



ARCHITECT

SYSTEM

en

HBsAg

IVD **REF** 6C36

84-5655/R8

B6C3B0

Read Highlighted Changes
Revised May, 2008

HBsAg

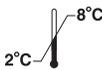


Customer Service

For additional product information, please contact your local customer service organization.

This package insert must be read carefully prior to use. 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.

Key to symbols used

REF	List Number	REACTION VESSELS	Reaction Vessels
IVD	<i>In Vitro</i> Diagnostic Medical Device	SAMPLE CUPS	Sample Cups
LOT	Lot Number	SEPTUM	Septum
	Expiration Date	REPLACEMENT CAPS	Replacement Caps
	Store at 2-8°C	SN	Serial Number
	CAUTION: Consult accompanying documents.	CONTROL NO.	Control Number
	Manufacturer	REAGENT LOT	Reagent Lot

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

NAME

ARCHITECT HBsAg

INTENDED USE

The ARCHITECT HBsAg assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of hepatitis B surface antigen (HBsAg) in human serum and plasma.

SUMMARY AND EXPLANATION OF TEST

Enzyme immunoassays for the detection of HBsAg were first described by Engvall and Perlmann¹⁻³ and Van Weemen and Schuurs⁴ in 1971. In 1976 and 1977, solid phase "sandwich" enzyme immunoassays were developed in which HBsAg was captured on a solid phase coated with polyclonal antibodies against HBsAg (anti-HBs) and then detected with anti-HBs conjugated to an enzyme.⁵⁻⁷ In the early 1980's, monoclonal anti-HBs based assays were developed for the detection of HBsAg.⁸⁻¹³ ARCHITECT HBsAg is a chemiluminescent microparticle immunoassay (CMIA) which uses microparticles coated with monoclonal anti-HBs for the detection of HBsAg.

HBsAg assays are routinely used to aid in the diagnosis of suspected hepatitis B viral (HBV) infection and to monitor the status of infected individuals, *i.e.*, whether the patient's infection has resolved or the patient has become a chronic carrier of the virus.¹⁴ For the diagnosis of acute or chronic hepatitis, HBsAg reactivity should be correlated with patient history and the presence of other hepatitis B serological markers. Samples nonreactive by ARCHITECT HBsAg are considered negative for HBsAg and need not be tested further. A reactive sample must be retested in duplicate by ARCHITECT HBsAg to determine whether it is repeatedly reactive. A sample which is found to be repeatedly reactive should be confirmed by a neutralizing confirmatory test utilizing human anti-HBs, such as the ARCHITECT HBsAg Confirmatory (9C94) assay. If the sample is neutralized, the sample is considered positive for HBsAg. It is recommended that confirmatory testing be performed prior to disclosure of HBV status.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT HBsAg assay is a two-step immunoassay, using chemiluminescent microparticle immunoassay (CMIA) technology, with flexible assay protocols referred to as Chemiflex, for the quantitative determination of HBsAg in human serum and plasma. In the first step, sample and anti-HBs coated paramagnetic microparticles are combined. HBsAg present in the sample binds to the anti-HBs coated microparticles. After washing, acridinium-labeled anti-HBs conjugate is added in the second step. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of HBsAg in the sample and the RLUs detected by the ARCHITECT *i** System optics.

The concentration of hepatitis B surface antigen in the specimen is determined using a previously generated ARCHITECT HBsAg calibration curve. If the concentration of the specimen is greater than or equal to 0.05 IU/mL, the specimen is considered reactive for HBsAg.

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

* *i* = immunoassay

REAGENTS

Reagent Kit, 100 Tests/500 Tests

NOTE: Some kit sizes are not available in all countries; please contact your local distributor.

ARCHITECT HBsAg Reagent Kit (6C36)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL per 100 test bottle/ 27.0 mL per 500 test bottle) Anti-HBs (Mouse, Monoclonal, IgM, IgG) Coated Microparticles in MES buffer with protein stabilizers. Minimum concentration: 0.0675% solids. Preservative: ProClin 300.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL per 100 test bottle/26.3 mL per 500 test bottle) Conjugate: Anti-HBs (Goat, IgG) Acridinium-Labeled Conjugate in MES buffer with protein stabilizers (Bovine and Human Plasma; nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.) Minimum concentration: 0.25 µg/mL. Preservative: ProClin 300.

Assay Diluent

ARCHITECT HBsAg Manual Diluent (6C36-40)

- **MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT HBsAg Manual Diluent containing recalcified human plasma; nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, anti-HCV, and anti-HBs. Preservative: Antimicrobial Agent and ProClin 300.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

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

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** containing 0.35 mol/L sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** containing phosphate buffered saline solution. Preservative: Antimicrobial Agent.

WARNINGS AND PRECAUTIONS

- **For *In Vitro* Diagnostic Use.**

-  **CAUTION: This product contains human sourced infectious 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, it is recommended that all human sourced materials be considered potentially infectious and handled with appropriate biosafety practices.**

Safety Precautions

- Microparticles, Conjugate and Manual Diluent contain methylisothiazolones which are components of ProClin and are classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



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

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

Handling Precautions

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

Storage Instructions

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

Indications of Reagent Deterioration

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

INSTRUMENT PROCEDURE

- The ARCHITECT HBsAg assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM prior to performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Human serum (including serum collected in serum separator tubes) or plasma collected in potassium EDTA, lithium heparin, sodium heparin, sodium citrate, ACD, CPDA-1, CP2D, CPD, and potassium oxalate may be used in the ARCHITECT HBsAg assay. Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient samples. Other anticoagulants have not been validated for use with the ARCHITECT HBsAg assay. Follow the tube manufacturer's processing instructions for serum or plasma collection tubes.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify the correct specimen types are used in the ARCHITECT HBsAg assay.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.

- This assay was designed and validated for use with human serum or plasma from individual patient and donor specimens. Pooled specimens must not be used since the accuracy of their test results has not been validated.
 - Do not use heat-inactivated specimens.
 - Do not use grossly hemolyzed specimens.
 - For optimal results, inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
 - **For optimal results, serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter. Such specimens may give inconsistent results and must be transferred to a centrifuge tube and centrifuged at least 10,000 RCF (Relative Centrifugal Force) for 10 minutes.**
 - 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.
 - 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.
 - **Gravity separation is not sufficient for specimen preparation. Specimens must be separated from clots or red blood cells using centrifugation as recommended by the tube manufacturer.**
 - Specimens may be stored on or off the clot or red blood cells for up to 14 days at 2-8°C.
 - If testing will be delayed more than 14 days, remove serum or plasma from the clot, serum separator, or red blood cells, and store frozen (-20°C or colder).
 - **Frozen specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing.**
 - 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.
 - No qualitative performance differences were observed between experimental controls and the 23 nonreactive or 23 spiked reactive specimens subjected to 6 freeze/thaw cycles. The quantitative performance differences observed were within normal assay variability; however, multiple freeze/thaw cycles should be avoided.
 - When shipped, specimens must be packaged and labeled in compliance with applicable state, federal, and international regulations covering the transport of specimens and infectious substances. Specimens may be shipped ambient, at 2-8°C (wet ice), or -20°C or colder (dry ice). Do not exceed the storage time limitations listed above. Prior to shipment, it is recommended that specimens be removed from the clot, serum separator, or red blood cells.
 - ARCHITECT HBsAg Calibrators and Controls must be mixed by gentle inversion prior to use.
 - No qualitative performance differences were observed between experimental controls and the 23 nonreactive or 23 spiked reactive specimens tested with elevated levels of triglycerides ($\leq 3,000$ mg/dL)*, protein (≤ 12 g/dL)*, bilirubin (≤ 20 mg/dL)*, and hemoglobin (≤ 500 mg/dL)*.
 - No qualitative performance differences were observed between experimental controls and the 30 nonreactive or 28 spiked reactive specimens tested with red blood cells at $\leq 0.4\%$ v/v.*
- * The quantitative performance differences observed were within normal assay variability.

PROCEDURE

Materials Provided

- 6C36 ARCHITECT HBsAg Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- 3M61-01 ARCHITECT HBsAg Calibrators
- 6C36-10 ARCHITECT HBsAg Controls
- 6C36-40 ARCHITECT HBsAg Manual Diluent
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

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

Assay Procedure

- Before loading the ARCHITECT HBsAg Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment:
 - **Invert the microparticle bottle 30 times.**
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
 - 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.
 - **If the microparticles do not resuspend, DO NOT USE; contact your local Abbott representative.**
- Order calibration, if necessary.
- Order tests.
 - For information on ordering patient specimens, calibrators, and controls, and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Load the ARCHITECT HBsAg Reagent Kit on the ARCHITECT *i* System. Verify that all necessary reagents are present. Ensure that septums are present on all reagent bottles.
- The minimum sample cup volume required to perform a single HBsAg test on the ARCHITECT *i* System is 150 μ L for the first HBsAg test plus 75 μ L for each additional HBsAg test from the same sample cup. No more than 10 replicates may be sampled from the same sample cup. Verify the minimum sample volume is present in the sample cup prior to running the test. The minimum sample cup volume is calculated by the system and is displayed on the Patient, Calibrator, and Control order screens and on the Orderlist report.
- For a sample that is priority loaded, with three or fewer replicates ordered, a smaller sample cup volume than is displayed on the order screen may be used. In this case, the minimum sample cup volume is 75 μ L for each replicate plus 50 μ L. For additional information on priority loading, refer to the ARCHITECT System Operations Manual, Section 5.
- To minimize the effects of evaporation, all samples (patient specimens, calibrators, and controls) must be tested within 3 hours of being placed on board the ARCHITECT *i* System. If the sample is on board the system for longer than 3 hours, additional sample volume is required. For additional 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.
- ARCHITECT HBsAg Calibrators and Controls must be mixed by gentle inversion prior to use. To obtain the recommended volume requirements for the ARCHITECT HBsAg Calibrators and Controls, hold the bottles **vertically**, and dispense 10 drops of each Calibrator (for two replicates) or 6 drops of each Control (for one replicate) into each respective sample cup.

- Load samples.
 - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN. The ARCHITECT *i* System performs the following functions:
 - Moves the sample carrier to the aspiration point.
 - Loads a reaction vessel (RV) into the process path.
 - Aspirates and transfers sample into the RV.
 - Advances the RV one position and transfers microparticles into the RV.
 - Mixes, incubates, and washes the reaction mixture.
 - Adds conjugate to the RV.
 - Mixes, incubates, and washes the reaction mixture.
 - Adds Pre-Trigger and Trigger Solutions.
 - Measures chemiluminescent emission to determine the presence of HBsAg in the sample.
 - Aspirates contents of RV to liquid waste and unloads RV to solid waste.
 - Calculates the result.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with a HBsAg value exceeding 250 IU/mL, are flagged with the code ">250.00 IU/mL" and may be diluted with the Manual Dilution Procedure.

- Manual dilutions should be performed as follows:
 - The suggested dilution for the ARCHITECT HBsAg assay is 1:500. It is recommended dilutions not exceed 1:999.
 - Add 25 μ L of the patient specimen to 475 μ L of ARCHITECT HBsAg Manual Diluent for a 1:20 dilution. Add 20 μ L of the 1:20 dilution to 480 μ L of ARCHITECT HBsAg Manual Diluent for a 1:500 dilution.
 - The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The dilution should be performed so that the diluted result reads greater than 0.05 IU/mL.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- To perform an ARCHITECT HBsAg calibration, test Calibrators 1 and 2 in duplicate. A single sample of all levels of HBsAg controls must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the Control package insert. Calibrators should be priority loaded.
- Calibration Range: 0 - 250 IU/mL.
- Once an ARCHITECT HBsAg calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
 - A reagent kit with a new lot number is used
 - Controls are out of range

For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

NOTE: It is recommended that the ARCHITECT HBsAg Positive Control 1, HBsAg Positive Control 2, and Negative Control be run in order to verify the calibration.

The recommended control requirement for the ARCHITECT HBsAg assay is a single sample of each control 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. Ensure that assay Control values are within the concentration ranges specified in the Control package insert.

NOTE: For special instructions on how to run controls with a value of 0 IU/mL (ARCHITECT HBsAg Negative Control) refer to the ARCHITECT HBsAg Control package insert.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT HBsAg assay belongs to method group 4.

RESULTS

The ARCHITECT HBsAg assay utilizes a 4 Parameter Logistic Curve Fit data reduction method (4PLC, Y-weighted) to generate a calibration Curve.

Interpretation of Results

- Specimens with concentration values < 0.05 IU/mL are considered nonreactive by the criteria of ARCHITECT HBsAg.
- Specimens with concentration values ≥ 0.05 IU/mL are considered reactive by the criteria of ARCHITECT HBsAg.
- All initially reactive specimens should be retested in duplicate. If both retest values are nonreactive, the specimen must be considered nonreactive for HBsAg. If either of the retest values is reactive, the specimen must be considered repeatedly reactive for HBsAg by the criteria of the ARCHITECT HBsAg.
- Repeatedly reactive samples should be tested by a neutralizing confirmatory test. Samples which are confirmed by neutralization with human anti-HBs must be considered positive for HBsAg.

NOTE: For details on configuring the ARCHITECT *i* System regarding grayzone and high reactive interpretations, refer to the ARCHITECT System Operations Manual, Section 2. The grayzone and high reactive 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

- 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 which employ mouse monoclonal antibodies.^{15,16} Additional clinical or diagnostic information may be required to determine patient status.
- If the HBsAg 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.
- Samples containing particulate matter or red blood cells must be centrifuged prior to running the assay.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- Do not use heat-inactivated specimens.
- 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.
- If you run ARCHITECT HBsAg on the same module as the ARCHITECT B12 assay, refer to labeling of the B12 assay for additional information and instructions regarding accumulation of protein in the sample probe.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The precision of ARCHITECT HBsAg was determined during clinical studies using three reagent lots. A panel composed of five unique members was tested in replicates of four with each reagent lot once daily for five days at three sites. Each daily run also included the ARCHITECT Positive Controls tested in duplicate at the beginning and end of the run. The intra-assay and inter-assay standard deviation (SD) and percent coefficient of variation (%CV) were determined with a variance component analysis¹⁷ for a random effects model¹⁸ (Table I).

TABLE I
ARCHITECT HBsAg Precision

Panel Members	Total No. Replicates	Grand Mean (IU/mL)	Intra-assay SD	Intra-assay %CV	Inter-assay ^a SD	Inter-assay ^a %CV	Total SD	Total %CV ^b
1	180	0.23	0.011	4.6	0.016	6.7	0.018	7.7
2	180	4.68	0.191	4.1	0.290	6.2	0.339	7.2
3	180	23.76	1.205	5.1	2.179	9.2	2.268	9.5
4	180	96.61	4.617	4.8	7.587	7.9	8.913	9.2
5	180	182.07	9.448	5.2	14.352	7.9	21.705	11.9
Positive Control 1	180	0.23	0.018	7.8	0.020	8.8	0.022	9.7
Positive Control 2	180	177.36	11.889	6.7	12.969	7.3	16.126	9.1

^a Inter-assay variability contains intra-assay variability.

^b Total assay variability contains intra-assay, inter-assay, inter-lot, inter-site variability.

Specificity

A total of 5043 serum and plasma specimens from volunteer whole blood donors, a low prevalence population for HBV infection, were evaluated by three clinical sites (Table II). The initial and repeat reactive rates were 0.46% (23/5043) and 0.16% (8/5043), respectively. Of the eight repeatedly reactive specimens, the presence of HBsAg was confirmed by specific neutralization with anti-HBs in one specimen.

Three of 500 specimens obtained from hospital patients were repeatedly reactive and confirmed positive for HBsAg. In 50 matched serum and plasma pairs, none of the specimens were repeatedly reactive. Only the matched plasma specimens are included in the ARCHITECT HBsAg specificity calculation. In 333 specimens from individuals with medical conditions unrelated to HBV infection and specimens containing potentially interfering substances, seven specimens were repeatedly reactive, and six of the seven specimens were confirmed positive for HBsAg.

TABLE II
Reactivity of the ARCHITECT HBsAg Assay in Specimens from Whole Blood Donors, Hospital Patients, Plasma Specimens from Matched Serum Plasma Pairs, Individuals with Medical Conditions Unrelated to HBV infection, and in Specimens Containing Potentially Interfering Substances

Category	Number Tested	IR* (% of Total)	RR* (% of Total)	Number of Confirmed Positive ^a (% of Repeatedly Reactive)
Volunteer Whole Blood Donors				
Serum	2537	7 (0.28%)	4 (0.16%)	1 (25.00%)
Plasma	2506	16 (0.64%)	4 (0.16%)	0 (0.00%)
Total Donors	5043	23 (0.46%)	8 (0.16%)	1 (12.50%)
Hospital Patients	500	3 (0.60%)	3 (0.60%)	3 (100.00%)
Plasma Specimens from Matched Serum/Plasma Pairs	50	0 (0.00%)	0 (0.00%)	0 (0.00%)
Medical Conditions Unrelated to HBV Infection and Potentially Interfering Substances ^b	333	8 (2.40%)	7 (2.10%)	6 (85.71%)

* IR = Initially Reactive; RR = Repeatedly Reactive

^a A specimen was confirmed positive for HBsAg if the non-neutralized specimen (with ARCHITECT HBsAg Confirmatory assay Pretreatment 2 added) exhibited an RLU greater than or equal to the ARCHITECT HBsAg Confirmatory assay cutoff value and if the neutralization with anti-HBs (Pretreatment 1) was 50% or greater.

^b Medical conditions unrelated to HBV infection and potentially interfering substances, included the following: anti-CMV (10), anti-EBV (10), anti-HSV (10), anti-HAV (10), anti-HCV (10), anti-HIV-1 (10), HBV vaccine recipients (10), rubella antibody (10), toxoplasma antibody (10), *E. coli* infections (10), yeast infections (10), syphilis (10), anti-nuclear antibody (10), rheumatoid factor (10), multiple myeloma (10), multiparous females (10), pregnant females (163), and alcoholic liver disease (10).

Sensitivity

The ARCHITECT HBsAg assay has a sensitivity of ≤ 0.05 IU/mL.

NOTE: In studies performed at Abbott Laboratories, using a HBsAg *ad/ay* reference panel, sensitivity results calculated by linear regression have ranged from 0.15 to 0.29 ng/mL.

A total of 503 serum and plasma specimens from 343 individuals known to be positive for HBsAg, 10 individuals with acute HBV infection, 50 individuals with chronic HBV infection, and 100 individuals at increased risk for HBV infection were tested. Of the 503 specimens, 408 (81.11%) were repeatedly reactive and confirmed positive by specific antibody neutralization (Table III).

TABLE III
Reactivity of the ARCHITECT HBsAg Assay in Selected Populations with HBV Infection and at Increased Risk for HBV Infection

Category	Number Tested	Number of Repeatedly Reactive (% of Total)	Number of Confirmed Positive (% of Repeatedly Reactive)
Preselected HBsAg Positive ^a	343	343 ^b (100.00%)	343 (100.00%)
Acute HBV Infection	10	10 (100.00%)	10 (100.00%)
Chronic HBV Infection	50	50 (100.00%)	50 (100.00%)
Increased Risk for HBV Infection ^c	100	5 ^d (5.00%)	5 (100.00%)
TOTAL	503	408 (81.11%)	408 (100.00%)

^a Previously confirmed positive by specific antibody neutralization.

^b Specimens were tested once.

^c Category included the following: intravenous drug users (25), hemodialysis patients (25), hemophilia patients (25), men sex men (25).

^d Two specimens were initially nonreactive and repeatedly reactive upon retest. Both specimens were confirmed positive for HBsAg and were included in the statistical analysis.

Overall Specificity and Sensitivity

Overall specificity and sensitivity were estimated from the results of 6429 serum and plasma specimens, tested with ARCHITECT HBsAg at six clinical sites. HBV seroconversion panels results were excluded from this calculation because the panels contained multiple bleeds from the same individual. Only the plasma specimens from the matched serum/plasma pairs were used so that these specimens would be represented once.

The overall specificity was estimated to be 99.87% (6001/6009) with a 95% confidence interval of 99.74% to 99.94%. The overall sensitivity was estimated to be 99.52% (418/420) with a 95% confidence interval of 98.29% to 99.94%.

Seroconversion

The ability of the ARCHITECT HBsAg assay to detect HBsAg was evaluated by testing 30 HBV seroconversion panels from blood and plasmapheresis donors who seroconverted over the course of their donation history. The panels were also tested by another HBsAg assay. The ARCHITECT HBsAg assay detected HBsAg three to five days (one bleed) earlier in 10 of the 30 panels. The comparator assay detected HBsAg three to 24 days (one to two bleeds) earlier in six of the 30 panels. Both assays exhibited equivalent detection of HBsAg in 14 of the 30 panels.

HBsAg Mutant Detection

HBsAg mutant susceptibility was evaluated with the ARCHITECT HBsAg assay. The most prevalent HBsAg mutant, the Gly→Arg 145 mutant (Glycine [GLY] to Arginine [ARG] mutation at amino acid position 145 of HBsAg), was readily detected in the ARCHITECT HBsAg assay with a sensitivity equivalent to detection of wild type HBsAg¹⁹.

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

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

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