

• the percent difference for the low positive sample was greater than or equal to -15%.

For the ARCHITECT HBsAg Qualitative Confirmatory Assay, the sample on board stability was acceptable if, when comparing the sample stored on-board the instrument for > 3 hours to the sample tested immediately upon loading on the instrument, there was no qualitative change on each low Positive Panel neutralized result.

For the ARCHITECT HBsAg Qualitative assay, the mean difference for the high negative sample is 0.02 S/CO, and the mean percent difference for the low positive sample is 5.7%. For the ARCHITECT HBsAg Qualitative Confirmatory assay, there were no qualitative changes to the low positive sample result interpretation.

The results support sample storage of up to 3 hours on board the ARCHITECT *i* System when tested using the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays.

Within-Assay Sample Carryover

A study was performed to evaluate the susceptibility of the ARCHITECT HBsAg Qualitative assay to within-assay sample carryover. Three replicates of wash buffer were tested to clear the system. A single replicate of an HBsAg negative sample was tested to serve as a sample that was not exposed to potential sample carryover (protected sample). This was followed by a single replicate of the HBsAg high positive sample (high sample, HBsAg concentration > 125,000 IU/mL), then by a single replicate of the HBsAg negative sample to serve as a sample exposed to potential sample carryover (unprotected sample). The sequence of wash buffer, protected negative sample, high sample, and unprotected negative sample was repeated an additional 11 times for a total of 12 iterations.

The difference between the unprotected negative sample mean and the protected negative sample mean was 0.10 S/CO for the ARCHITECT *i* 2000_{SR}, demonstrating the ARCHITECT HBsAg Qualitative assay is not susceptible to within-assay sample carryover.

High Dose Hook Effect

A study was performed to characterize the performance of the ARCHITECT HBsAg Qualitative assay when used to test specimens containing high levels of HBsAg that have the potential to cause a high dose hook effect. The study results also apply to the ARCHITECT HBsAg Qualitative Confirmatory assay since the microparticle, conjugate, and ancillary wash buffer reagents are identical between the two assays.

To perform the study two HBsAg-positive human plasma specimens with HBsAg concentrations of 3235 IU/mL and 53650 IU/mL were used as the positive stocks. Serial dilutions of the positive stock samples were prepared using recalcified HBsAg-negative human plasma. Each dilution level (undiluted through 1:100,000,000) and the recalcified HBsAg-negative human plasma were tested in a minimum of 12 replicates on one ARCHITECT *i* 2000SR instrument using one lot each of reagents, calibrators, and controls. The ARCHITECT HBsAg Qualitative assay was considered not susceptible to high dose hook effect if each positive stock tested at undiluted had a reactive result. Both of the positive stocks were reactive when tested undiluted.

The ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory interpretations are not impacted by high dose hook effect.

Stability Studies

All performance studies were conducted using the ARCHITECT *i* 2000/*i* 2000_{SR}

Systems.

ARCHITECT HBsAg Qualitative Reagent Developmental and Transport Simulation Stabilities

The developmental stability is an on-going study to establish the stability (expiration dating) of the ARCHITECT HBsAg Qualitative Reagents at the intended storage condition of 2 to 8°C and during on-board storage. Testing is performed on three lots of 100-test kit reagents and two lots of 500-test kit reagents.

In addition, the developmental stability includes the in-use condition. The in-use condition simulates customer use over time. In-use condition testing is performed on one lot of 100-test kit reagents.

The transport simulation study tests reagents after they have been subjected to potential ambient transport conditions. Transport simulation testing is performed on one lot of 100-test kit reagents.

The intended storage condition results provide evidence that the ARCHITECT HBsAg Qualitative Reagents will work as intended and will meet the specification performance requirements if given a shelf life of 8 months. The results generated for in use and on-board storage conditions also support 8 months of dating for ARCHITECT HBsAg Qualitative Reagents.

ARCHITECT HBsAg Qualitative Confirmatory Reagent Developmental and Transport Simulation Stability Studies

The developmental stability is an on-going study to establish the stability (expiration dating) of the ARCHITECT HBsAg Qualitative Confirmatory Reagents at the intended storage condition of 2 to 8°C and during on-board storage. Testing is performed on three lots of reagents.

In addition, the developmental stability includes the in-use condition. The in-use condition simulates customer use over time. In-use condition testing is performed on one lot of 100-test kit reagents.

The transport simulation study tests reagents after they have been subjected to potential ambient transport conditions. Transport simulation testing is performed on one lot of 100-test kit reagents.

The intended storage condition results provide evidence that the ARCHITECT HBsAg Qualitative Confirmatory Reagents will work as intended and will meet the specification performance requirements if given a shelf life of 8 months. The

results generated for in use and on-board storage conditions also support 8 months of dating for ARCHITECT HBsAg Qualitative Confirmatory Reagents.

ARCHITECT HBsAg Qualitative Calibrator and Control Developmental and Transport Simulation Stability Studies

The developmental stability studies are on-going studies to establish the expiration dating of the ARCHITECT HBsAg Qualitative Calibrators and Controls at the intended storage condition of 2 to 8°C. Intended storage stability testing is performed on three lots each of calibrators and controls.

In addition, the calibrator and control developmental stability includes the in-use condition. The in-use condition for the calibrators and controls simulates customer use over time. In-use condition testing is performed using one lot each of calibrators and controls.

The transport simulation study tests calibrators and controls after they have been subjected to potential ambient transport conditions. Transport simulation condition testing is performed using one lot each of calibrators and controls.

The intended storage condition results provide evidence that the ARCHITECT HBsAg Qualitative Calibrators and Controls will work as intended and will meet the specification performance requirements if given a shelf life of 8 months. The results generated for in use condition also support 8 months of dating for ARCHITECT HBsAg Qualitative Calibrators and Controls.

ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent Recommended Storage Stability

The ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent has the same formulation as the ARCHITECT HBsAg Qualitative Negative Control. Therefore, the data used to support the stability of the ARCHITECT HBsAg Qualitative Negative Control are also used to support the stability of the ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent.

Reagent On Board Evaluation

A study was performed to evaluate the performance of the ARCHITECT HBsAg Qualitative reagents when stored on board the ARCHITECT i 2000SR while the instrument was in continuous running mode (on board evaluation). A minimum of 17 time points were performed over at least a 31-day period.

Two controls and three panels were tested as follows:

• Negative Control

• Positive Control

• High negative panel with a target S/CO value of 0.80

• Low positive panel with a target S/CO value of 1.20

• Moderate positive (release) panel with a target S/CO value of 3.50

The reagent on board evaluation for the ARCHITECT HBsAg Qualitative assay was considered acceptable if the shift from baseline over the course of 30 days was

• < + 0.15 S/CO for the high negative panel

• > –15% for the positive control and low positive and release panels

Across all instruments, the test mean percent shifts ranged from -4.5% to 3.8% for the positive control, -3.2% to 3.0% for the low positive panel, and -3.3 % to 2.8% for the release panel. The test mean S/CO shifts ranged from 0.00 S/CO to 0.02 S/CO for the negative control and -0.03 S/CO to 0.04 S/CO for the high negative panel. The reference mean percent shifts ranged from -3.2% to 1.8% for the positive control, -4.3% to -0.4% for the low positive panel, and -5.5 % to -1.5% for the release panel. The reference mean S/CO shifts ranged from -0.01 to 0.06 S/CO for the negative control and -0.04 S/CO to 0.04 S/CO for the high negative panel.

The results support a 30 day reagent storage of the ARCHITECT HBsAg Qualitative reagent kit on board the ARCHITECT i System while the instrument is in continuous running mode.

Microbial Challenge Characterization

A Microbial Challenge Characterization (MCC) evaluation was performed for the ARCHITECT HBsAg Qualitative reagents, Calibrator, and Controls and ARCHITECT HBsAg Qualitative Confirmatory reagents. The MCC 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, to determine that the product is adequately protected.

The AET evaluation was performed to establish the level of antimicrobial protection provided by the preservative formulation of the ARCHITECT HBsAg Qualitative Reagents, Calibrators, and Controls and the ARCHITECT HBsAg

Qualitative Confirmatory Reagents and Manual Diluent. The ARCHITECT HBsAg Qualitative Calibrator 2 (LN 4P53Q-01) and the ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent (LN 4P54P-01) have the same formulation as the ARCHITECT HBsAg Qualitative Negative Control (LN 4P53L-01). Therefore, the results used to support the AET stability of the ARCHITECT HBsAg Qualitative Negative Control can be used to support the AET stability of the ARCHITECT HBsAg Qualitative Calibrator 2 and ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent.

The AET testing was performed per Abbott's procedures and based on guidance from the U.S. Pharmacopeia-National Formulary (USP-NF) General Chapter 51, Antimicrobial Effectiveness Test, to determine the concentrations and types of microbial organisms inoculated and evaluated in the test.

The AET test results classified the materials tested into three groups based on the observed microbial counts displayed. The groups were cidal, static or neither static or cidal. For all of the materials tested, the results were cidal for all microbial groups that were evaluated. For each study, the reference conditions for each on-test material showed no evidence of microbial growth throughout the study.

The MIC evaluation was performed to demonstrate the effect of the microbial bioburden and/or its by-products on the assay performance of the ARCHITECT HBsAg Qualitative Reagent. The on-test materials and their antimicrobial formulations were selected based on Abbott's procedures.

The ARCHITECT HBsAg Qualitative Reagents were considered not sensitive to a bioburden level of 103 to 104 CFU/mL if: for the positive control and each panel, the percent difference point estimate in S/CO units between the reference and test conditions was greater or equal to -15%, for the negative control, when each inoculated replicate S/CO was less than or equal to 0.85, and the difference of the test condition mean S/CO was less than or equal to + 0.15 S/CO from the reference condition mean S/CO. If the above criteria were not met, the ARCHITECT HBsAg Qualitative Reagents were considered sensitive to the bioburden level tested.

All individual negative control S/CO results were < 0.27 S/CO. The difference in negative control mean S/CO ranged from -0.01 to 0.01 S/CO. The positive control percent differences ranged from -2.1% to 1.6%. The ARCHITECT HBsAg Qualitative Reagents were not sensitive to any microbial organisms when inoculated at 103 to 104 CFU/mL.

The overall conclusion of the MCC evaluation indicated that the level of

antimicrobial protection provided by the preservative formulation for ARCHITECT HBsAg Qualitative Reagents, Calibrators, and Controls and ARCHITECT HBsAg Qualitative Confirmatory Reagents is adequate. In addition, the MCC results for the Negative Control apply to the ARCHITECT HBsAg Qualitative Calibrator 2 and ARCHITECT HBsAg Qualitative Confirmatory Manual Diluent.

X. SUMMARY OF CLINICAL STUDIES

A prospective multi-center study was conducted to evaluate the precision of the ARCHITECT HBsAg Qualitative assay and the agreement between the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays and a comparator HBsAg/HBsAg confirmatory assay using clinical specimens from the intended use diagnostic populations.

There were no adverse device events during the clinical investigation. The study was conducted at three clinical testing sites.

System Reproducibility (5-Day Precision)

A study was conducted to validate the precision performance of the ARCHITECT HBsAg Qualitative assay based on guidance from the NCCLS document EP5-A2 and CLSI document EP15-A2. Three lots each of ARCHITECT HBsAg Qualitative Reagents, Calibrators, and Controls were tested at each of three clinical testing sites. The ARCHITECT HBsAg Qualitative Negative Control and Positive Control, a high negative panel member (targeted to 0.80 S/CO), a low positive panel member (targeted to 1.20 S/CO), and a moderate positive panel member (targeted to 3.50 S/CO) were assayed in replicates of four at two separate times per day for five days. The results are presented in the following table

Table 4
ARCHITECT HBsAg Qualitative System Reproducibility (5-Day Precision)
All Sites, All Reagent Lots

ARCHITECT *i* 2000/*i* 2000$_{SR}$

Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)[a]		Precision with Additional Component of Between-Site[b]		Precision with Additional Component of Between-Lot[b]		Precision with Additional Components of Site and Lot (Overall)[b]	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Negative Control	360	0.17	0.028	NA	0.031	NA	0.031	NA	0.034	NA	0.034	NA	0.035	NA
Positive Control	360	3.45	0.066	1.9	0.070	2.0	0.073	2.1	0.087	2.5	0.137	4.0	0.137	4.0
High Negative	360	0.77	0.037	4.8	0.061	7.9	0.061	7.9	0.063	8.3	0.061	7.9	0.063	8.3
Low Positive	360	1.28	0.066	5.1	0.066	5.1	0.066	5.1	0.069	5.4	0.075	5.9	0.075	5.9
Moderate Positive	360	3.64	0.134	3.7	0.138	3.8	0.138	3.8	0.153	4.2	0.188	5.2	0.188	5.2

[a] Total variability contains within-run, between-run, and between-day variance components.
[b] Includes the lot-site interaction component.

Expected Results and Method Comparison

Description of Patient Population

Of the 2800 specimens tested and analyzed in the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory clinical study, 1279 specimens were from individuals at increased risk of HBV infection due to lifestyle, behavior, occupation, or known exposure event; 675 specimens were from individuals with signs and symptoms of hepatitis infection; 8 specimens were from subjects with clinically diagnosed acute HBV infection; 67 specimens were from subjects with clinically diagnosed chronic infection defined by the presence of HBsAg for >= 6 months; 29 specimens were classified as based on four-marker HBV reference testing; 22 specimens were classified as chronic based on four-marker HBV reference testing; and 720 specimens were from pregnant females.

Study Design

Each specimen was tested using the ARCHITECT HBsAg Qualitative assay and, if warranted, the ARCHITECT HBsAg Qualitative Confirmatory assay at one of the three clinical testing sites. Each specimen was also tested with the HBsAg and HBsAg confirmatory (where required) comparator methods at a reference laboratory.

Specimens from the increased risk of HBV infection, signs and symptoms of hepatitis infection, and acute and chronic HBV infection populations were also tested with three HBV reference assays, each detecting a unique serological marker (anti-HBc IgM, total anti-HBc, and anti-HBs). HBV classification was based on the reference marker patterns presented in Table 5. The classification used was a modification of the National Centers of Infectious Diseases of the Centers for Disease Control and Prevention (CDC) interpretation of Viral Hepatitis B Panel testing.

Supplemental testing was performed for specimen results that were discordant between the ARCHITECT HBsAg Qualitative and ARCHITECT HBsAg Qualitative Confirmatory assays and the comparator HBsAg and HBsAg confirmatory assays to better characterize the specimen.

Table 5: HBV Classification

HBV Reference Markers				
HBsAg	Anti-HBc IgM	Total Anti-HBc	Anti-HBs	HBV Classification
+	–	–	–	Acute
+	I	+	–	Acute
+	+	+	–	Acute
+	–	+	–	Chronic
+	–	+	+	Chronic
+	–	–	+	Chronic
+	+	+	+	Late acute/recovering [a]
–	+	+	+	Recovering acute
–	+	+	–	Recovering acute/undetectable HBsAg
–	+	–	+	Recovering acute
–	+	–	–	Possible recovering acute,
–	I	+	+	Distantly immune
–	I	+	–	Possible distantly immune, anti-HBs not
–	–	+	–	Distantly immune, anti-HBs not detected
–	–	+	+	Immune due to natural infection
–	–	–	+	Immune due to HBV vaccination
–	–	–	–	Susceptible

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

[a] One additional marker pattern was observed during the clinical study.

Expected Results

Increased Risk of HBV Infection Population

Of the 2800 specimens tested in the ARCHITECT HBsAg Qualitative clinical study, 1279 specimens were from individuals with increased risk of HBV infection. All 1279 individuals were at risk for HBV infection due to lifestyle, behavior, occupation, or a known exposure event but were asymptomatic and reported no current signs or symptoms of hepatitis.

The increased risk population (n=1279) consisted of the following race/ ethnic groups: 598 (46.76%) Caucasian, 470 (36.75%) African American, 159 (12.43%) Hispanic, 25 (1.95%) Asian, 2 (0.16%) American Indian/Alaska Native, and 25 (1.95%) were from other ethnic groups. Samples were collected from geographically diverse locations within the US.

The distribution of ARCHITECT HBsAg Qualitative results by age group and gender for the increased risk of HBV infection population is presented in the following table.

Table 6:
Assay Results by Age Range and Gender
Individuals at Increased Risk of HBV Infection

Age Range (Years)	Gender	ARCHITECT HBsAg Qualitative Result		Total
		Number of Reactive (%)	Number of Nonreactive (%)	
10 to 19	Female	1 (7.69)	12 (92.31)	13
	Male	2 (18.18)	9 (81.82)	11
20 to 29	Female	2 (1.12)	176 (98.88)	178
	Male	2 (1.36)	145 (98.64)	147
30 to 39	Female	3 (2.65)	110 (97.35)	113
	Male	8 (4.71)	162 (95.29)	170
40 to 49	Female	1 (0.63)	159 (99.38)	160
	Male	4 (1.90)	206 (98.10)	210
50 to 59	Female	5 (5.05)	94 (94.95)	99
	Male	12 (11.21)	95 (88.79)	107
60 to 69	Female	4 (11.11)	32 (88.89)	36
	Male	0 (0.00)	17 (100.00)	17
70 to 79	Female	0 (0.00)	5 (100.00)	5
	Male	0 (0.00)	9 (100.00)	9
80 to 89	Female	0 (0.00)	2 (100.00)	2
	Male	0 (0.00)	0 (0.00)	0
Unknown	Female	0 (0.00)	1 (100.00)	1
	Male	0 (0.00)	1 (100.00)	1
Total		*44 (3.44)*	*1235 (96.56)*	*1279*

Results – ARCHITECT HBsAg Qualitative

Increased Risk of HBV Infection and Signs and Symptoms of Hepatitis Infection Populations

Of the 2800 specimens tested and analyzed, 1954 specimens were from individuals at increased risk of HBV infection and signs and symptoms of hepatitis infection populations.

Specimens (n=1954) from these populations consisted of the race/ethnic groups: 970 (49.64%) Caucasian, 598 (30.60%) African American, 311 (15.92%) Hispanic, 40 (2.05%) Asian, 5 (0.26%) American Indian/Alaska Native, 30 (1.54%) Other.

The positive percent agreement between the ARCHITECT HBsAg Qualitative assay results and the comparator HBsAg assay final interpretation for the increased risk of HBV infection and signs and symptoms of hepatitis infection populations combined was 97.83% (90/92) with a 95% exact confidence interval of 92.37% to 99.74% while the negative percent agreement was 99.30% (1849/1862) with a 95% exact confidence interval of 98.81% to 99.63%.

The negative percent agreement and positive percent agreement results for the increased risk of HBV infection and signs and symptoms of hepatitis infection populations by HBV classification are presented in the following table.

Table 7
Percent Agreement by HBV Classification
Individuals at Increased Risk of HBV Infection and Individuals with Signs and Symptoms of Hepatitis Infection
ARCHITECT HBsAg Qualitative Interpretation and Comparator HBsAg Final Interpretation
N = 1954

HBV Classification	Positive Percent Agreement (%)	95% Confidence Interval (%)	Negative Percent Agreement (%)	95% Confidence Interval (%)
Acute	100.00 (7/7)	(59.04, 100.00)	NA	NA
Chronic	97.65 (83/85)	(91.76, 99.71)	NA	NA
Recovering Acute	NA	NA	100.00 (9/9)	(66.37, 100.00)
Recovering Acute, Undetectable HBsAg	NA	NA	100.00 (3/3)	(29.24, 100.00)
Distantly Immune, Anti-HBs Not Detected	NA	NA	97.44 (114/117)	(92.69, 99.47)
Immune Due to Natural Infection	NA	NA	98.21 (219/223)	(95.47, 99.51)
Immune Due to HBV Vaccination	NA	NA	100.00 (414/414)	(99.11, 100.00)
Susceptible	NA	NA	99.45 (1090/1096)	(98.81, 99.80)
Total	*97.83 (90/92)*	*(92.37, 99.74)*	*99.30 (1849/1862)*	*(98.81, 99.63)*

NA = Not Applicable

Acute and Chronic HBV Infection Populations

Of the 2800 specimens tested and analyzed, 126 were from pre-selected specimens from individuals with acute and chronic HBV infection.

The percent agreement between the ARCHITECT HBsAg Qualitative assay results and the comparator HBsAg assay final interpretation for the individuals with acute and chronic HBV infection is presented in the following table.

Table 8: Percent Agreement
Individuals with Acute or Chronic HBV Infection
ARCHITECT HBsAg Qualitative Interpretation and
Comparator HBsAg Final Interpretation

Specimen Category	Positive Percent Agreement (%)	95% Confidence Interval (%)	Negative Percent Agreement (%)	95% Confidence Interval (%)
Individuals with Acute HBV Infection	97.30 (36/37)	(85.84, 99.93)	NA	NA
Individuals with Chronic HBV Infection	100.00 (86/86)	(95.80, 100.00)	66.67 (2/3)	(9.43, 99.16)
Total	99.19 (122/123)	(95.55, 99.98)	66.67 (2/3)	(9.43, 99.16)

NA = Not Applicable

Comparison of Results

The ARCHITECT HBsAg Qualitative assay results were compared with the comparator HBsAg assay final interpretation for each of the HBV classifications for the increased risk of HBV infection and signs and symptoms of hepatitis infection populations (n = 1954) and the acute or chronic HBV infection populations (n=126). The results are presented in the following table.

Table 9: Comparison of Results
Individuals at Increased Risk of HBV Infection and
Signs and Symptoms of Hepatitis Infection
ARCHITECT HBsAg Qualitative Interpretation and
Comparator HBsAg Final Interpretation

HBV Classification	Comparator HBsAg Final Interpretation				Total
	Confirmed Positive [a]		Negative/Not Confirmed		
	ARCHITECT HBsAg Qualitative Result		ARCHITECT HBsAg Qualitative Result		
	Reactive	Nonreactive	Reactive	Nonreactive	
	N	N	N	N	N
Acute	47	1	0	0	48
Chronic	160	2	0	0	162
Late Acute, Recovering	5	0	0	0	5

Recovering Acute	0	0	0	9	9
Recovering Acute, Undetectable HBsAg	0	0	0	3	3
Distantly Immune, Anti-HBs Not Detected	0	0	3	115	118
Immune Due to Natural Infection	0	0	5	220	225
Immune Due to HBV Vaccination	0	0	0	414	414
Susceptible	0	0	6	1090	1096
Total	**212**	**3** [b]	**14** [c]	**1851**	**2080**

[a] The comparator HBsAg final positive interpretation includes retesting and confirmatory testing according to the comparator package inserts.

[b] All 3 specimens were positive for an additional marker (anti HBc, or anti-HBs) or had DNA present (assay sensitivity of 169 copies/mL).

[c] Of these 14 specimens, 1 specimen was not confirmed on the ARCHITECT HBsAg Qualitative Confirmatory assay, 10 specimens were positive for an additional marker (anti-HBc, anti HBs or anti-HBe) or had DNA present, and 3 specimens had no additional markers or DNA present.

Increased Risk Population Testing

In addition to the 1279 specimens from individuals at increased risk tested at 3 clinical sites, 498 specimens from hemodialysis patients were tested at Abbott Laboratories. The following table compares the ARCHITECT HBsAg Qualitative results and comparator HBsAg assay final interpretations for each risk factor for this overall increased risk population. The results are presented in the following table.

Table 10: Increased Risk Population Testing
ARCHITECT HBsAg Qualitative Interpretation and
Comparator HBsAg Final Interpretation

	Comparator HBsAg Assay Final Interpretation				
	Confirmed Positive		**Negative/Not Confirmed**		
	ARCHITECT HBsAg Qualitative Result		**ARCHITECT HBsAg Qualitative Result**		
Specimen Category	**Reactive (N)**	**Nonreactive (N)**	**Reactive (N)**	**Nonreactive (N)**	**Total (N)**
Multiple Sex Partners	23	1	3	876	903
Injecting Drug User (IDU)	2	0	1	116	119
Men who have Sex with Men (MSM)	1	0	1	9	11
Sexual Contact with HBV	2	0	0	22	24
Household Contact with HBV	6	0	0	43	49
Occupational Exposure Incident	2	0	1	163	166
Hemodialysis Patient	2	0	0	499	501 [a]
Perinatal Exposure to HBV	2	0	0	2	4

Total	**40**	**1**	**6**	**1730**	**1777**

[a] Of these 501 specimens, 3 specimens were tested at clinical sites and 498 specimens were tested at Abbott Laboratories.

Pregnant Female Population

For the pregnant female population (n=720), the positive percent agreement was 100.00% (1/1) with a 95% confidence interval of 2.50% to 100.00% and the negative percent agreement was 100.00% (719/719) with a 95% confidence interval of 99.49% to 100.00% for the ARCHITECT HBsAg Qualitative interpretation versus the comparator HBsAg final interpretation.

The pregnant female population (n=720) consisted of the following race/ ethnic groups: 48 (6.67%) Caucasian, 74 (10.28%) African American, 573 (79.58%) Hispanic, 15 (2.08%) Asian, 2 (0.28%) American Indian/Alaska Native, and 8 (1.11%) from other ethnic groups.

Pediatric Population

Of the 2800 specimens in the clinical study, 142 specimens were from a pediatric population aged 17 to 21. In addition, 68 specimens from pediatric individuals aged 4 to 18 who were at increased risk of HBV infection were tested at Abbott Laboratories.

The distribution of ARCHITECT HBsAg Qualitative reactive and nonreactive results by age range and gender is presented in the following table.

Table 12:
Assay Results by Age Range and Gender
Pediatric Specimens

Age Range (Years)	Gender	ARCHITECT HBsAg Qualitative Result		Total
		Reactive N (%)	Nonreactive N (%)	
>4 to 12	Female	1 (5.26)	18 (94.74)	19
	Male	0 (0.00)	22 (100.00)	22
>12 to 18	Female	0 (0.00)	23 (100.00)	23
	Male	0 (0.00)	7 (100.00)	7
>18 to 21	Female	2 (1.75)	112 (98.25)	114
	Male	3 (12.00)	22 (88.00)	25
Total		**6 (2.86)**	**204 (97.14)**	**210**

For the pediatric specimens (n=210);

The negative percent agreement NPA was 99.51% (203/204) with a 95% confidence interval of 97.30% to 99.99%

The positive percent agreement was 83.33% (5/6) with a 95% confidence interval of 35.88% to 99.58% for the ARCHITECT HBsAg Qualitative result versus the comparator HBsAg final interpretation.

Results – ARCHITECT HBsAg Qualitative Confirmatory

Of the 2800 specimens tested in this study, 234 specimens were tested using the ARCHITECT HBsAg Qualitative Confirmatory assay and/or comparator HBsAg confirmatory assay. The results are presented by specimen category in the following table.

Table 13:
Comparison of Results by Specimen Category
ARCHITECT HBsAg Qualitative Confirmatory Interpretation and
Comparator HBsAg Confirmatory Interpretation

Specimen Category	Comparator HBsAg Confirmatory Interpretation				Total
	Confirmed Positive [a]		Negative/Not Confirmed		
	ARCHITECT HBsAg Qualitative Confirmatory Interpretation		ARCHITECT HBsAg Qualitative Confirmatory Interpretation		
	Confirmed Positive	Negative/ Not Confirmed	Confirmed Positive	Negative/ Not Confirmed	
	N	N	N	N	N
Increased Risk of HBV Infection	37	2	5	4	48
Signs and Symptoms of Hepatitis Infection	52	1	7	1	61
Individuals with Acute HBV Infection	36	1	0	0	37
Individuals with Chronic HBV Infection	86	0	1	0	87
Pregnant Females	1	0	0	0	1
Total	**212**	**4**	**13**	**5**	**234**

[a] The comparator HBsAg final positive interpretation includes retesting and confirmatory testing according to the comparator package inserts.

Of the 234 specimens that required confirmation by either assay, 233 specimens from the increased risk of HBV infection, signs and symptoms of hepatitis infection, acute and chronic HBV infection populations were classified by HBV infection. The confirmatory results are presented by HBV classification in the following table.

Table 14: Comparison of Results by HBV Classification
Individuals at Increased Risk of HBV Infection, Individuals with Signs and Symptoms of Hepatitis Infection,
and Individuals with Acute or Chronic HBV Infection
ARCHITECT HBsAg Qualitative Confirmatory Interpretation and
Comparator HBsAg Confirmatory Interpretation

HBV Classification	Comparator HBsAg Confirmatory Interpretation				Total
	Confirmed Positive [a]		Negative/Not Confirmed		
	ARCHITECT HBsAg Qualitative Confirmatory Interpretation		ARCHITECT HBsAg Qualitative Confirmatory Interpretation		
	Confirmed Positive	Negative/Not Confirmed	Confirmed Positive	Negative/Not Confirmed	
	N	N	N	N	N
Acute	47	1	0	0	48
Chronic	159	3	0	0	162
Late Acute, Recovering	5	0	0	0	5
Distantly Immune, Anti-HBs Not Detected	0	0	3	1	4
Immune Due to Natural Infection	0	0	5	0	5
Immune Due to HBV Vaccination	0	0	0	1	1
Susceptible	0	0	5	3	8
Total	**211**	**4** [b]	**13** [c]	**5**	**233**

[a] The comparator HBsAg final positive interpretation includes retesting and confirmatory testing according to the comparator package inserts.

[b] All 4 specimens were positive for an additional marker (anti-HBc, or anti-HBs) or had DNA present (assay sensitivity of 169 copies/mL).

[c] Of these 13 specimens, 10 specimens were positive for an additional marker (anti-HBc, anti-HBs, or anti-HBe) or had DNA present and 3 specimens had no markers or DNA present.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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 FDA Microbiology Devices Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM NONCLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

As an *in-vitro* diagnostic test the ARCHITECT HBsAg Qualitative and the ARCHITECT HBsAg Qualitative Confirmatory involve removal of blood from an individual for testing purposes. The test, therefore, presents no more safety hazard to an individual being tested than other tests where blood is drawn.

False positive and false negative results are discussed in Section VIII. There were no adverse effects of the device reported while the study was conducted.

B. Effectiveness Conclusions

- The ARCHITECT HBsAg Qualitative and the ARCHITECT HBsAg Qualitative Confirmatory Assays demonstrated acceptable analytical sensitivity as determined by limit of detection studies comparing with the WHO International Standard and through seroconversion studies.
- The ARCHITECT HBsAg Qualitative precision around the assay cut-off and across the assay range was within acceptable limits (%CV less than 5% for internal repeatability and less than 10% for within laboratory reproducibility).
- The Assay demonstrated the analytical ability to detect all the HBV genotypes A through H and the ability to detect the HBsAg mutant Thr-123-Ala and other HBsAg mutants (including Gly-145-Arg) when compared to the comparator HBsAg assay
- The analytical specificity studies showed that there are no concerns with endogenous interferents at physiological levels, or with potential cross reactive agents.
- The Assays demonstrated equivalent performance with serum and plasma samples.
- Sample stability with the ARCHITECT HBsAg Qualitative assays was demonstrated to be valid for up to 7 days (2-8°C) or for 24 hours at 15-30°C and can withstand 3 freeze/thaw cycles.
- The claimed reagent stability information was adequately substantiated by analytical study results. The real-time stability information provided supports a shelf life of 8 month when stored at 2-8°C.
- The clinical performance was evaluated in an ethnically diverse population representative of the intended use population and representative of the different HBV classification groups. The positive and negative percent agreement values for both the ARCHITECT HBsAg Qualitative and the ARCHITECT HBsAg Qualitative Confirmatory assays were acceptable.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the instructions for use. The submitted clinical studies have shown that the ARCHITECT HBsAg Qualitative and the ARCHITECT HBsAg Qualitative Confirmatory Assays, when compared to

reference clinical laboratory procedures, has a similar ability to detect the presence of HBsAg in specimens from persons with signs and symptoms of hepatitis and in persons at risk for hepatitis B infection. The rate of false positivity and false negativity are within acceptable limits compared to the reference assay. It has been shown that the device has no demonstrable cross-reactivity with the majority of viruses or organisms that may cause clinical hepatitis. Therefore, this device should benefit the physician in the diagnosis and management of HBV.

XIII. CDRH DECISION

CDRH issued an approval order on April 12, 2012.

The applicant's manufacturing facilities were inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. 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.