ARCHITECT Anti-HBc IgM

REF 6C33-27
REF 6C33-22

en
Anti-HBc IgM
6C33
G60417R04
B6C3W0

Read Highlighted Changes: Revised July 2019.

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

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 THE 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.[1-5] Hepatitis B surface antigen (HBsAg) will generally also be present as a serological marker of an acute infection,[6-8] but there are reports of HBsAg being undetectable.[9, 10]

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.[6-8] The concentrations are generally lower than those associated with acute infections and may rise and fall with exacerbation of the disease.[11-15] 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, HBeAg, 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.[6, 8, 11, 16]

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.

1. Prediluted sample and anti-human IgM (mouse monoclonal) coated paramagnetic microparticles are combined. The human IgM present in the sample binds to the anti-human IgM (mouse monoclonal) coated microparticles.
2. After washing, anti-HBc specific IgM binds to the acridinium-labeled rHBcAg conjugate that is added.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of anti-HBc IgM in the sample and the RLUs detected by the ARCHITECT iSystem optics.

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 an active calibration. If the chemiluminescent signal in the reaction is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-HBc IgM.

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

REAGENTS

Kit Contents

ARCHITECT Anti-HBc IgM 6C33

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT iSystems. Please contact your local distributor.

REF	6C33-27	6C33-22
Σ	100	400
MICROPARTICLES	1 x 5.6 mL	4 x 5.6 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 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 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

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and 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.[17-20]

The following warnings and precautions apply to: CONJUGATE	
	
WARNING:	Contains Polyethylene glycol octylphenyl ether (Triton X-405)
H319	Causes serious eye irritation.
Prevention	
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337+P313	If eye irritation persists: Get medical advice / attention.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the 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.
  - 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.

When handling microparticle vials, change gloves that have contacted human plasma/sera, since introduction of human IgM may result in a neutralized microparticle.

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

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage. Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. 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.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

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

The ARCHITECT Anti-HBc IgM assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to 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.

NOTE: For details on configuring the ARCHITECT iSystem 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

Specimen Types

Validated specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human serum	Serum
	Serum separator tubes
Human plasma	Potassium EDTA
	Sodium citrate
	Sodium heparin
	ACD
	CPDA-1
	CPD
	Potassium oxalate

- Other anticoagulants have not been validated for use with the ARCHITECT Anti-HBc IgM assay.
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum or plasma.
- The instrument 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 assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed
  - obvious microbial contamination
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.

- 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.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- 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,
  - they require repeat testing, or
  - they were frozen and thawed.
- 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 ≥ 10,000 RCF for 10 minutes to remove particulate matter and to ensure consistency in the results.
- 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.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- 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.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	2-8°C	≤ 7 days
	-20°C or colder	--

Specimens may be stored on or off the clot or red blood cells.

Remove serum or plasma from the clot, serum separator, or red blood cells if stored longer than the maximum 2-8°C storage time 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.

Avoid multiple freeze/thaw cycles.

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 (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), triglycerides (≤ 3,000 mg/dL), protein (≤ 12 g/dL), or red blood cells (≤ 0.4% v/v).

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- It is recommended that specimens be removed from the clot, serum separator, or red blood cells.
- Ship ambient, at 2-8°C (wet ice), or -20°C or colder (dry ice).
- Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

6C33 ARCHITECT Anti-HBc IgM Reagent Kit

Materials Required but not Provided

- ARCHITECT Anti-HBc IgM Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 6C33-02 ARCHITECT Anti-HBc IgM Calibrators
- 6C33-11 ARCHITECT Anti-HBc IgM Controls
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT 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 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, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Carefully snap the septum onto the top of the bottle.
- Load the reagent kit on the ARCHITECT iSystem.
  - 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.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 64 µL

    Sample volume for each additional test from same sample cup: 14 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 14 µL

- > 3 hours on board: Additional sample volume 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 ARCHITECT Anti-HBc IgM Calibrators and Controls. Make sure the calibrators and controls are completely thawed before mixing. Allow sufficient time for thawing.
  - Mix calibrator(s) and controls THOROUGHLY by low speed vortex or gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 5 drops

    for each control: 5 drops
- 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. Perform maintenance more frequently when required by laboratory 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

- Test Calibrator 1 and 2 in replicates of three. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Once an ARCHITECT Anti-HBc IgM 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 or
  - 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 iSystem calculates the cutoff rate (CO) from the mean RLU of three replicates for Calibrator 1 and Calibrator 2 and stores the results.

Cutoff RLU = [(Calibrator 2 mean RLU - Calibrator 1 mean RLU) x 0.75] + Calibrator 1 mean RLU

The cutoff RLU is stored for each reagent lot calibration.

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

S/CO = 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 (6C33-02) package insert.

Interpretation of Results

S/CO values	Interpretation
< 1.00	Nonreactive
≥ 1.00	Reactive

For details on configuring the ARCHITECT iSystem to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2.

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

- For diagnostic purposes, results should be used in conjunction with patient history and other hepatitis markers for diagnosis of acute or chronic infection.
- If the anti-HBc IgM results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- 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[21] using a mixed analysis of variance model.[22] 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 SD	Intra-run %CV	Inter-run[a] SD	Inter-run[a] %CV
Calibrator 1[b]	516	0.03	0.004	13.34	0.004	13.56
Calibrator 2[b]	516	1.33	0.059	4.45	0.059	4.45
Negative Control[c]	516	0.03	0.003	11.40	0.003	12.83
Positive Control[c]	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

[a] Inter-run variability contains intra-run variability.

[b] The results for Calibrator 1 and Calibrator 2 include three separate lots combined for each calibrator.

[c] 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[b]) 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 n	Reactive n	Reactive %
Random Blood Donors	1136[a,b]	0	0.00
Hospitalized Patients	498[b]	0	0.00
Total	1634[b]	0	0.00

[a] Included 560 plasma and 576 serum specimens.

[b] 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 third 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. A total of nine specimens were reactive by AxSYM CORE-M[e]. 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 n	Reactive n	Reactive %
Potentially Interfering Substances or Other Conditions	161[a]	1[b]	0.62
High Risk of Blood Transmissible Infections	75[c]	1[d]	1.33
Chronic HBV Infection	80[e]	8	10.00

[a] 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.

[b] One specimen (dialysis patient) was reactive by ARCHITECT Anti-HBc and nonreactive by ARCHITECT HBsAg.

[c] 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.

[d] One specimen (MSM) was reactive by ARCHITECT HBsAg and ARCHITECT Anti-HBc.

[e] 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.

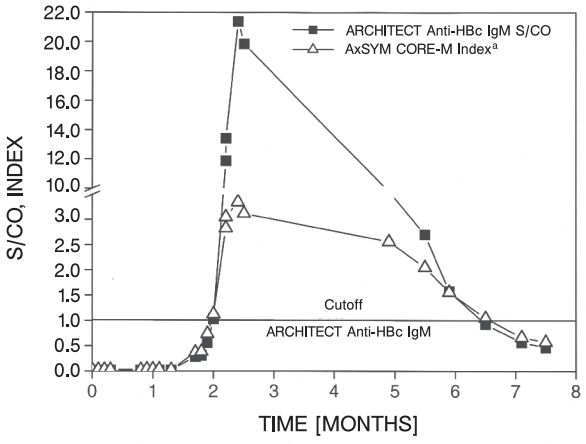
Sensitivity

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 (≥ 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.

FIGURE 1: Example of a Serial Bleed from a Hepatitis B Patient



[a] AxSYM CORE-M grayzone range: 0.80 to 1.20 Index.

Assay Comparison

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[a]
AxSYM CORE-M	Reactive	212	0
	Grayzone Reactive	8	7[b]
	Nonreactive	3	1932[c]

[a] Includes grayzone results (range 0.50 to 0.99 S/CO).

[b] Five were grayzone by ARCHITECT Anti-HBc IgM.

[c] Eleven were grayzone by ARCHITECT Anti-HBc IgM.

BIBLIOGRAPHY

1. Lindsay KL, Nizze JA, Koretz R, et al. Diagnostic usefulness of testing for anti-HBc IgM in acute hepatitis B. *Hepatol* 1986;6:1325-1328.
2. Chau KH, Hargie MP, Decker RH, et al. Serodiagnosis of recent hepatitis B infection by IgM class anti-HBc. *Hepatology* 1983;3(2):142-149.
3. Wang A-X, Coulepis AG, Hui Z, et al. Immunoglobulin M antibodies against hepatitis B core antigen in patients with chronic hepatitis B infection. *Pathol* 1984;16:83-85.
4. Eble K, Clemens J, Krenc C, et al. Differential diagnosis of acute viral hepatitis using rapid, fully automated immunoassays. *J Med Virol* 1991;33:139-150.
5. Gerlich WH, Uy A, Lambrecht F, et al. Cutoff levels of immunoglobulin M antibody against viral core antigen for differentiation of acute, chronic, and past hepatitis B virus infections. *J Clin Microbiol* 1986;24:288-293.
6. Decker RH. Diagnosis. In: Zuckerman AJ, Thomas HC, eds. *Viral hepatitis - Scientific basis and clinical management.* New York: Churchill Livingstone, 1993:165-184.
7. Hollinger FB. Hepatitis B Virus. In: Fields BN, Knipe DM, Howley PM, et al., eds. *Fields virology. Third ed* Philadelphia: Lippincott-Raven Publishers, 1996:2752-2757.
8. Martin P, Friedman LS, Dienstag JL. Diagnostic Approach. In: Zuckerman AJ, Thomas HC, eds. *Viral hepatitis - Scientific basis and clinical management.* New York: Churchill Livingstone, 1993:393-409.
9. Papaevangelou G, Roumeliotou-Karayannis A, Tassopoulos N, et al. Diagnostic value of anti-HBc IgM in high HBV prevalence areas. *J Med Virol* 1984;13:393-399.
10. Gerlich WH, Luer W, Thomssen R, et al. Diagnosis of acute and inapparent hepatitis B virus infections by measurement of IgM antibody to hepatitis B core antigen. *J Infect Dis* 1980;142:95-101.
11. Colloredo G, Bellati G, Leandro G, et al. Quantitative analysis of IgM anti-HBc in chronic hepatitis B patients using a new “gray-zone” for the evaluation of “borderline” values. *J Hepatol* 1996;25:644-648.
12. Bänninger P, Altorfer J, Frösner GG, et al. Prevalence and significance of anti-HBc IgM (radioimmunoassay) in acute and chronic hepatitis B and in blood donors. *Hepatol* 1983;3:337-342.
13. Mels GC, Bellati G, Leandro G, et al. Fluctuations in viremia, aminotransferases and IgM antibody to hepatitis B core antigen in chronic hepatitis B patients with disease exacerbations. *Liver* 1994;14:175-181.
14. Kiyosawa K, Sodeyama T, Franca STM, et al. Serial assay for IgM anti-HBc in patients with anti-HBe-positive chronic hepatitis and its significance for long-term prognosis. *J Med Virol* 1988;24:241-250
15. Maruyama T, Schödel F, Iino S, et al. Distinguishing between acute and symptomatic chronic hepatitis B virus infection. *Gasteroenterol* 1994;106:1006-1015.
16. Tassopoulos NC, Papatheodoridis GV, Kalantzakis Y, et al. Differential diagnosis of acute HBsAg positive hepatitis using IgM anti-HBc by a rapid, fully automated microparticle enzyme immunoassay. *J Hepatol* 1997;26:14-9.
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; December 2009.
19. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
20. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition.* CLSI Document M29-A4. Wayne, PA: CLSI; 2014.
21. Box GEP, Hunter WG, Hunter JS. *Statistics for experimenters; an introduction to design, data analysis, and model building.* New York, NY: John Wiley & Sons, Inc, 1978:510-539, 571–583.
22. SAS Institute, Inc. SAS Technical Report P-229, *SAS/STAT Software: Changes and enhancements,* Release 6.07. Cary, NC: SAS Institute Inc, 1992:289–366.

Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTROL NO.	Control Number
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCT OF GERMANY	Product of Germany
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: EYE IRRITANT	Warning: Causes serious eye irritation.
WASH BUFFER	Wash Buffer

The following U.S. Patents are relevant to the ARCHITECT iSystem 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

Abbott GmbH & Co. KG
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580

CE 0123

Customer Service: Contact your local representative or find country-specific contact information on www.abbottdiagnostics.com

Revised July 2019.

Abbott