



**Anti-HBc IgM**

**REF** 6C33

**B6C330**

**36-6144/R4**



# Anti-HBc IgM

This package insert must be read carefully prior to 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.

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### Key to symbols used

<b>REF</b>	List Number	<b>LOT</b>	Lot Number
<b>IVD</b>	For <i>In Vitro</i> Diagnostic Use	<b>CALIBRATORS</b>	Calibrator Kit
	Store at 2-8°C	<b>CONTROLS</b>	Control Kit
	CAUTION: Handle human sourced materials as potentially infectious. Consult instructions for use. (Infection Risk)	<b>ASSAY CD-ROM</b>	Assay CD-ROM
	Expiration Date	<b>SN</b>	Serial Number
	Consult instructions for use.	<b>CONTROL NO.</b>	Control Number
	ABBOTT Max-Planck-Ring 2 65205 Wiesbaden Germany +49-6122-580	<b>REAGENT LOT</b>	Reagent Lot
	ABBOTT Max-Planck-Ring 2 65205 Wiesbaden Germany +49-6122-580	<b>REACTION VESSELS</b>	Reaction Vessels
	Legal Manufacturer	<b>SAMPLE CUPS</b>	Sample Cups
		<b>SEPTUM</b>	Septum
		<b>REPLACEMENT CAPS</b>	Replacement Caps

**CE** 0088  
ABBOTT  
Max-Planck-Ring 2  
65205 Wiesbaden  
Germany  
+49-6122-580

**CE**  
ABBOTT  
Max-Planck-Ring 2  
65205 Wiesbaden  
Germany  
+49-6122-580

Legal Manufacturer

## NAME

ARCHITECT® Anti-HBc IgM

## INTENDED USE

The ARCHITECT Anti-HBc IgM assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the qualitative detection of IgM antibody to hepatitis B core antigen (anti-HBc IgM) in human serum and plasma and is indicated for use as an aid in the diagnosis of acute or recent hepatitis B viral infection.

## SUMMARY AND EXPLANATION OF TEST

The ARCHITECT Anti-HBc IgM assay utilizes acridinium-labeled recombinant hepatitis B virus core antigen (rHBcAg) conjugate for the detection of anti-HBc IgM. Viral specific IgM antibody has been detected in most acute viral infections and is a reliable marker of acute disease. The concentrations of anti-HBc IgM rise rapidly in patients with acute infection; high levels of anti-HBc IgM have been detected in patients with acute hepatitis B viral infection.<sup>1-5</sup> Hepatitis B surface antigen (HBsAg) will generally also be present as a serological marker of an acute infection,<sup>6-8</sup> but there are reports of HBsAg being undetectable.<sup>9-10</sup> In the convalescent phase, anti-HBc IgM will persist after the disappearance of HBsAg and decrease slowly over time. In the absence of information about any other hepatitis B virus (HBV) markers, it must be considered that an individual with detectable levels of anti-HBc IgM may be actively infected with HBV or that the infection may have resolved. Anti-HBc IgM may also be present in patients with chronic hepatitis B viral infection.<sup>6-8</sup> The concentrations are generally lower than those associated with acute infections and may rise and fall with exacerbation of the disease.<sup>11-15</sup> Differentiation of acute and chronic hepatitis B viral infection solely on the basis of viral markers, which are also frequently present, such as HBsAg, anti-HBs, HBcAg, anti-HBe, and anti-HBc, is difficult because most of these markers occur in both acute and chronic disease. Since there is high correlation of high anti-HBc IgM concentrations with acute hepatitis B viral infection, the test for anti-HBc IgM may serve as an aid to distinguish acute hepatitis illness due to HBV versus superimposed infections by other possible agents such as hepatitis A, hepatitis C, or delta virus.<sup>6,8,11,16</sup>

## BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Anti-HBc IgM assay is a two-step immunoassay for the qualitative detection of anti-HBc IgM in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex®.

In the first step, prediluted sample and anti-human IgM (mouse monoclonal) coated paramagnetic microparticles are combined. Human IgM present in the sample binds to the anti-human IgM (mouse monoclonal) coated microparticles. After washing, the anti-HBc specific IgM binds to the acridinium-labeled rHBcAg conjugate that is added in the second step. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction vessel (RV). The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-HBc IgM in the sample and the RLUs detected by the ARCHITECT *i* \* optical system. The presence or absence of anti-HBc IgM in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from a previous ARCHITECT Anti-HBc IgM calibration. If the chemiluminescent signal of the reaction is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-HBc IgM by the ARCHITECT Anti-HBc IgM assay.

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

\* *i* = immunoassay

## REAGENTS

### Reagent Kit, 100 Tests

ARCHITECT Anti-HBc IgM Reagent Kit (6C33)

- **MICROPARTICLES** 1 or 4 Bottle(s) (5.6 mL) Microparticles: Anti-human IgM (mouse monoclonal) coated microparticles in TRIS buffer with protein (bovine, goat) stabilizers. Minimum concentration: 0.12% solids. Preservatives: Antimicrobial Agents.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL) Conjugate: Acridinium-labeled hepatitis B virus core antigen (*E. coli*, recombinant) conjugate in succinate buffer with protein (bovine) stabilizer. Minimum concentration: 0.4 µg/mL. Preservatives: Antimicrobial Agents.

## 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. Preservatives: Antimicrobial Agents.

## WARNINGS AND PRECAUTIONS

- **IVD For In Vitro Diagnostic 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.

## Safety Precautions

**CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens,<sup>17</sup> Biosafety Level 2<sup>18</sup> or other appropriate biosafety practices<sup>19-22</sup> should be used for materials that contain or are suspected of containing infectious agents.

- ARCHITECT *i* Trigger Solution contains sodium hydroxide (NaOH) and is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



R41	Risk of serious damage to eyes.
S25	Avoid contact with eyes.
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.
S36/39	Wear suitable protective clothing and eye/face protection.
S46	If swallowed, seek medical advice immediately and show this container or label.

- **Information for European customers: For product not classified as dangerous per European Directive 1999/45/EC - Safety data sheet available for professional user on request.**
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

## Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Prior to loading the ARCHITECT Anti-HBc IgM 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 microparticle vials, change gloves that have contacted human plasma/sera, since introduction of human IgM may result in a neutralized microparticle.
- Prior to placing the septum on an uncapped reagent bottle, squeeze the septum in half to confirm that the slits are open. If the slits appear sealed, continue to gently squeeze the septum to open the slits.
- Once a septum has been placed on an open 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

-  The ARCHITECT Anti-HBc IgM 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, reagents are stable until the expiration date.
- The ARCHITECT Anti-HBc IgM Reagent Kit may be stored onboard 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 they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with the septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, you must 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 will require retesting. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

### INSTRUMENT PROCEDURE

- The ARCHITECT Anti-HBc IgM assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM prior to performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.  
**NOTE:** For details on configuring the ARCHITECT *i* System to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2, Subsection Assay Settings, Configure assay parameters dialog window – Interpretation.
- 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

- Human serum (including serum collected in serum separator tubes) or plasma collected in potassium EDTA, sodium citrate, sodium heparin, ACD, CPDA-1, CPD, or potassium oxalate may be used in the ARCHITECT Anti-HBc IgM assay. Other anticoagulants have not been validated for use with the ARCHITECT Anti-HBc IgM assay. Follow the manufacturer's processing instructions for serum or plasma collection tubes.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify the correct specimen types are used in the ARCHITECT Anti-HBc IgM assay.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- This assay was designed and validated for use with human serum or plasma from individual patient and donor specimens. Pooled specimens must not be used since the accuracy of their test results has not been validated.
- Do not use heat-inactivated specimens.
- Do not use grossly hemolyzed specimens.
- Specimens with obvious microbial contamination should not be used.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- For optimal results, inspect all samples for bubbles and foaming. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results or aspiration errors.

- Specimens from heparinized patients may be partially coagulated and erroneous results could occur due to the presence of fibrin. To prevent this phenomenon, draw the specimen prior to heparin therapy.
- For optimal results, serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter.
- Gravity separation is not sufficient for specimen preparation. Specimens must be separated from clots or red blood cells using centrifugation as recommended by the tube manufacturer.
- After specimens have been processed per the collection tube manufacturer's instructions, they must be transferred to a centrifuge tube and centrifuged at  $\geq 10,000$  RCF (Relative Centrifugal Force) for 10 minutes if:
  - they contain red blood cells, clots, or particulate matter, or
  - they require repeat testing, or
  - they were frozen and thawed.**Transfer clarified specimen to a sample cup or secondary tube for testing.
- Specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing or inversion. Visually inspect the specimens for the absence of stratification. If layering or stratification is observed, repeat until specimens are visibly homogeneous. Centrifuge at  $\geq 10,000$  RCF for 10 minutes to remove particulate matter and to ensure consistency in the results.
- 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.
- Specimens may be stored on or off the clot or red blood cells for up to 7 days at 2-8°C. If testing will be delayed more than 7 days, remove serum or plasma from the clot, serum separator, or red blood cells and store frozen at -20°C or colder.
- No qualitative performance differences were observed between experimental controls and the 25 nonreactive or 25 spiked reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.
- No qualitative performance differences were observed between experimental controls and the 25 nonreactive or the 25 spiked reactive specimens tested with elevated levels of bilirubin ( $\leq 20$  mg/dL), hemoglobin ( $\leq 500$  mg/dL), triglycerides ( $\leq 3,000$  mg/dL), protein ( $\leq 12$  g/dL), or red blood cells ( $\leq 0.4\%$  v/v).
- When shipped, specimens must be packaged and labeled 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 -20°C or colder (dry ice). Do not exceed the storage time limitations listed above. Prior to shipment, it is recommended that specimens be removed from the clot, serum separator, or red blood cells.

### PROCEDURE

#### Materials Provided

- 6C33 ARCHITECT Anti-HBc IgM Reagent Kit

#### Materials Required but not Provided

- ARCHITECT *i* System
- ARCHITECT *i* **ASSAY CD-ROM**
- 6C33-01 ARCHITECT Anti-HBc IgM **CALIBRATORS**
- 6C33-10 ARCHITECT Anti-HBc IgM **CONTROLS**
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.
- For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

#### Assay Procedure

- Before loading the ARCHITECT Anti-HBc IgM Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment.
  - 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 ABBOTT representative.**
- Once the microparticles have been resuspended, remove and discard the cap. Wearing clean gloves, remove a septum from the bag.
- Squeeze the septum in half to confirm that the slits are open. Carefully snap the septum onto the top of the bottle.
- Order calibration, if necessary.
- For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens, calibrators, and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Load the ARCHITECT Anti-HBc IgM Reagent Kit on the ARCHITECT *i* System. Verify that all necessary reagents are present. Ensure that septums are present on all reagent bottles.
- 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 evaporations verify adequate cup volume is present prior to running the test.
  - Priority: 64  $\mu$ L for the first Anti-HBc IgM test plus 14  $\mu$ L for each additional Anti-HBc IgM test from the same sample cup.
  - $\leq$  3 hours onboard: 150  $\mu$ L for the first Anti-HBc IgM test plus 14  $\mu$ L for each additional Anti-HBc IgM test from the same sample cup.
  - $>$  3 hours onboard: additional sample volume is required. Refer to the ARCHITECT System Operations Manual, Section 5, for information on sample evaporation and volumes.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare Calibrators and Controls.
  - Make sure the ARCHITECT Anti-HBc IgM Calibrators and Controls are completely thawed before mixing. Allow sufficient time for thawing.
  - ARCHITECT Anti-HBc IgM Calibrators and Controls should be mixed THOROUGHLY by low speed vortex or inversion prior to use.
  - To obtain the recommended volume requirements for the ARCHITECT Anti-HBc IgM Calibrators and Controls, hold the bottles vertically and dispense 5 drops of each calibrator or 5 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. The ARCHITECT *i* System performs the following functions:
  - Moves the sample to the aspiration point.
  - Loads a reaction vessel (RV) into the process path.
  - Aspirates and transfers an aliquot of the sample into the RV.
  - Moves the RV one position and adds ARCHITECT *i* Wash Buffer to dilute the sample.
  - Aspirates microparticles and an aliquot of the diluted sample and transfers it to a new RV.
  - Mixes, incubates, and washes the reaction mixture.
  - Adds conjugate to the RV.
  - Mixes, incubates, and washes the reaction mixture.
  - Adds Pre-Trigger and Trigger Solutions.
  - Measures chemiluminescent emission to detect the presence of anti-HBc IgM in the sample.
  - Aspirates contents of RV to liquid waste and unloads RV to solid waste.
  - Calculates the result.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your Laboratory requires more frequent maintenance, follow those procedures.

**NOTE:** The ARCHITECT Anti-HBc IgM assay performs a sample predilution, and therefore requires two RVs per test.

## Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT Anti-HBc IgM assay.

## Calibration

- To perform an ARCHITECT Anti-HBc IgM calibration, test Calibrators 1 and 2 in replicates of three. A single sample of all levels of ARCHITECT Anti-HBc IgM Controls must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the control package insert. Calibrators should be priority loaded.
- Once an ARCHITECT Anti-HBc IgM calibration is accepted and stored, all subsequent samples may be tested without further calibration unless one or more of the following occur:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

## QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT Anti-HBc IgM assay is that a single sample of both controls be tested once every 24 hours each day of use for each reagent lot. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

The ARCHITECT Anti-HBc IgM Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and must be retested. Recalibration may be indicated.

## Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT Anti-HBc IgM assay belongs to method group 5.

## RESULTS

### Calculation

The ARCHITECT *i* System calculates the cutoff rate (CO) from the mean RLU of three replicates for Calibrator 1 and Calibrator 2 and stores the results.

$$\text{Cutoff RLU} = [(\text{Calibrator 2 mean RLU} - \text{Calibrator 1 mean RLU}) \times 0.75] + \text{Calibrator 1 mean RLU}$$

The cutoff RLU is stored for each reagent lot calibration.

The ARCHITECT *i* System calculates a result based on the ratio of the sample RLU(s) to the cutoff RLU for each specimen and control.

$$S/CO = \text{sample RLU/cutoff RLU}$$

Example: If the Specimen RLU = 25,000  
and the CO = 19,500  
 $25,000/19,500 = 1.28$   
 $S/CO = 1.28$

The ARCHITECT Anti-HBc IgM Calibrator 2 has been referenced against the Paul-Ehrlich-Institute, Langen, Germany, HBc Referenzserum IgM 84 (IgM anti-HBc). For details, refer to the ARCHITECT Anti-HBc IgM Calibrator Kit (6C33-01) package insert.

### Interpretation of Results

- Specimens with S/CO values  $<$  1.00 are considered nonreactive by the ARCHITECT Anti-HBc IgM assay.
- Specimens with S/CO values  $\geq$  1.00 are considered reactive by the ARCHITECT Anti-HBc IgM assay.

**NOTE:** For details on configuring the ARCHITECT *i* System to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2, Subsection Assay Settings, Configure assay parameters dialog window-Interpretation.

### 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

- If the anti-HBc IgM results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with patient history and other hepatitis markers for diagnosis of acute or chronic infection.
- **Specimens that have been frozen and thawed and specimens containing red blood cells, clots, or particulate matter must be centrifuged prior to running the assay.**
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- Do not use heat-inactivated specimens.
- Do not use grossly hemolyzed specimens.
- Specimens with obvious microbial contamination should not be used.
- Specimens from heparinized patients may be partially coagulated and erroneous results could occur due to the presence of fibrin. To prevent this phenomenon, draw the specimen prior to heparin therapy.
- Specimens from patients with high levels of IgM, e.g. specimens from patients with multiple myeloma, may show depressed values when tested with assay kits that use reagents containing anti-human IgM.

## SPECIFIC PERFORMANCE CHARACTERISTICS

### Precision

The precision of ARCHITECT Anti-HBc IgM was determined during the clinical evaluation using a panel consisting of one nonreactive member, three diluted anti-HBc IgM reactive members, controls, and calibrators. Two sites tested two different lots of the controls and calibrators across two reagent lots (four combinations), and one site tested three different lots of controls and calibrators across three reagent lots (nine combinations). All members were tested in triplicate in four runs for two or four days. The intra-run and inter-run standard deviations (SD) and percent coefficient of variation (%CV) were analyzed with a variance components analysis<sup>23</sup> using a mixed analysis of variance model.<sup>24</sup> Data are summarized in Table 1.

TABLE 1

ARCHITECT Anti-HBc IgM Reproducibility, Three Sites, Three Lots

Panel Member	Total n	Mean S/CO	Intra-run		Inter-run <sup>a</sup>	
			SD	%CV	SD	%CV
Calibrator 1 <sup>b</sup>	516	0.03	0.004	13.34	0.004	13.56
Calibrator 2 <sup>b</sup>	516	1.33	0.059	4.45	0.059	4.45
Negative Control <sup>c</sup>	516	0.03	0.003	11.40	0.003	12.83
Positive Control <sup>c</sup>	516	3.23	0.124	3.84	0.133	4.13
Panel 1	204	0.03	0.003	12.48	0.004	14.53
Panel 2	204	0.47	0.020	4.19	0.032	6.80
Panel 3	204	0.93	0.033	3.59	0.041	4.38
Panel 4	204	7.91	0.249	3.15	0.372	4.70

CV = coefficient of variation, n = sample size, S/CO = sample to cutoff, SD = standard deviation

<sup>a</sup> Inter-run variability contains intra-run variability.

<sup>b</sup> The results for Calibrator 1 and Calibrator 2 include three separate lots combined for each calibrator.

<sup>c</sup> The results for the negative and positive controls include three separate lots combined for each control.

### Specificity

A total of 1634 random blood donor and hospitalized patient specimens was tested at three clinical sites. None of the 1634 specimens were reactive by ARCHITECT Anti-HBc IgM. The specificity of ARCHITECT Anti-HBc IgM in this population was 100.00% (1631/1631<sup>b</sup>) with a 95% confidence interval of 99.77-100.00%. The data are summarized in Table 2.

TABLE 2  
Specificity Results Using Random Blood Donors and Hospitalized Patients

Population	Number	Reactive	
	n	n	%
Random Blood Donors	1136 <sup>a,b</sup>	0	0.00
Hospitalized Patients	498 <sup>b</sup>	0	0.00
Total	1634 <sup>b</sup>	0	0.00

<sup>a</sup> Included 560 plasma and 576 serum specimens.

<sup>b</sup> Six specimens (four random blood donors, two hospitalized patients) were grayzone reactive by ARCHITECT Anti-HBc IgM if a 0.50 to 0.99 S/CO grayzone range was applied. Three of these specimens were ARCHITECT Anti-HBc (total antibody) reactive (one random blood donor, two hospitalized patients). These three specimens were excluded from the specificity calculation due to the presence of total Anti-HBc antibodies. For the remaining three specimens no other HBV serological markers were detected.

A total of 161 specimens from individuals with potentially interfering substances and other conditions (CMV-IgM, EBV-IgM, HCV, HIV-1, HSV-IgM, HAV total antibody, HAV-IgM, rubella, HBV vaccine recipients, total Anti-HBc high reactive, toxoplasmosis, syphilis, urinary tract infections, rheumatoid factor, antinuclear autoantibodies [ANA], alcoholic cirrhosis, pregnant females [first and second trimester], multiple myeloma [IgM], multiparous females, dialysis patients, other liver disease) were tested by ARCHITECT Anti-HBc IgM.

Seventy five specimens from individuals with high risk of blood transmissible infections (intravenous drug users [IVDU], men who have sex with men [MSM], hemophiliacs) were tested by ARCHITECT Anti-HBc IgM.

A population of 80 specimens from patients diagnosed with chronic hepatitis B was tested by ARCHITECT Anti-HBc IgM. Eight specimens (10.00%) were reactive by ARCHITECT Anti-HBc IgM. All eight were also reactive by AxSYM CORE-M<sup>®</sup>. A total of nine specimens were reactive by AxSYM CORE-M<sup>®</sup>. The data for these three populations are summarized in Table 3.

TABLE 3  
Potentially Interfering Substances or Other Conditions, High Risk of Blood Transmissible Infections, and Chronic HBV Infection Specimens

Population	Number	Reactive	
	n	n	%
Potentially Interfering Substances or Other Conditions	161 <sup>a</sup>	1 <sup>b</sup>	0.62
High Risk of Blood Transmissible Infections	75 <sup>c</sup>	1 <sup>d</sup>	1.33
Chronic HBV Infection	80 <sup>e</sup>	8	10.00

<sup>a</sup> Two specimens (one HCV, one toxoplasmosis) were grayzone reactive if a 0.50 to 0.99 S/CO grayzone range was applied. Both were reactive by ARCHITECT Anti-HBc (total antibody) and nonreactive by ARCHITECT HBsAg.

<sup>b</sup> One specimen (dialysis patient) was reactive by ARCHITECT Anti-HBc and nonreactive by ARCHITECT HBsAg.

<sup>c</sup> Two specimens (IVDU) were grayzone reactive if a 0.50 to 0.99 S/CO grayzone range was applied. Both were reactive by ARCHITECT Anti-HBc and nonreactive by ARCHITECT HBsAg.

<sup>d</sup> One specimen (MSM) was reactive by ARCHITECT HBsAg and ARCHITECT Anti-HBc.

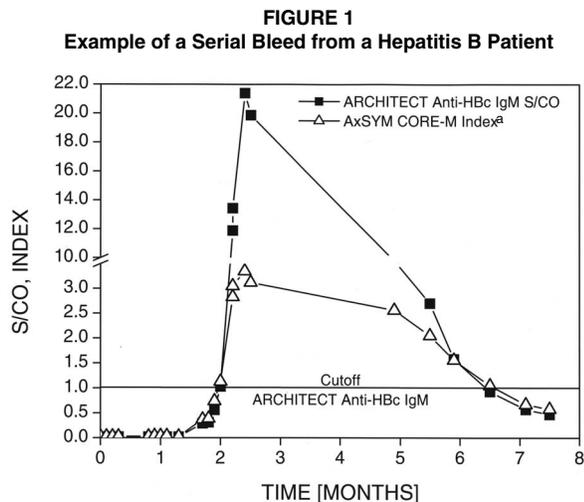
<sup>e</sup> Six additional specimens were grayzone reactive if a 0.50 to 0.99 S/CO grayzone range was applied. The same additional number of specimens was grayzone reactive by AxSYM CORE-M.

### Sensitivity

In a total of 212 specimens from patients with acute hepatitis B, all were reactive by ARCHITECT Anti-HBc IgM. The sensitivity was 100.00% (212/212) with a 95% confidence interval of 98.28-100.00%.

**NOTE:** Four additional specimens, initially classified as acute HBV specimens, were excluded from the sensitivity calculation. Of these, three specimens were concordantly nonreactive by ARCHITECT Anti-HBc IgM and AxSYM CORE-M. The fourth specimen was nonreactive by ARCHITECT HBsAg.

The sensitivity of ARCHITECT Anti-HBc IgM is set so that a reactive result ( $\geq 1.00$  S/CO) implies acute or recent hepatitis B infection. An example of a serial bleed panel from a hepatitis B patient is shown in Figure 1.



<sup>a</sup> AxsYM CORE-M grayzone range: 0.80 to 1.20 Index.

#### Comparison to a Commercially Available Anti-HBc IgM Assay

A total of 2162 specimens (random blood donors, hospitalized patients, potentially interfering substances or other conditions, high risk of blood transmissible infections, acute HBV infection, and chronic HBV infection) were tested by ARCHITECT Anti-HBc IgM and AxsYM CORE-M. The agreement between the two methods was 99.54% (2152/2162). The data are summarized in Table 4.

**TABLE 4**  
Comparison of ARCHITECT Anti-HBc IgM with AxsYM CORE-M

		ARCHITECT Anti-HBc IgM	
		Reactive	Nonreactive <sup>a</sup>
AxsYM CORE-M	Reactive	212	0
	Grayzone Reactive	8	7 <sup>b</sup>
	Nonreactive	3	1932 <sup>c</sup>

<sup>a</sup> Includes grayzone results (range 0.50 to 0.99 S/CO).

<sup>b</sup> Five were grayzone by ARCHITECT Anti-HBc IgM.

<sup>c</sup> Eleven were grayzone by ARCHITECT Anti-HBc IgM.

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

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