ARCHITECT HBeAg

REF 6C32-27
REF 6C32-37

en
HBeAg
6C32
G6-5476/R02
B6C3X0

Read Highlighted Changes: Revised February 2015.

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 HBeAg

INTENDED USE

The ARCHITECT HBeAg assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of hepatitis B e antigen (HBeAg) in human serum and plasma and is indicated for use as an aid in the diagnosis and monitoring of hepatitis B viral infection.

The ARCHITECT HBeAg assay can also be used for the quantitative determination of HBeAg. Refer to ARCHITECT HBeAg Quantitative Calibrators package insert (7P24-01) for instructions and further information.

SUMMARY AND EXPLANATION OF THE TEST

HBeAg determinations can be used to monitor the progress of hepatitis B viral infection. HBeAg is first detectable in the early phase of hepatitis B viral infection, after the appearance of hepatitis B surface antigen (HBsAg).[1] The titers of both antigens rise rapidly during the period of viral replication in acute infection. The presence of HBeAg correlates with increased numbers of infectious virus (Dane particles), the occurrence of core particles in the nucleus of the hepatocyte, and the presence of hepatitis B virus specific DNA and DNA polymerase in serum.[1] HBeAg may persist together with HBsAg in chronic hepatitis B viral infection. However, a subset of chronic hepatitis B patients have no detectable HBeAg in serum, but are positive for antibody to HBeAg (anti-HBe); these patients may also be positive for serum hepatitis B virus DNA.[2]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

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

1. Sample, assay diluent, and anti-HBe (mouse, monoclonal) coated paramagnetic microparticles are combined. HBeAg present in the sample binds to the anti-HBe coated microparticles.
2. After washing, acridinium-labeled anti-HBe conjugate 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 HBeAg in the sample and the RLUs detected by the ARCHITECT iSystem optics.

The presence or absence of HBeAg 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 less than the cutoff signal, then the specimen is considered nonreactive for HBeAg.

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

REAGENTS

Kit Contents

ARCHITECT HBeAg 6C32

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

REF	6C32-27	6C32-37
Σ	100	500
MICROPARTICLES	1 x 6.6 mL	1 x 27.0 mL
CONJUGATE	1 x 5.9 mL	1 x 26.3 mL
ASSAY DILUENT	1 x 3.9 mL	1 x 16.1 mL

MICROPARTICLES Antibody to hepatitis B e antigen (mouse, monoclonal) coated microparticles in phosphate buffer with protein (bovine) stabilizer. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and other antimicrobial agents.

CONJUGATE Acridinium-labeled antibody to hepatitis B e antigen (mouse, monoclonal) conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.04 µg/mL. Preservative: ProClin 300.

ASSAY DILUENT Phosphate buffer with recalcified human plasma and protein (bovine) stabilizer. Preservatives: ProClin 300 and a second antimicrobial agent.

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 contains human-sourced and/or potentially infectious components. Refer to the **REAGENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[3-6]

The human plasma used in the Assay Diluent is nonreactive for HBeAg, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.

The following warnings and precautions apply to: MICROPARTICLES / CONJUGATE / ASSAY DILUENT	
	
WARNING	Contain methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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.

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 HBeAg assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to performing the assay.

The assay file number for ARCHITECT HBeAg Qualitative Assay is 305 (HBeAgQual).

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.

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-B CPDA-1 CPD Potassium oxalate

- Other anticoagulants have not been validated for use with the ARCHITECT HBeAg assay.
- 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.
- Performance has not been established using cadaver specimens or 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

- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.
- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed
  - obvious microbial 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.
- For accurate results, serum and plasma specimens must be free of fibrin, red blood cells, or other particulate matter.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.

  Specimens must be separated from clots or red blood cells using the centrifugation instructions recommended by the collection tube manufacturer.
- 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.
- 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.
- **Mix thawed specimens by inverting 180 degrees from upright and return, for a total of 10 inversion cycles. 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.
- 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 (-20°C or colder).

No qualitative performance differences were observed between experimental controls and the 23 nonreactive or 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 22 nonreactive or the 22 spiked reactive specimens tested with elevated levels of hemoglobin (≤ 500 mg/dL) or triglycerides (≤ 3,000 mg/dL).

No qualitative performance differences were observed between experimental controls and the 23 nonreactive or the 23 spiked reactive specimens tested with elevated levels of bilirubin (≤ 20 mg/dL).

No qualitative performance differences were observed between experimental controls and the 25 nonreactive or the 25 spiked reactive specimens tested with elevated levels of 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.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

6C32 ARCHITECT HBeAg Reagent Kit

Materials Required but not Provided

- ARCHITECT HBeAg Assay file (Assay file number 305) obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 6C32-01 ARCHITECT HBeAg Calibrators
- 6C32-10 ARCHITECT HBeAg 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: 80 µL

    Sample volume for each additional test from same sample cup: 30 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 30 µL
  - > 3 hours on board: Additional sample volume required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT HBeAg Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 4 drops

    for each control: 4 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.

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT HBeAg assay.

Calibration

- Test Calibrators 1 and 2 in replicates of three. Calibrators should be priority loaded.

  A single sample of each qualitative 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.

  Refer to ARCHITECT HBeAg Calibrators package insert (6C32-01) and ARCHITECT HBeAg Controls package insert (6C32-10).
- Once an ARCHITECT HBeAg 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 minimum control requirement for the ARCHITECT HBeAg assay is that a single sample of both controls be tested once every 24 hours each day of use. 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 HBeAg Control values must be within the acceptable ranges specified in the control package insert (6C32-10). If a control is out of its specified range, the associated test results are invalid and samples 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 HBeAg assay belongs to method group 5.

RESULTS

The ARCHITECT iSystem calculates the ARCHITECT HBeAg Calibrator 1 (Cal 1) and Calibrator 2 (Cal 2) mean chemiluminescent signals (RLUs) from three replicates of each calibrator and stores the results.

Calculation

The ARCHITECT iSystem calculates an ARCHITECT HBeAg result based on the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

- Cutoff RLU = [(Cal 2 mean RLU - Cal 1 mean RLU) x 0.1] + Cal 1 mean RLU
- The cutoff RLU is stored for each reagent lot calibration.
- S/CO = Sample RLU/Cutoff RLU

Example:

If the Sample RLU = 1800 and the

Cutoff RLU = 1000, then

1800/1000 = 1.800

S/CO = 1.800

Interpretation of Results

Initial Results

S/CO values	Instrument Flag	Instrument Interpretation	Retest Procedure
< 1.000	NONREACTIVE	Nonreactive	No retest required.
≥ 1.000	REACTIVE	Reactive	Retest in duplicate.

Duplicate Retest Results

Instrument Interpretation	Specimen Classification
Both results nonreactive	Specimen considered nonreactive for HBeAg.
One or both results reactive	Specimen considered repeatedly reactive for HBeAg.

All initially reactive specimens should be transferred to a centrifuge tube, recentrifuged at ≥ 10,000 RCF for 10 minutes and retested in duplicate.

For details on configuring the ARCHITECT iSystem regarding grayzone and high reactive interpretations, refer to the ARCHITECT System Operations Manual, Section 2. The grayzone and high reactive result interpretation is an editable parameter, and should be utilized per end user requirements.

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 or monitoring purposes, results should be used in conjunction with patient history and other hepatitis markers for diagnosis or monitoring of acute or chronic infection.
- In the presence of anti-HBe, immune complex formation might occur which can lead to lower HBeAg results.
- If the HBeAg results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT HBeAg that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.[7, 8]

  ARCHITECT HBeAg reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. 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.[9]

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The precision of the ARCHITECT HBeAg assay for reactive specimens (S/CO ≥ 1.000) is ≤ 10%. A study was performed using a panel consisting of one nonreactive member, four diluted HBeAg reactive members, controls, and calibrators. Two external sites tested two different lots of the controls and calibrators across two reagent lots (every combination), and an internal site tested three different lots of controls and calibrators across three reagent lots (every combination). All panel members were tested in replicates of three per run. The intra-run and inter-run standard deviations (SD) and percent coefficient of variation (%CV) were analyzed with a variance components analysis[10] using a mixed analysis of variance model.[11] The data from this study are summarized in Table 1.

Table 1: ARCHITECT HBeAg Precision*

Panel Member	Total n	Mean S/CO	Intra-run SD	Intra-run %CV	Inter-run** SD	Inter-run** %CV
Calibrator 1	516	0.309	0.042	13.61	0.043	13.92
Calibrator 2	516	7.223	0.281	3.88	0.321	4.44
Negative Control	516	0.368	0.046	12.40	0.049	13.36
Positive Control	516	3.869	0.120	3.09	0.172	4.43
Panel 1	204	0.389	0.088	22.63	0.090	22.99
Panel 2	204	1.164	0.049	4.19	0.057	4.86
Panel 3	204	4.375	0.148	3.38	0.171	3.91
Panel 4	204	169.903	4.110	2.42	6.367	3.75
Panel 5	204	1191.234	24.793	2.08	39.426	3.31

* Representative performance data are shown. Results obtained in individual laboratories may vary.

** Inter-run variability contains intra-run variability.

Specificity

The ARCHITECT HBeAg assay specificity for random blood donor specimens is ≥ 99.5%. A study on a total of 1309 random blood (serum and plasma) donor specimens was performed at two clinical sites. All 1309 were nonreactive by ARCHITECT HBeAg. The data from this study are summarized in Table 2.

The ARCHITECT HBeAg assay specificity for hospitalized patient specimens is > 99.0%. A study on a total of 498 hospitalized patient specimens was performed at one clinical site. Seven were reactive by ARCHITECT HBeAg and were also positive for HBsAg. The remaining 491 specimens were nonreactive by ARCHITECT HBeAg. The data from this study are summarized in Table 2.

Table 2: ARCHITECT HBeAg Specificity Results Using Specimens from Random Blood Donors and Hospitalized Patients*

Population	Number of Specimens Tested	Initially Reactive	Repeatedly Reactive	Number of Positives by Supplemental Testing**
Random Blood Donors	1309	0	0	0
Hospitalized Patients	498	7	7	7
Total	1807	7	7	7

* Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

** Supplemental testing on HBeAg repeatedly reactives was performed with an HBsAg assay.

A study was performed in which a total of 155 specimens from individuals with potentially interfering substances and disease states other than HBV (CMV, EBV, anti-HAV, anti-HCV, anti-HIV-1, HSV, rubella, HBV vaccine recipients, syphilis, urinary tract infections, rheumatoid factor, anti-nuclear autoantibodies [ANA], toxoplasmosis, alcoholic cirrhosis, pregnant females, multiple myeloma, multiparous females, dialysis patients, human anti-mouse antibodies [HAMA]) were tested by ARCHITECT HBeAg. The data from this study are summarized in Table 3.

A study was performed in which 75 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 HBeAg. Four specimens were reactive by ARCHITECT HBeAg and were also positive for HBsAg. The data from this study are summarized in Table 3.

Table 3: ARCHITECT HBeAg Specificity Results Using Potentially Interfering and High Risk Specimens*

Population	Number of Specimens Tested	Initially Reactive	Repeatedly Reactive	Number of Positives by Supplemental Testing**
Potentially Interfering Substances	155	0	0	0
High Risk of Blood Transmissible Infections	75	4	4	4

* Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

** Supplemental testing on HBeAg repeatedly reactives was performed with an HBsAg assay.

Sensitivity

The ARCHITECT HBeAg assay sensitivity is ≥ 99.5%. A study was performed in which a total of 206 specimens, which were pre-characterized reactive for HBeAg and HBsAg, were all reactive by ARCHITECT HBeAg. The data from this study are summarized in Table 4.

Table 4: ARCHITECT HBeAg Sensitivity Results Using Specimens Pre-characterized Reactive for HBeAg*

Population	Number of specimens Tested	Reactive
Pre-characterized HBeAg Reactives	206	206

* Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

The ARCHITECT HBeAg assay sensitivity at the cutoff is < 0.5 PEI U/mL. A study was performed in which a total of 93 specimens from individuals clinically or serologically classified with different stages of HBV infection were tested by ARCHITECT HBeAg. Twenty-seven out of 36 acute specimens were reactive and 9 were nonreactive. Out of 57 chronic specimens, 18 were reactive and 39 were nonreactive.

Assay Comparison

A total of 2702 specimens (random blood donors, hospitalized patients, potentially interfering substances, high risk of blood transmissible infections, acute HBV infection, chronic HBV infection, other HBV positives, and seroconversion panels) were tested by ARCHITECT HBeAg and AxSYM HBe 2.0. The agreement between the two methods was 99.30% (2683/2702).

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Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY DILUENT	Assay Diluent
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: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer

The following US 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

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

Revised February 2016.

Abbott

ARCHITECT HBeAg Controls

REF 6C32-10

en
HBeAg
6C32
G5-3175 / R04
C6C320

Read Highlighted Changes: Revised November 2014.

INTENDED USE

The ARCHITECT HBeAg Controls are for the verification of the accuracy and precision of the ARCHITECT iSystem when used for the qualitative detection of Hepatitis B e Antigen (HBeAg) in human serum and plasma. Refer to the ARCHITECT HBeAg reagent package insert for additional information.

CONTENTS

- 1 Bottle (8 mL) of ARCHITECT HBeAg Negative Control. Recalcified human plasma. Preservative: Antimicrobial Agents.
- 1 Bottle (8 mL) of ARCHITECT HBeAg Positive Control. Recombinant DNA-derived HBeAg in TRIS buffer with protein (bovine) stabilizer. Preservatives: Antimicrobial Agents.
- The controls are at the following ranges and approximate concentrations:

Control	Color	Approximate Concentration (PEI U/mL)	Range (S/CO)
CONTROL −	none	0.0	0.000 - 0.800
CONTROL +	Blue[a]	0.7	2.026 - 6.077

[a] Dye: Acid Blue No. 9

STANDARDIZATION

Concentration standardized against the Reference Standard of the Paul Ehrlich Institute, Langen, Germany.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[1-4]
- The human plasma used in the Negative Control is nonreactive for HBeAg, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.

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.

STORAGE

- Controls are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Controls may be used immediately after removal from 2-8°C storage.

Prior to use, mix by gentle inversion (5-10 times).

After each use, tightly close the caps and return the controls to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline–Third Edition*. CLSI Document M29-A3. Wayne, PA: CLSI; 2005.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CONTROL −	Negative Control
CONTROL +	Positive Control
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
RANGE	Range
REF	List Number

Abbott GmbH & Co. KG
Max-Planck-Ring 2
65205 Wiesbaden
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CE
0088

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

Revised November 2014.

Abbott

ARCHITECT HBeAg Calibrators

REF 6C32-01

en
HBeAg
6C32
G5-3174 / R03
S6C320

Read Highlighted Changes: Revised November 2014.

INTENDED USE

The ARCHITECT HBeAg Calibrators are for the calibration of the ARCHITECT iSystem when used for the qualitative detection of Hepatitis B e Antigen (HBeAg) in human serum and plasma. Refer to the ARCHITECT HBeAg reagent package insert for additional information.

CONTENTS

2 Bottles (4 mL) of ARCHITECT HBeAg Calibrators. Calibrator 1 contains TRIS buffer with protein (bovine) stabilizer. Calibrator 2 contains recombinant DNA-derived HBeAg in TRIS buffer with protein (bovine) stabilizer. Preservatives: Antimicrobial Agents.

The calibrators are at the following approximate concentrations:

Calibrator	Approximate Concentration (PEI U/mL)
CAL 1	0.0
CAL 2	1.3

STANDARDIZATION

Concentration standardized against the Reference Standard of the Paul Ehrlich Institute, Langen, Germany.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- 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.[1-4]

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.

STORAGE

- Calibrators are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Calibrators may be used immediately after removal from 2-8°C storage.

Prior to use, mix by gentle inversion (5-10 times).

After each use, tightly close the caps and return the calibrators to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services, *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed. Washington, DC: US Government Printing Office, December 2009.
3. World Health Organization, *Laboratory Biosafety Manual*, 3rd ed. Geneva: World Health Organization, 2004.
4. Clinical and Laboratory Standards Institute (CLSI), *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline - Third Edition*. CLSI Document M29-A3. Wayne, PA: CLSI, 2005.

Key to Symbols

	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CAL 1	Calibrator 1
CAL 2	Calibrator 2
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
REF	List Number

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

Revised November 2014.

Abbott

ARCHITECT
Anti-HBe Calibrator

REF 6C34-01

en
Anti-HBe
6C34
G4-7810 / R05
S6C340

Read Highlighted Changes: Revised July 2015.

INTENDED USE

The ARCHITECT Anti-HBe Calibrator is for the calibration of the ARCHITECT iSystem when used for the qualitative detection of antibody to Hepatitis B e Antigen (Anti-HBe) in human serum and plasma. Refer to the ARCHITECT Anti-HBe reagent package insert for additional information.

CONTENTS

1 Bottle (4 mL) of ARCHITECT Anti-HBe Calibrator 1. Recalcified nonreactive human plasma. Preservative: Sodium Azide.

The calibrator is at the following approximate concentration:

Calibrator	Color	Concentration (PEI U/mL)
CAL 1	Green[a]	0.0

[a]Dye: Green (Acid Yellow No.23 and Acid Blue No.9)

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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 the calibrator is nonreactive for anti-HBe, HBeAg, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CAL 1	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

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.

STORAGE

- Calibrator is stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Calibrator may be used immediately after removal from 2-8°C storage.

Prior to use, mix by gentle inversion (5-10 times).

After each use, tightly close the cap and return the calibrator to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CAL 1	Calibrator 1
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
REF	List Number

Abbott GmbH & Co. KG
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Customer Service: Contact your local representative or find country-specific contact information on www.abbottdiagnostics.com

Revised July 2015.

Abbott

ARCHITECT
Anti-HBe Controls

REF 6C34-10

en

Anti-HBe
6C34
G5-9346 / R06
C6C340

Read Highlighted Changes: Revised July 2015.

INTENDED USE

The ARCHITECT Anti-HBe Controls are for the verification of the accuracy and precision of the ARCHITECT iSystem when used for the qualitative detection of antibody to Hepatitis B e Antigen (anti-HBe) in human serum and plasma. Refer to the ARCHITECT Anti-HBe reagent package insert for additional information.

CONTENTS

2 Bottles (8 mL each) of ARCHITECT Anti-HBe Controls are recalcified human plasma. The negative control is nonreactive. The positive control is reactive for anti-HBe. Preservative: Sodium Azide.

The controls are at the following ranges and approximate concentrations:

		Approximate Concentration	Control Range	
Control	Color	(PEI U/mL)	S/CO	(% Inhibition)
CONTROL -	none	0.00	1.30 - 2.70	-35.0 - 35.0
CONTROL +	Blue[a]	0.38	0.21 - 0.80	60.0 - 89.5

[a] Dye: Acid Blue No. 9

STANDARDIZATION

Concentration standardized against the Reference Standard of the Paul Ehrlich Institute, Langen, Germany.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[1-4]
- The human plasma used in the negative control is nonreactive for anti-HBe, HBeAg, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2.
- The human plasma used in the positive control is reactive for anti-HBe, and nonreactive for HBeAg, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2.

The following warnings and precautions apply to CONTROL - , CONTROL +	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

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.

STORAGE

- Controls are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Controls may be used immediately after removal from 2-8°C storage.

Prior to use, mix by gentle inversion (5-10 times).

After each use, tightly close the caps and return the controls to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual.* 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL -	Negative Control
CONTROL +	Positive Control
INHIBITION	Inhibition
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
RANGE	Range
REF	List Number

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

Revised July 2015.

Abbott

ARCHITECT Anti-HBe

REF 6C34-25
REF 6C34-20
REF 6C34-35

en
Anti-HBe
6C34
G6-0570/R06
B6C340

Read Highlighted Changes: Revised February 2016.

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-HBe

INTENDED USE

The ARCHITECT Anti-HBe assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of antibody to hepatitis B e antigen (anti-HBe) in human serum and plasma and is indicated as an aid in the diagnosis and monitoring of hepatitis B viral infection.

SUMMARY AND EXPLANATION OF THE TEST

Hepatitis B e antigen (HBeAg) and its antibody (anti-HBe) are found in association with hepatitis B viral infection.[1] HBeAg is first detectable in the early phase of hepatitis B viral infection, after the appearance of hepatitis B surface antigen (HBsAg).[2] The titers of both antigens rise rapidly during the period of viral replication in acute infection. Seroconversion from HBeAg to anti-HBe during acute hepatitis B infection is usually indicative of resolution of infection and a reduced level of infectivity. A negative HBeAg result may indicate (1) early acute infection before the peak of viral replication or (2) early convalescence when HBeAg has declined below detectable levels. The presence of anti-HBe serves to distinguish between these two phases.[3] A subset of chronic hepatitis B patients have no detectable HBeAg in serum, but are positive for anti-HBe; these patients may also be positive for serum hepatitis B virus DNA.[4]

Additionally HBe antigen/antibody seroconversion is used as an indicator of virological response when treating patients with chronic hepatitis B.[5]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

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

1. Sample, neutralizing reagent, and anti-HBe (mouse, monoclonal) coated paramagnetic microparticles are combined. The anti-HBe present in the sample binds to the recombinant HBeAg present in the neutralizing reagent. Unbound recombinant HBeAg is available to bind to the anti-HBe coated microparticles.
2. After washing, acridinium-labeled anti-HBe conjugate is added to create a reaction mixture.
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 an inverse relationship between the amount of anti-HBe in the sample and the RLUs detected by the ARCHITECT iSystem optics.

The presence or absence of anti-HBe 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 of the reaction is greater than the cutoff signal, then the sample is considered nonreactive for anti-HBe.

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

REAGENTS

Kit Contents

ARCHITECT Anti-HBe 6C34

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

REF	6C34-25	6C34-20	6C34-35
Σ	100	400	500
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL
NEUTRALIZING REAGENT	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL

MICROPARTICLES Antibody to Hepatitis B e Antigen (mouse, monoclonal) coated microparticles in phosphate buffer with protein (bovine) stabilizer. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and other Antimicrobial Agents.

CONJUGATE Acridinium-labeled antibody to Hepatitis B e Antigen (mouse, monoclonal) conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.08 µg/mL. Preservative: ProClin 300.

NEUTRALIZING REAGENT Hepatitis B e Antigen (recombinant DNA) in TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 6.7 PEI U/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.[6-9]

The following warnings and precautions apply to: MICROPARTICLES / CONJUGATE	
	
WARNING	Contain methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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.

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-HBe 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.

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.

Alternate Result Units

The default result unit for the ARCHITECT Anti-HBe assay is S/CO (Sample to Cutoff ratio). An alternate result unit, %Inh (Percent Inhibition), may be selected for reporting results by editing assay parameter "Result concentration units", to %Inh. For information on editing the Result concentration units, refer to the ARCHITECT System Operations Manual, Section 2.

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-B CPDA-1 CPD Potassium oxalate

- Other specimen collection tube types have not been validated with this assay.
- Performance has not been established for the use of cerebrospinal specimens or the use of body fluids other than human serum and 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
- 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.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.
- 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 accurate results, serum and plasma specimens must be free of fibrin, red blood cells, or other particulate matter.
- No qualitative performance differences were observed between experimental controls and the 22 nonreactive or the 22 spiked reactive specimens tested with elevated levels of hemoglobin (≤ 500 mg/dL) or triglycerides (≤ 3,000 mg/dL).
- No qualitative performance differences were observed between experimental controls and the 23 nonreactive or the 23 spiked reactive specimens tested with elevated levels of bilirubin (≤ 20 mg/dL).
- No qualitative performance differences were observed between experimental controls and the 25 nonreactive or the 25 spiked reactive specimens tested with elevated levels of protein (≤ 12 g/dL), or red blood cells (≤ 0.4% v/v).

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 red blood cells, clots, or particulate matter,
  - they require repeat testing, or
  - they were frozen and thawed.

  Transfer clarified specimens to a sample cup or secondary tube for testing.
- **Mix thawed specimens by inverting 180 degrees from upright and return, for a total of 10 inversion cycles. 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.
- 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.
- 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	15-30°C	≤ 3 days
	2-8°C	≤ 7 days

Specimens may be stored on or off the clot or red blood cells for up to 7 days at 2-8°C or off the clot or red blood cells for 3 days at 15-30°C.

Plasma specimens that have been stored at 2-8°C more than three days without removal from red blood cells should be re-centrifuged before analysis, to avoid erroneous results.

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 (-20°C or colder).

No qualitative differences were observed between experimental controls and the 23 nonreactive or spiked reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

6C34 ARCHITECT Anti-HBe Reagent Kit

Materials Required but not Provided

- ARCHITECT Anti-HBe Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 6C34-01 ARCHITECT Anti-HBe Calibrator
- 6C34-10 ARCHITECT Anti-HBe 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: 150 µL

    Sample volume for each additional test from same sample cup: 100 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 100 µL
  - > 3 hours on board: Additional sample volume required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT Anti-HBe Calibrator and Controls.
  - Mix calibrator(s) and controls by gentle inversion (5-10 times) before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 10 drops

    for each control: 4 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.

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT Anti-HBe assay.

Calibration

- Test Calibrator 1 in replicates of three. The calibrator 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-HBe 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 minimum control requirement for the ARCHITECT Anti-HBe assay is that a single sample of both the 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-HBe 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 samples 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-HBe assay belongs to method group 5.

RESULTS

The ARCHITECT iSystem calculates the ARCHITECT Anti-HBe Calibrator 1 mean chemiluminescent signal (RLU) from 3 replicates and stores the result.

Calculation

The ARCHITECT iSystem calculates an ARCHITECT Anti-HBe result based on the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

- Cutoff RLU = Calibrator 1 mean RLU x 0.5
- The cutoff RLU is stored for each reagent lot calibration.
- S/CO = Sample RLU/Cutoff RLU

Example:

If the Sample RLU = 15000 and the

Cutoff RLU = 30000, then

15000/30000 = 0.50

S/CO = 0.50

The ARCHITECT iSystem calculates the percent inhibition (%Inh) of the sample RLU relative to the Calibrator 1 mean RLU.

$$\% \text{ Inhibition} = \frac{\text{Calibrator 1 Mean RLU - Sample RLU}}{\text{Calibrator 1 Mean RLU}} \times 100$$

Example:

If the Sample RLU = 15000 and the

Calibrator 1 Mean RLU = 60000, then

$$\frac{60000-15000}{60000} \times 100 = 75$$

% Inhibition = 75

Interpretation of Results

- Specimens with S/CO values > 1.00 are considered nonreactive by the ARCHITECT Anti-HBe assay and need not be tested further.
- Specimens with S/CO values ≤ 1.00 are considered reactive by the ARCHITECT Anti-HBe assay.
- Specimens with %Inh < 50* are considered nonreactive by the ARCHITECT Anti-HBe assay.
- Specimens with %Inh ≥ 50* are considered reactive by the ARCHITECT Anti-HBe assay.
- Samples with S/CO values > 3.0 or %Inh < -50 may be reactive for HBeAg and should be tested for HBeAg.
- All initially reactive specimens should be transferred to a centrifuge tube, recentrifuged at ≥ 10,000 RCF for 10 minutes and retested in duplicate. If both retest values are nonreactive, the specimen must be considered nonreactive for anti-HBe. If either of the retest values is reactive, the specimen must be considered repeat reactive for anti-HBe by the criteria of ARCHITECT Anti-HBe.
- For details on configuring the ARCHITECT iSystem to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2.

* **NOTE:** Due to mathematical rounding a sample result of, for example, 49.8%Inh equals 50%Inh and is considered reactive by the ARCHITECT Anti-HBe assay.

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-HBe 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.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits that employ mouse monoclonal antibodies.[10, 11] ARCHITECT Anti-HBe reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. 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.[12]

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The precision of the ARCHITECT Anti-HBe assay across the control range (0.21 - 2.70 S/CO) is ≤ 10%. A study was performed using a panel consisting of one nonreactive member, four diluted anti-HBe reactive members, controls, and the calibrator. Two external sites tested two different lots of the controls and the calibrator across two reagent lots (every combination), and an internal site tested three different lots of controls and calibrator across three reagent lots (every combination). All panel members were tested in replicates of three per run. The intra-run and inter-run standard deviations (SD) and percent coefficient of variation (%CV) were analyzed with a variance components analysis[13] using a mixed analysis of variance model[14]. The data from this study are summarized in Table 1.

Table 1: ARCHITECT Anti-HBe Precision*

Panel member	Total n	Mean S/CO	Intra-run SD	Intra-run %CV	Inter-run** SD	Inter-run** %CV
Calibrator 1	516	2.00	0.096	4.79	0.097	4.83
Negative Control	516	1.97	0.086	4.38	0.095	4.80
Positive Control	516	0.51	0.027	5.29	0.029	5.68
Panel 1	204	0.11	0.006	5.64	0.007	6.55
Panel 2	204	0.23	0.008	3.72	0.010	4.48
Panel 3	204	0.47	0.018	3.76	0.022	4.66
Panel 4	204	0.93	0.044	4.75	0.047	5.04
Panel 5	204	1.70	0.080	4.69	0.084	4.93

* Representative performance data are shown. Results obtained in individual laboratories may vary.

** Inter-run variability contains intra-run variability.

Specificity

The ARCHITECT Anti-HBe assay specificity for random blood donor specimens is ≥ 99.5%.

A study on a total of 1310 random blood (serum and plasma) donor specimens was performed at two clinical sites. Six specimens were reactive by ARCHITECT Anti-HBe and were also reactive for anti-HBc. The remaining 1304 specimens were nonreactive by ARCHITECT Anti-HBe. The data from this study are summarized in Table 2.

The ARCHITECT Anti-HBe assay specificity for hospitalized patient specimens is > 99.0%.

A study on a total of 498 hospitalized patient specimens was performed at one clinical site. Sixty-three specimens were reactive by ARCHITECT Anti-HBe and were also reactive for anti-HBc. The remaining 435 specimens were nonreactive by ARCHITECT Anti-HBe. The data from this study are summarized in Table 2.

Table 2: ARCHITECT Anti-HBe Specificity Results Using Specimens from Random Blood Donors and Hospitalized Patients*

Population	Number of Specimens Tested	Initial Reactive	Repeat Reactive	Number of Reactives by Supplemental Testing**
Random Blood Donors	1310	6	6	6
Hospitalized Patients	498	64	63	53
Total	1808	70	69	59

* Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

** Supplemental testing on anti-HBe repeat reactives was performed with an anti-HBc assay.

A study was performed in which a total of 155 specimens from individuals with potentially interfering substances and disease states other than HBV (CMV, EBV, anti-HAV, anti-HCV, anti-HIV-1, HSV, rubella, HBV vaccine recipients, syphilis, urinary tract infections, rheumatoid factor, anti-nuclear autoantibodies [ANA], toxoplasmosis, alcoholic cirrhosis, pregnant females, multiple myeloma, multiparous females, dialysis patients, human anti-mouse antibodies [HAMA]) were tested by ARCHITECT Anti-HBe. Seven specimens were reactive by ARCHITECT Anti-HBe and were also reactive for anti-HBc. The data from this study are summarized in Table 3.

A study was performed in which 75 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-HBe. Fifteen specimens were reactive by ARCHITECT Anti-HBe and were also reactive for anti-HBc. The data from this study are summarized in Table 3.

Table 3: ARCHITECT Anti-HBe Specificity Results Using Potentially Interfering Substances and High Risk Specimens*

Population	Number of Specimens Tested	Initial Reactive	Repeat Reactive	Number of Reactives by Supplemental Testing**
Potentially Interfering Substances	155	7	7	7
High Risk of Blood Transmissible Infections	75	15	15	15

* Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

** Supplemental testing on anti-HBe repeat reactives was performed with an anti-HBc assay.

Sensitivity

The ARCHITECT Anti-HBe assay sensitivity is ≥ 99.5%. A study was performed in which a total of 206 specimens, which were pre-characterized reactive for anti-HBe and anti-HBc, were all reactive by ARCHITECT Anti-HBe. The data from this study are summarized in Table 4.

Table 4: ARCHITECT Anti-HBe Sensitivity Results Using Specimens Pre-characterized Reactive for Anti-HBe*

Population	Number of Specimens Tested	Reactive
Pre-characterized Anti-HBe Reactives	206	206

* Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

The ARCHITECT Anti-HBe assay sensitivity at the cut-off is ≤ 0.45 PEI U/mL.

A study was performed in which a total of 93 specimens from individuals clinically or serologically classified with different stages of HBV infection were tested by ARCHITECT Anti-HBe. Seventeen out of 36 acute specimens were reactive and 19 were nonreactive. Out of 57 chronic specimens, 36 were reactive and 21 were nonreactive.

Assay Comparison

A total of 2605 specimens (random blood donors, hospitalized patients, potentially interfering substances, high risk of blood transmissible infections, acute HBV infection, chronic HBV infection, other HBV positives, and seroconversion panels) were tested by ARCHITECT Anti-HBe and AxSYM Anti-HBe 2.0. The agreement between the two methods was 99.19% (2584/2605).

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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
NEUTRALIZING REAGENT	Neutralizing Reagent
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: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer

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Revised February 2016.

Abbott

ARCHITECT
Anti-HBc IgM Calibrators

REF 6C33-02

en
Anti-HBc IgM
6C33
G5-8958 / R01
S6C3W0

INTENDED USE

The ARCHITECT Anti-HBc IgM Calibrators are for the calibration of the ARCHITECT iSystem when used for the qualitative detection of IgM antibody to Hepatitis B core antigen (anti-HBc IgM) in human serum and plasma. Refer to the ARCHITECT Anti-HBc IgM reagent package insert for additional information.

CONTENTS

- 1 Bottle (4 mL) of ARCHITECT Anti-HBc IgM Calibrator 1. Recalcified nonreactive human plasma. Preservatives: ProClin 950, ProClin300 and other antimicrobial agents.
- 1 Bottle (4 mL) of ARCHITECT Anti-HBc IgM Calibrator 2. Recalcified human plasma reactive for anti-HBc IgM. Preservatives: ProClin 950, ProClin300 and other antimicrobial agents.

The Calibrators are at the following approximate concentrations:

Calibrator	Concentration (PEI U/mL)
CAL 1	0
CAL 2	67

STANDARDIZATION

Concentration standardized against the Reference Standard of the Paul Ehrlich Institute, Langen, Germany.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use

CAUTION: This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[1-4]

The human plasma used in Calibrator 1 is nonreactive for HBsAg, anti-HIV-1/HIV-2, anti-HCV, anti-HBs, and HIV-1 RNA or HIV-1 Ag.

The human plasma used in Calibrator 2 is reactive for anti-HBc IgM, reactive or nonreactive for HBsAg and nonreactive for anti-HIV-1/HIV-2, anti-HCV, and HIV-1 RNA or HIV-1 Ag.

The following warnings and precautions apply to: CAL 1 / CAL 2	
WARNING	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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.

STORAGE

- Calibrators are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Calibrators may be used immediately after removal from 2-8°C storage.

Prior to use, mix by gentle inversion (5-10 times).

After each use, tightly close the caps and return the calibrators to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Biological risks
	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CAL 1	Calibrator 1
CAL 2	Calibrator 2
HEPATITIS B RISK	Hepatitis B Risk
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
REF	List Number
WARNING: SENSITIZER	Warning: May cause an allergic reaction.

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Created June 2015.

Abbott

ARCHITECT
Anti-HBc IgM Controls

REF 6C33-11

en
Anti-HBc IgM
6C33
G6-0340 / R02
C6C3W0

INTENDED USE

The ARCHITECT Anti-HBc IgM Controls are for the verification of the calibration of the ARCHITECT iSystem when used for the qualitative detection of IgM antibody to Hepatitis B core antigen (anti-HBc IgM) in human serum and plasma. Refer to the ARCHITECT Anti-HBc IgM reagent package insert for additional information.

CONTENTS

2 Bottles (8 mL each) of ARCHITECT Anti-HBc IgM Controls are prepared in recalcified human plasma.

- The Negative Control is nonreactive. Preservatives: ProClin 950, ProClin 300, and other antimicrobial agents.
- The Positive Control is reactive for anti-HBc IgM. Preservatives: ProClin 950, ProClin 300, and other antimicrobial agents.

The controls are at the following ranges and approximate concentrations:

Control	Color	Dye	Concentration (PEI U/mL)	Range (S/CO)
CONTROL -	Natural	None	0	0 - 0.25
CONTROL +	Blue	Acid Blue No. 9	150	1.608 - 4.825

STANDARDIZATION

Concentration standardized against the Reference Standard of the Paul Ehrlich Institute, Langen, Germany.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use

CAUTION: This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[1-4]

The human plasma used in Negative Control is nonreactive for HBsAg, anti-HIV-1/HIV-2, anti-HCV, anti-HBs, and HIV-1 RNA or HIV-1 Ag.

The human plasma used in Positive Control is reactive for Anti-HBc IgM, reactive or non reactive for HBsAg and nonreactive for anti-HIV-1/HIV-2, anti-HCV, and HIV-1 RNA or HIV-1 Ag.

The following warnings and precautions apply to: CONTROL - / CONTROL +	
WARNING	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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.

STORAGE

- Controls are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Controls may be used immediately after removal from 2-8°C storage.

Prior to use, mix by gentle inversion (5-10 times).

After each use, tightly close the caps and return the controls to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual.* 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Biological risks
	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CONTROL -	Negative Control
CONTROL +	Positive Control
HEPATITIS B RISK	Hepatitis B Risk
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
RANGE	Range
REF	List Number
WARNING: SENSITIZER	Warning: May cause an allergic reaction.


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Revised August 2015.

Abbott

ARCHITECT Anti-HBc IgM

REF 6C33-27
REF 6C33-22

en
Anti-HBc IgM
6C33
G60417R03
B6C3W0

Read Highlighted Changes: Revised December 2017.

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.[5, 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.

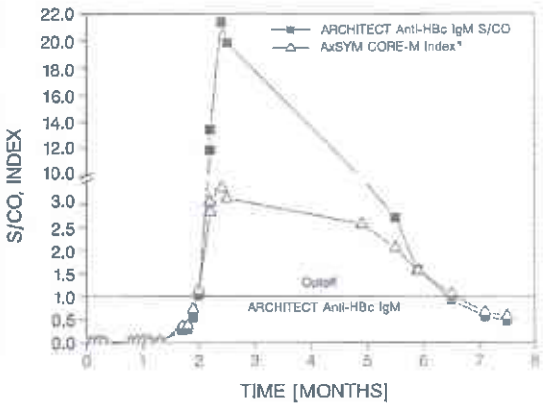
Sensitivity

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.

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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

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CE
0088

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

Revised December 2017.

Abbott

ARCHITECT
Anti-HCV Calibrator

REF 6C37-01

en

Anti-HCV
6C37
G4-7728 / R05
S6C3A0

Read Highlighted Changes: Revised November 2014.

INTENDED USE

The ARCHITECT Anti-HCV Calibrator is for the calibration of the ARCHITECT iSystem when used for the qualitative detection of antibody to Hepatitis C virus (anti-HCV) in human serum and plasma. Refer to the ARCHITECT Anti-HCV reagent package insert for additional information.

CONTENTS

1 Bottle (4 mL) of ARCHITECT Anti-HCV Calibrator is prepared in recalcified human plasma (inactivated); reactive for anti-HCV. Preservative: Sodium Azide.

Calibrator	Color
CAL 1	Green*

* Dyes: Acid Yellow No. 23 and Acid Blue No. 9

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[1-4]
- The human plasma used in the Calibrator is reactive for anti-HCV and nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CAL 1	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

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.

STORAGE

- Calibrator is stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Calibrator should be mixed by gentle inversion prior to use.

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Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CAL 1	Calibrator 1
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
REF	List Number

Abbott GmbH & Co. KG
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CE 0088

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

Revised November 2014.

Abbott

ARCHITECT
Anti-HCV Controls

REF 6C37-10

en

Anti-HCV
6C37
G4-7729 / R06
C6C3B0

Read Highlighted Changes: Revised November 2014.

INTENDED USE

The ARCHITECT Anti-HCV Controls are for the verification of the calibration of the ARCHITECT iSystem when used for the qualitative detection of antibody to Hepatitis C virus (anti-HCV) in human serum and plasma.

Refer to the ARCHITECT Anti-HCV reagent package insert for additional information.

CONTENTS

2 Bottles (8 mL each) of ARCHITECT Anti-HCV Controls are prepared in recalcified human plasma (inactivated). The Positive Control is reactive for anti-HCV. Preservative: Sodium Azide.

The controls are at the following:

Control	Color	Titer	Control Range S/CO
CONTROL −	Natural	N/A*	≤ 0.60
CONTROL +	Blue**	≥ 1:1	1.71 - 5.13

* Not Applicable.

** Dye: Acid Blue No. 9

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. 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.[1-4]
- The human plasma used in the Negative Control is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2.
- The human plasma used in the Positive Control is reactive for anti-HCV and nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CONTROL − / CONTROL +	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

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.

STORAGE

- Controls are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR ANALYSIS

Controls should be mixed by gentle inversion prior to use.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline–Third Edition*. CLSI Document M29-A3. Wayne, PA: CLSI; 2005.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL −	Negative Control
CONTROL +	Positive Control
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
PRODUCT OF GERMANY	Product of Germany
RANGE	Range
REF	List Number
TITER	Titer

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

CE
0088

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

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