

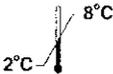
CORE

CUSTOMER SERVICE

UNITED STATES: 1-877-4ABBOTT

Caution: United States Federal Law restricts this device to sale and distribution by or on the order of a physician, or to a clinical laboratory; and use is restricted to, by, or on the order of a physician.

This package insert must be read carefully before product use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used	
REF	List Number
IVD	<i>In Vitro</i> Diagnostic Medical Device
	Store at 2-8°C
LOT	Lot Number
	Expiration Date
	Consult instructions for use
SN	Serial Number
REACTION VESSELS	Reaction Vessels
SAMPLE CUPS	Sample Cups
SEPTUMS	Septums
REPLACEMENT CAPS	Replacement Caps
REAGENT LOT	Reagent Lot
CONTROL NO.	Control Number

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NAME

ARCHITECT CORE

INTENDED USE

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.

Warning: 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.

Assay performance characteristics have not been established when the ARCHITECT CORE assay is used in conjunction with other manufacturers' assays for specific hepatitis markers. Users are responsible for establishing their own performance characteristics.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients. Users are responsible for establishing their own assay performance characteristics in these populations.

SUMMARY AND EXPLANATION OF THE TEST

The ARCHITECT CORE assay utilizes microparticles coated with recombinant hepatitis B virus core antigen (rHBcAg) for the detection of anti-HBc antibodies. Anti-HBc antibody determinations can be used as an indicator of current or past HBV infection. Anti-HBc antibodies are found in serum shortly after the appearance of hepatitis B surface antigen (HBsAg) in acute HBV infections. They will persist after the disappearance of HBsAg and before the appearance of detectable antibody to HBsAg (anti-HBs).¹⁷ In the absence of information about any other HBV markers, it must be considered that an individual with detectable levels of anti-HBc antibodies may be actively infected with HBV or that the infection may have resolved, leaving the person immune.¹⁸ Anti-HBc antibodies may be the only serological marker of HBV infection and potentially infectious blood.¹⁶

The presence of anti-HBc antibodies does not differentiate between acute or chronic hepatitis B infection.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

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. 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.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100/500 Tests

NOTE: Some kit sizes are not available for use on all ARCHITECT *i* Systems. Please contact your local distributor.

ARCHITECT CORE Reagent Kit (6L22)

- **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.
- **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.
- **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.
- **SPECIMEN DILUENT** 1 or 4 Bottle(s) (5.36 mL/23.72 mL) specimen diluent containing reductant in MOPSO buffer.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-trigger solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger solution containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

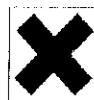
- **WASH BUFFER** Wash buffer containing phosphate buffered saline solution. Preservative: antimicrobial agent.

WARNINGS AND PRECAUTIONS

- **For In Vitro Diagnostic Use.**

Safety Precautions

- **CAUTION: This product requires the handling of human specimens. It is recommended that all human sourced materials are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens¹⁷. Biosafety Level 2¹⁸ or other appropriate biosafety practices^{19,20} should be used for materials that contain or are suspected of containing infectious agents.**
- The ARCHITECT CORE Microparticles contain methylisothiazolones, which are components of ProClin, and are classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



- R43 May cause sensitization by skin contact.
- S24 Avoid contact with skin.
- S35 This material and its container must be disposed of in a safe way.
- S37 Wear suitable gloves.
- S46 If swallowed, seek medical advice immediately and show this container or label.

- The ARCHITECT CORE Assay Diluent contains methylisothiazolones, which are components of ProClin, and polyethylene glycol octylphenyl ether, which is a component of Triton X. The ARCHITECT CORE Assay Diluent is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



- R36 Irritating to eyes.
- R43 May cause sensitization by skin contact.
- S24 Avoid contact with skin.
- S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
- S35 This material and its container must be disposed of in a safe way.
- S37 Wear suitable gloves.
- S39 Wear eye/face protection.
- S46 If swallowed, seek medical advice immediately and show this container or label.

- The conjugate contains sodium azide. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagents beyond the expiration date.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Before loading the ARCHITECT CORE Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- **To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.**
- **When handling conjugate vials, change gloves that have contacted human serum or plasma, since introduction of human antibody will result in a neutralized conjugate.**
- Once a septum has been placed on the reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- 
- 2°C** The ARCHITECT CORE Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
 - When stored and handled as directed, the reagents are stable until the expiration date.
 - The ARCHITECT CORE Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
 - Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, initiate a scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- This test is designed for use on the ARCHITECT *i* Systems (*i* 2000 and *i* 2000_{enh}).
- The ARCHITECT CORE assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* System Assay CD-ROM before performing the assay. For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

- The following specimen tube types were verified for use with the ARCHITECT CORE assay:

Glass	Plastic
<ul style="list-style-type: none"> Serum 	<ul style="list-style-type: none"> Serum Serum separator Lithium heparin plasma separator Sodium heparin Dipotassium EDTA

- Assay performance characteristics have not been established for any specimen matrices other than serum or plasma (dipotassium EDTA, lithium heparin, sodium heparin).
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT CORE assay.

Specimen Conditions

- Do not use specimens with the following conditions:
 - heat-inactivated
 - pooled
 - grossly hemolyzed
 - obvious microbial contamination
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum and plasma.
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.** Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.

- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at > 10,000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
 - they contain fibrin, red blood cells, or other particulate matter or
 - they were frozen and thawed.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.
- Transfer clarified specimen to a sample cup or secondary tube for testing.

Storage

- Specimens may be stored on or off the clot, red blood cells, or separator gel for
 - up to 3 days at room temperature (study performed at 23 to 30°C) or
 - up to 7 days at 2-8°C.
- If testing will be delayed more than 3 days for specimens stored at room temperature or more than 7 days for specimens stored at 2-8°C, remove serum or plasma from the clot, red blood cells, or separator gel and store at -20°C or colder.
- Avoid more than three freeze/thaw cycles.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped ambient, at 2-8°C (wet ice), or frozen (dry ice). Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided:

- 6L22 ARCHITECT CORE Reagent Kit

Materials Required but not Provided:

- ARCHITECT *i* System
- ARCHITECT *i* System Assay CD-ROM
- 6L22-01 ARCHITECT CORE Calibrator
- 6L22-10 ARCHITECT CORE Controls (or other control material)
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUMS**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the specified volumes.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT CORE Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
 - Invert the microparticle bottle 30 times.**
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
 - If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
 - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Handling Precautions** section of this package insert.

- Load the ARCHITECT CORE Reagent Kit on the ARCHITECT *i* System.
 - Verify that all necessary reagents are present.
 - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
 - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
 - If utilizing ARCHITECT system software version 5.0 or higher, refer to the ARCHITECT System Operations Manual, Section 5 for information on ordering patient specimens and controls.
 - If utilizing an ARCHITECT system software version lower than 5.0, use the following instructions to order patient specimens and controls:
 - For information on ordering patient specimens and the positive control and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
 - Use the following instructions to order a negative control (nonreactive for anti-HBc antibodies):
 - Order a negative control as a patient specimen, not as a Control.
 - Manually verify the validity of the negative control every time it is run. Because the control is run as a patient specimen, a result will not be flagged by the ARCHITECT *i* System if it is outside the acceptable control range.
- To troubleshoot control values that fall outside the control range, refer to the ARCHITECT System Operations Manual, Section 10.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
 - Priority: 75 µL for first CORE test plus 25 µL for each additional CORE test from the same sample cup.
 - ≤ 3 hours on board: 150 µL for the first CORE test plus 25 µL for each additional CORE test from the same sample cup.
 - > 3 hours on board: Replace with a fresh sample (patient specimens, controls, and calibrator).
 - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrator and controls.
 - Mix the ARCHITECT CORE Calibrator and Controls by gentle inversion before use.
 - To obtain the recommended volume requirements for the ARCHITECT CORE Calibrator and Controls, hold the bottles **vertically** and dispense 5 drops of the calibrator or 4 drops of each control into each respective sample cup.
- Load samples.
 - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. When a laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedure

- Specimens cannot be diluted for the ARCHITECT CORE assay.

Calibration

- To perform an ARCHITECT CORE calibration, test the calibrator in triplicate. The calibrator should be priority loaded.
- A single sample of each control level must be tested to evaluate the assay calibration.
 - Order controls as described above.
 - Ensure that assay control values are within the S/CO ranges specified in the control package insert.
- Once an ARCHITECT CORE calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
 - A reagent kit with a new lot number is used.
 - Controls are out of range.

QUALITY CONTROL PROCEDURES

The ARCHITECT CORE Controls are in a serum matrix made from recalcified plasma. The user should provide alternate control material for plasma when necessary.

The recommended control requirement for the ARCHITECT CORE assay is that a single sample of each control level be tested once every 24 hours each day of use. Additional controls may be tested in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Control values must be within the ranges specified in the control package insert. If a control result is confirmed to be out of its specified range, any test results generated since the last acceptable control results must be evaluated to determine if test results may have been adversely affected.^{21,22} Adversely affected test results are invalid, and these samples must be retested. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

RESULTS

Calculations

- 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 CORE Calibrator 1 mean RLU by 1.0.

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

- The ARCHITECT *i* System calculates the S/CO result for each specimen and control as follows:

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

Interpretation of Results

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 HBV; anti-HBc antibodies were detected in the sample which suggests either on-going or previous HBV infection.

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- Current methods for the detection of anti-HBc antibodies may not detect all infected individuals. A nonreactive test result does not exclude the possibility of exposure to or infection with HBV.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).^{23,24} Such specimens may show either falsely elevated or depressed values when tested with assay kits (such as ARCHITECT CORE) that employ mouse monoclonal antibodies.²³
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.²⁵ Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert for specimen limitations.

EXPECTED RESULTS

Due to geographic locations or demographics, assay results obtained in individual laboratories may vary from data presented.

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. Testing of these specimens was performed at three clinical sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

The increased risk population (n=1,254) consisted of the following race/ethnic groups:

- 635 (50.64%) Caucasian
- 385 (30.70%) African-American
- 177 (14.11%) Hispanic
- 28 (2.23%) Asian
- 2 (0.16%) American Indian/Alaska Native
- 25 (1.99%) Other
- 2 (0.16%) Unknown

The 1,254 specimens from the increased risk population were obtained from the following collection locations:

- 399 (31.82%) from St. Petersburg, FL
- 250 (19.94%) from Galveston, TX
- 163 (13.00%) from Dallas, TX
- 121 (9.65%) from Miami, FL
- 111 (8.85%) from Plymouth, MA
- 94 (7.50%) from Chicago, IL
- 49 (3.91%) from Denver, CO
- 34 (2.71%) from High Point, NC
- 33 (2.63%) from Colton, CA

A total of 231 (18.42%) specimens in the increased risk population were reactive in the ARCHITECT CORE assay. The number of ARCHITECT CORE reactive results observed for the increased risk population at each collection location was:

- 67 (16.79%) from St. Petersburg, FL
- 28 (11.20%) from Galveston, TX
- 29 (17.79%) from Dallas, TX
- 34 (28.10%) from Miami, FL
- 19 (17.12%) from Plymouth, MA
- 38 (40.43%) from Chicago, IL
- 13 (26.53%) from Denver, CO
- 0 (0.00%) from High Point, NC
- 3 (9.09%) from Colton, CA

Of the 1,254 specimens, 590 (47.05%) were female and 664 (52.95%) were male. The age was not reported for two specimens. Of the remaining 1,252 specimens, the mean age was 39 years (age range: 17 to 82 years). The distribution of ARCHITECT CORE reactive and nonreactive results among the increased risk population by age and gender (n=1,254) is summarized in the following table.

Age Group (years)	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
10-19	F	1 (7.69)	12 (92.31)	13
	M	1 (12.50)	7 (87.50)	8
20-29	F	13 (7.22)	167 (92.78)	180
	M	6 (4.41)	130 (95.59)	136
30-39	F	8 (6.72)	111 (93.28)	119
	M	26 (14.53)	153 (85.47)	179
40-49	F	37 (25.00)	111 (75.00)	148
	M	51 (24.29)	159 (75.71)	210
50-59	F	18 (20.93)	68 (79.07)	86
	M	37 (36.63)	64 (63.37)	101
60-69	F	14 (40.00)	21 (60.00)	35
	M	9 (46.00)	11 (55.00)	20
70-79	F	3 (60.00)	2 (40.00)	5
	M	6 (66.67)	3 (33.33)	9
80-89	F	1 (33.33)	2 (66.67)	3
	M	0 (0.00)	1 (100.00)	1
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

SPECIFIC PERFORMANCE CHARACTERISTICS

Assay results obtained in individual laboratories may vary from data presented.

Precision

The ARCHITECT CORE assay is designed to have a Total CV of $\leq 10\%$ for the ARCHITECT CORE Positive Control and a low positive panel targeted to 1.20 S/CO, and less than or equal to a total SD of 0.10 S/CO for a high negative panel targeted to 0.80 S/CO.

System Reproducibility

A five-day precision study was performed for the ARCHITECT CORE assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP15-A2.²⁶ Testing was conducted at three clinical sites using three lots each of ARCHITECT CORE Reagents, Calibrator, and Controls per site. Two levels of controls and panels were assayed in replicates of four at two separate times of day for 5 days. The data are summarized in the following table.

Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)		Precision with Additional Component of Between-Site*		Precision with Additional Component of Between-Lot*		Precision with Additional Components of Site and Lot (Overall)*	
			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	NA	0.015	NA	0.015	NA	0.020	NA	0.039	NA	0.041	NA

NA = not applicable

* Includes site-lot interaction variance component.

Within-Laboratory Precision

A 20-day precision study was performed for the ARCHITECT CORE assay based on guidance from the CLSI document EP5-A2.²⁷ Testing was conducted at Abbott Laboratories using three ARCHITECT CORE assay reagent lots, three calibrator lots, one control lot, and two instruments. Two levels of controls and panels were assayed in replicates of three (to obtain a minimum of two replicates) at two separate times of day for 20 different days. The data are summarized in the following table.

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	NA	0.018	NA
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	NA	0.015	NA

NA = not applicable

Clinical Performance

A prospective multi-center study was conducted to evaluate the ability of the ARCHITECT CORE assay to detect IgG and IgM antibodies to anti-HBc in a group of individuals that would normally be tested in a clinical situation. Of the 2,259 specimens tested and analyzed in the ARCHITECT CORE clinical study, 1,254 specimens were obtained from individuals living in the United States with increased risk of HBV infection due to lifestyle, behavior, occupation, disease state, or a known exposure event, and 625 specimens were obtained from individuals living in the United States exhibiting signs and symptoms of hepatitis infection (Population 1).

The 1,879 specimens in Population 1 were obtained from the following collection locations:

- 470 (25.01%) from St. Petersburg, FL
- 329 (17.51%) from Chicago, IL
- 278 (14.80%) from Galveston, TX
- 264 (14.05%) from Dallas, TX
- 182 (9.69%) from Miami, FL
- 176 (9.37%) from Denver, CO
- 111 (5.91%) from Plymouth, MA
- 35 (1.86%) from Colton, CA
- 34 (1.81%) from High Point, NC

Population 1 (n=1,879) consisted of the following race/ethnic groups:

- 937 (49.87%) Caucasian
- 531 (28.26%) African-American
- 323 (17.19%) Hispanic
- 48 (2.55%) Asian
- 4 (0.21%) American Indian/Alaska Native
- 34 (1.81%) Other
- 2 (0.11%) Unknown

Of the 1,879 specimens in Population 1, 850 (45.24%) were female and 1,029 (54.76%) were male. The age was not reported for two specimens. Of the remaining 1,877 specimens, the mean age was 42 years (age range: 17 to 83 years).

Specimens were also prospectively collected in Vietnam from 97 individuals at increased risk of HBV infection and 127 individuals with signs and symptoms of hepatitis infection (Population 2). The 224 specimens in Population 2 were 100.00% Vietnamese, and 124 (55.36%) were female and 100 (44.64%) were male. The mean age was 37 years (age range: 18 to 68 years).

Each specimen was tested using a comparator anti-HBc assay and three HBV reference assays, each detecting a unique serological marker (HBsAg, IgM anti-HBc, and anti-HBs). The HBV classification was determined for each specimen based on the reactivity patterns of the four HBV serological marker results. The comparator and reference assays were from a single manufacturer and during the clinical study, all comparator and reference testing was performed following manufacturer's instructions. Each specimen was also tested at one of three clinical sites located in Galveston, TX; Hershey, PA; or Milwaukee, WI using the ARCHITECT CORE assay.

Results by Specimen Classification

Following testing with the comparator anti-HBc assay and the three reference HBV assays, Population 1 specimens were assigned an HBV classification using the reactive (+) and nonreactive (-) patterns. There were 15 unique reference marker patterns observed in the ARCHITECT CORE clinical study for Population 1.

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

† Indeterminate

Following testing with the comparator anti-HBc assay and the three reference HBV assays, Population 2 specimens were assigned an HBV classification using the reactive (+) and nonreactive (-) patterns. There were 10 unique reference marker patterns observed in the ARCHITECT CORE clinical study for Population 2.

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

† Indeterminate

Comparison of Results

The following table compares the ARCHITECT CORE assay results with comparator anti-HBc assay results for each of the HBV classifications for Population 1. The data are summarized in the following table.

HBV Classification	Anti-HBc Comparator				Total
	Reactive		Negative		
	ARCHITECT CORE Interpretation		ARCHITECT CORE Interpretation		
	Reactive n (%)	Nonreactive n (%)	Reactive n (%)	Nonreactive n (%)	
Early Acute	0 (0.00)	0 (0.00)	4 (0.21) ^a	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 (0.32) ^b	0 (0.00)	0 (0.00)	219 (11.66)
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 (0.27) ^c	0 (0.00)	0 (0.00)	107 (5.69)
Immune Due to HBV Vaccination	0 (0.00)	0 (0.00)	17 (0.90) ^d	324 (17.24)	341 (18.15) ^e
Susceptible	0 (0.00)	0 (0.00)	7 (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 (0.11) ^f	50 (2.66)	52 (2.77)
Total	455 (24.22)	11 (0.59)	30 (1.60)	1363 (73.60)	1879 (100.00)

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- 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.
- 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.
- 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. 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, positive for anti-HBe, equivocal 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 HBV DNA; 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.
- 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.
- 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.

The following table compares the ARCHITECT CORE assay results with comparator anti-HBc assay results for each of the HBV classifications for Population 2. The data are summarized in the following table.

HBV Classification	Anti-HBc Comparator				
	Reactive		Negative		Total
	ARCHITECT CORE Interpretation		ARCHITECT CORE Interpretation		
Reactive n (%)	Nonreactive n (%)	Reactive n (%)	Nonreactive 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 (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 (8.48)	21 (9.38)	40 (17.86)
Susceptible	0 (0.00)	0 (0.00)	3 (1.34)	28 (12.50)	31 (13.84)
Total	151 (67.41)	0 (0.00)	23 (10.27)	50 (22.32)	224 (100.00)

- 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.
- 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.
- Although serological HBV classification indicates immune due to HBV vaccination, all 40 were recorded as not vaccinated.
- 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 table below summarizes the percent agreement between ARCHITECT CORE and the comparator anti-HBc assay for Population 1 by HBV classification.

HBV Classification	Positive Percent Agreement %	95% Confidence Interval	Negative Percent Agreement %	95% Confidence Interval
Early Acute	NA	NA	71.43 (10/14)	41.90 - 91.61
Acute	100.00 (11/11)	71.51 - 100.00	NA	NA
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	NA	NA
Recovering Acute/Undetectable HBsAg	100.00 (4/4)	39.76 - 100.00	NA	NA
Immune Due to Natural Infection	97.26 (213/219)	94.13 - 98.99	NA	NA
Distantly Immune/Anti-HBs Unknown	100.00 (37/37)	90.51 - 100.00	NA	NA
Distantly Immune/Anti-HBs Not Detected	95.33 (102/107)	89.43 - 98.47	NA	NA
Immune Due to HBV Vaccination	NA	NA	95.01 (324/341)	92.14 - 97.07
Susceptible	NA	NA	99.30 (997/1004)	98.57 - 99.72
Early Recovery	100.00 (1/1)	2.50 - 100.00	NA	NA
Unknown	NA	NA	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

NA - not applicable

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

The table below summarizes the percent agreement between ARCHITECT CORE and the comparator anti-HBc assay for Population 2 by HBV classification.

HBV Classification	Positive Percent Agreement %	95% Confidence Interval	Negative Percent Agreement %	95% Confidence Interval
Early Acute	NA	NA	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	NA	NA
Distantly Immune/Anti-HBs Unknown	100.00 (5/5)	47.82 - 100.00	NA	NA
Distantly Immune/Anti HBs Not Detected	100.00 (16/16)	79.41 - 100.00	NA	NA
Immune Due to HBV Vaccination	NA	NA	52.50 (21/40)	36.13 - 68.49
Susceptible	NA	NA	90.32 (28/31)	74.25 - 97.96
Total	100.00 (151/151)	97.59 - 100.00	68.49 (50/73)	56.56 - 78.87

NA - not applicable

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

Percent of Positive Specimens and Percent Agreement for Individuals Diagnosed with Acute and Chronic HBV Infection

The performance of the ARCHITECT CORE assay was evaluated by testing prospectively-collected specimens from six individuals diagnosed with acute HBV infection and 50 individuals diagnosed with chronic HBV infection. Acute status was defined for the six specimens by the four HBV serological marker results. The percent of positive ARCHITECT CORE specimens for individuals with documented 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 with documented 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.

For the surplus pediatric specimens, the negative percent agreement between the ARCHITECT CORE assay results and the comparator anti-HBc assay results was 98.99% (98/99, with a 95% confidence interval of 94.50% to 99.97%). The positive percent agreement between the ARCHITECT CORE assay results and the comparator anti-HBc assay results was 100.00% (1/1, with a 95% confidence interval of 2.50% to 100.00%). The distribution of the ARCHITECT CORE reactive and nonreactive results for the surplus pediatric population is summarized by age and gender in the following table.

Age Group (years)	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
2-12	F	0 (0.00)	17 (100.00)	17
	M	0 (0.00)	33 (100.00)	33
13-18	F	0 (0.00)	22 (100.00)	22
	M	2 (18.18)	9 (81.82)	11
19-21	F	0 (0.00)	12 (100.00)	12
	M	0 (0.00)	5 (100.00)	5
Total		2 (2.00)	98 (98.00)	100

For the prospectively-collected pediatric specimens (Population 1, Population 2, and chronic specimens), the negative percent agreement between the ARCHITECT CORE assay results and the comparator anti-HBc assay results was 96.63% (86/89, with a 95% confidence interval of 90.46% to 99.30%). The positive percent agreement between the ARCHITECT CORE assay results and the comparator anti-HBc assay results 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 prospectively-collected pediatric population is summarized by age and gender in the following table.

Age Group (years)	Gender	ARCHITECT CORE Result		Total
		Reactive n (%)	Nonreactive n (%)	
2-18	F	1 (25.00)	3 (75.00)	4
	M	2 (50.00)	2 (50.00)	4
19-21	F	17 (28.81)	42 (71.19)	59
	M	6 (13.33)	39 (86.67)	45
Total		26 (23.21)	86 (76.79)	112

Analytical Specificity

The ARCHITECT CORE assay was evaluated for potential cross-reactivity for specimens from individuals with medical conditions unrelated to HBV infection. The specimens were tested using the ARCHITECT CORE assay and the comparator anti-HBc assay. The final results for each of the specimens were compared between the two assays. The data are summarized in the following table.

**Reactivity of the ARCHITECT CORE Assay
in Individuals with Medical Conditions Unrelated to HBV Infection**

Category	n	Comparator Anti-HBc Assay			
		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 ^a	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 ^a	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
Rubcola 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 Virus (anti-VZV positive)	10	8	0	0	2
Yeast infection	9	8	0	0	1
Total	153	125	0	2	26

^a NR = Nonreactive, R = Reactive

^a 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.

Carryover

The ARCHITECT CORE assay was evaluated for susceptibility to within-assay sample carryover by comparing the results of a high anti-HBc sample with a concentration of approximately 7,763 Paul-Ehrlich-Institute (PEI) units/mL tested before a low anti-HBc sample with a target S/CO value of 0.80 (S/CO range: 0.60 to 0.99). HBV positive specimens up to 7,763 PEI units/mL caused less than an average of 0.05 S/CO change in subsequent test results, indicating that no within-assay sample carryover was present.

Analytical Sensitivity

The ARCHITECT CORE assay is designed to have an analytical sensitivity of < 1.0 PEI units/mL. The analytical sensitivity of the ARCHITECT CORE assay was determined using four-PEI standard member panels that were tested with three reagent lots using each of three calibrator lots. The ARCHITECT CORE mean analytical sensitivity 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.

Interference

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

- Bilirubin < 20 mg/dL
- Hemoglobin < 500 mg/dL
- Total Protein < 12 g/dL
- Triglycerides < 3000 mg/dL

Tube Type Matrix Comparison

The following tube types are acceptable for use with the ARCHITECT CORE assay:

- Glass: serum
- Plastic: serum, serum separator, lithium heparin plasma separator, sodium heparin, and dipotassium EDTA

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 the following table.

Tube Type	Distribution of Absolute % Differences	
	≤ 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)

Seroconversion Panels

The ability of the ARCHITECT CORE assay to detect anti-HBc was evaluated by testing seven seroconversion panels obtained from two commercial vendors across three ARCHITECT CORE reagent lots. 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. The data for all three reagent lots are summarized in the following table.

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 evaluate whether neonate samples may be tested with the ARCHITECT CORE assay. Cord blood serum was used as a surrogate for neonate serum. Twenty two matched cord blood and maternal serum samples were spiked with anti-HBc positive stock to yield a high negative sample (target S/CO 0.80) and a low positive sample (target S/CO 1.20). The distribution of the percent differences per analyte level is listed in the following table.

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)

BIBLIOGRAPHY

1. Hoofnagle JH, Gerety RJ, Barker LF. Antibody to hepatitis-B-virus core in man. *Lancet* 1973;ii:869-73.
2. Szmuness W, Hoofnagle JH, Stevens CE, et al. Antibody against the hepatitis type B core antigen. A new tool for epidemiologic studies. *Am J Epidemiol* 1976;104(3):256-62.
3. Hoofnagle JH, Seef LB, Buskell-Bales Z, et al. Serologic responses in HB. In: Vyas GN, Cohen SN, Schmid R, editors. *Viral Hepatitis*. Philadelphia, PA: Franklin Institute Press; 1978:219-42.
4. Krugman S, Overby LR, Mushahwar IK, et al. Viral hepatitis, type B: Studies on natural history and prevention re-examined. *N Engl J Med* 1979;300(3):101-6.
5. Zito DR, Gurdak RG, Tucker FL, et al. Hepatitis B virus serology: Loss of antibody to surface antigen. *Am J Clin Pathol* 1987;88(2):229-31.
6. Gillin N. Hepatitis B: Diagnosis, Prevention, and Treatment. *Clin Chem* 1997;43(8B):1500-6.
7. Koff RS. Viral Hepatitis. In: Schiff I, Schiff ER, editors. *Diseases of the Liver*. 7th ed. Philadelphia: JB Lippincott, 1993:492-577.
8. Dodd RY, Popovsky MA, Members of the Scientific Section Coordinating Committee. Antibodies to hepatitis B core antigen and the infectivity of the blood supply. *Transfusion* 1991;31(5):443-9.
9. Seef LB, Beebe GW, Hoofnagle JH, et al. A serologic follow-up of the 1942 epidemic of post-vaccination hepatitis in the United States Army. *N Engl J Med* 1987;316(16):965-70.
10. Katchaki JN, Siem TH, Brouwer R, et al. Detection and significance of anti-HBc in the blood bank; preliminary results of a controlled prospective study. *J Virol Methods* 1980;2:119-25.
11. Lander JJ, Gilnick GL, Golb LH, et al. Anticore antibody screening of transfused blood. *Vox Sang* 1978;34:77-80.
12. Hoofnagle JH, Seef LB, Buskell-Bales Z, et al. Type B hepatitis after transfusion with blood containing antibody to hepatitis B core antigen. *N Engl J Med* 1978;298(25):1379-83.
13. Koziol DE, Holland PV, Alling DW, et al. Antibody to hepatitis B core antigen as a paratological marker for non-A, non-B hepatitis agents in donated blood. *Ann Intern Med* 1986;104:488-95.
14. AuBuchon JP, Sandler SG, Fang CT, et al. American Red Cross experience with routine testing for hepatitis B core antibody. *Transfusion* 1989;29:230-2.
15. Stevens CE, Aach RD, Hollinger FB, et al. Hepatitis B virus antibody in blood donors and the occurrence of non-A, non-B hepatitis in transfusion recipients: An analysis of the transfusion-transmitted viruses study. *Ann Intern Med* 1984;101(6):733-8.
16. Raimondo G, Pollicino T, Cacciola I, et al. Occult hepatitis B virus infection. *J Hepatology* 2007;46:160-170.
17. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
18. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; January 2007.
19. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
20. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline - Third Edition*. CLSI Document M29-A3. Wayne, PA: CLSI; 2005.
21. Centers for Medicare and Medicaid Services, Department of Health and Human Services. 42 CFR 493.1202. *Standard; Moderate or high complexity testing, or both: Effective from September 1, 1992 to December 31, 2002*. Paragraph (c). http://edocket.access.gpo.gov/cfr_2002/octqtr/pdf/42cfr493.1202.pdf. Accessed March 13, 2009.
22. Clinical and Laboratory Standards Institute. *Statistical Quality Control for Quantitative Measurement Procedures; Principles and Definitions; Approved Guideline - Third Edition*. CLSI Document C24-A3. Wayne, PA: CLSI; 2006.
23. Primus FJ, Kelley EA, Hansen HJ, et al. "Sandwich"-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34(2):261-264.
24. Schreff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45:879-885.
25. Boscatto LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
26. Clinical and Laboratory Standards Institute. *User Verification of Performance for Precision and Trueness: Approved Guideline - Second Edition*. CLSI Document EP15-A2. Wayne, PA: CLSI; 2005.
27. Clinical and Laboratory Standards Institute. *Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline - Second Edition*. CLSI Document EP5-A2. Wayne, PA: CLSI; 2004.

The following U.S. Patents are relevant to the ARCHITECT System or its components. There are other such patents and patent applications in the United States and worldwide.

5 468 646	5 543 524	5 545 739
5 565 570	5 669 819	5 783 699

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Manufactured for
Abbott Laboratories, Abbott Park IL
by
Abbott Diagnostics International, LTD, Barceloneta, Puerto Rico
March 2009
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In Vitro Test
REF 6L22-10
XX-XXXX/RI

ARCHITECT® SYSTEM

CORE

Controls

Key to symbols used

	Reference		Lot
	In Vitro Diagnostic		Control
	8°C		Control
	2°C		Control
	Warning		

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In Vitro Test
REF: BL22-01
XX-XXX/RT

ARCHITECT® SYSTEM

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Calibrator

Key to symbols used

REF	Lot	LOT	Lot
IVD	Reference Range	X	Reference Range
37°C	Temperature	CAL	Calibrator
2°C	Temperature		
!	Caution		

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REF: BL22-01

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INTENDED USE

The ARCHITECT CORE Calibrator is used for the calibration of the ARCHITECT System. 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.

PRINCIPLES OF THE PROCEDURE

The ARCHITECT System utilizes two color reaction light units (RLU) from two weak RLU at three replicates or Calibrator 1. The absorbance of the calibrator is assessed against a parameter of the environment. In accuracy, the cutoff RLU is calculated as follows:

$$\text{Cutoff RLU} = \text{Calibrator 1 Mean RLU} \times 1.6$$

The readable calibration is stored by the ARCHITECT System for use with any reagent kit. Further, the addition should be used in conjunction with control samples to determine the validity of the calibration.

WARNINGS AND PRECAUTIONS

- For *In Vitro* Diagnostic Use.



CAUTION: This product contains human sourced and/or potentially infectious components. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infectious. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens, Biosafety Level 2 or other appropriate biosafety practices, should be used for materials that contain or are suspected of containing infectious agents.

- The human plasma used in calibrator 1 is inactive for anti-HBc and anti-HBs, and is non-infective by HBsAg, HBeAg, HBeI, HBeS, or HBeIc, HIV-1, HIV-2, and anti-HCV.
- Calibrator 1 contains methylglucosylamines, which are components of PEG-20 and is classified per applicable European Community (EC) Directives as a "very low" following the appropriate Risk, R, and Safety (S) phrases.



- R40 May cause sensitization by skin contact
- S26 Avoid contact with skin
- S33 This material and its container must be disposed of in a safe way
- S37 Wear suitable gloves
- S46 If swallowed, seek medical advice immediately and show this container or label

- This product contains sodium azide. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operators Manual, Section 8.

MATERIALS PROVIDED

- 1 Bottle (4 mL) ARCHITECT CORE Calibrator 1, anti-HBc positive human plasma, reconstituted anti-HBc negative human plasma, Calibrator 1 in green and contains 3.00 Bus Day No. 9 and Anti Yellow Day No. 23 Preservative solution 0.50 and 0.50mL each

STANDARDIZATION

ARCHITECT CORE Calibrator 1, concentration is standardized against the reference standard of the Paul Ehrlich Institute, Lander, Germany.

The calibrator is at the following concentrations:

Calibrator	Concentration
ARCHITECT CORE Calibrator 1	0.5 IU/mL
ARCHITECT CORE Calibrator 2	0.5 IU/mL

PREPARATION AND STORAGE

- The calibrator is liquid ready to use. No preparation is required.
 - When stored and handled as directed, the calibrator is stable until the expiration date.
 - The calibrator must be stored at 2-8°C. Do not store at temperatures below 0°C or above 10°C.
 - Refer to the ARCHITECT CORE assay reagent package insert for the assay and general stability information.
 - 20°C
- 20 / 1
Store at 2-8°C

QUALITY CONTROL PROCEDURES

Refer to the ARCHITECT CORE assay reagent package insert and ARCHITECT System Operators Manual for additional information.

- A single sample of each control level must be tested to ensure the assay calibration. For information on setting controls, refer to the ARCHITECT System Operators Manual, Section 5.

- Ensure that assay control values are within the ranges specified in the control package insert.
- Once an ARCHITECT CORE calibration is accepted and stored, all subsequent samples may go through direct future calibration checks.
- A reagent kit with a new lot number is used.
- Controls are out of range.

PROCEDURE

- ARCHITECT CORE Calibrator 1 must be mixed by gentle inversion before use.
- To perform a calibration, refer to the calibration 1 in the package insert. The calibration should be done daily.
- To obtain the recommended to the manufacturer for the ARCHITECT CORE Calibrator 1, hold the bottle vertically and dispense 5 drops of the calibrator into the sample cup.
- For information on setting calibrations, refer to the ARCHITECT System Operators Manual, Section 5.

BIBLIOGRAPHY

- US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Occupational safety and health airborne pathogens
- US Department of Health and Human Services, Bureau of Microbiological and Biodefense, 5th ed. Washington, DC: US Government Printing Office, January 2007
- World Health Organization, Laboratory Biosafety Manual, 3rd ed. Geneva: World Health Organization, 2004
- Centers for Disease Control and Prevention, Protection of Laboratory Workers from Contagiously Acquired Infections, *Annals of the New York Academy of Sciences*, 1025:105-111, 2003

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March 2009

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