



HAVAb-IgM

REF 6C30

B6C300

56-0241/R3



HAVAb-IgM

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

Note Changes Highlighted

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July 2004

Key to symbols used			
REF	List Number	CAL 1	Calibrator 1
IVD	For <i>In Vitro</i> Diagnostic Use	CONTROL -	Negative Control
	Store at 2-8°C	CONTROL +	Positive Control
	CAUTION: Handle human sourced materials as potentially infectious. Consult instructions for use. (Infection Risk)	ASSAY CD-ROM	Assay CD-ROM
LOT	Lot Number	SN	Serial Number
	Expiration Date	CONTROL NO.	Control Number
	Consult instructions for use.	REAGENT LOT	Reagent Lot
	Legal Manufacturer	REACTION VESSELS	Reaction Vessels
	Legal Manufacturer	SAMPLE CUPS	Sample Cups
		SEPTUM	Septum
		REPLACEMENT CAPS	Replacement Caps

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

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

Legal Manufacturer

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

NAME

ARCHITECT® HAVAb-IgM

INTENDED USE

The ARCHITECT HAVAb-IgM assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV) in human serum and plasma. The ARCHITECT HAVAb-IgM assay is indicated for use as an aid in the diagnosis of acute or recent hepatitis A viral infection.

SUMMARY AND EXPLANATION OF TEST

The ARCHITECT HAVAb-IgM assay determines the presence of IgM anti-HAV in human serum and plasma. Hepatitis A is a self-limiting disease and is often a subclinical disorder, particularly in children. Since symptomatic hepatitis A virus (HAV) infections can be clinically indistinguishable from infection with hepatitis B or C virus, serological testing is an important tool to achieve proper diagnosis. During the acute phase of HAV infection, IgM anti-HAV appears in the patient's serum and is nearly always detectable at the onset of symptoms.¹⁻⁴ In most cases, IgM anti-HAV response usually peaks within the first month of illness and can persist for up to six months.^{5,6}

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT HAVAb-IgM assay is a two-step immunoassay for the qualitative detection of IgM anti-HAV in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex®. In the first step, prediluted sample, assay diluent, and hepatitis A virus (human) coated paramagnetic microparticles are combined. IgM anti-HAV present in the sample binds to the hepatitis A virus (human) coated microparticles. After washing, the IgM anti-HAV binds to the anti-human IgM acridinium-labeled conjugate that 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 IgM anti-HAV in the sample and the RLUs detected by the ARCHITECT *i*® system optics. The presence or absence of IgM anti-HAV in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an ARCHITECT HAVAb-IgM calibration. Specimens with signal to cutoff (S/CO) values > 1.20 are considered reactive for IgM anti-HAV. Specimens with S/CO values of 0.80 to 1.20 are considered grayzone reactive. Specimens with S/CO values < 0.80 are considered nonreactive.

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

**i* = immunoassay

REAGENTS

Reagent Kit, 100 Tests

ARCHITECT HAVAb-IgM Reagent Kit (6C30)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL) Microparticles: Hepatitis A virus (human) coated microparticles in TRIS buffer. Minimum concentration: 0.08% solids. Preservatives: ProClin® 300 and other Antimicrobial Agents.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL) Conjugate: Anti-human IgM (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.01 µg/mL. Preservatives: ProClin 300 and other Antimicrobial Agents.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (10.0 mL) Assay Diluent: HAVAb-IgM Assay Diluent containing protein (bovine) stabilizer in TRIS buffer. Preservatives: ProClin 300 and other Antimicrobial Agents.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

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

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35M sodium hydroxide.


ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: Antimicrobial Agents.

WARNINGS AND PRECAUTIONS

- **IVD** For *In Vitro* Diagnostic Use.
- Package instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

-  **CAUTION:** This product contains human sourced and/or potentially infectious components. For a specific listing, refer to the REAGENTS section of this package insert. Components sourced from human blood have been tested and found to be nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, and anti-HIV-1/HIV-2. 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,⁷ Biosafety Level 2⁸ or other appropriate biosafety practices^{9,10} should be used for materials that contain or are suspected of containing infectious agents. These precautions include, but are not limited to, the following:

- Wear gloves when handling specimens or reagents.
- Do not pipette by mouth.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in areas where these materials are handled.
- Clean and disinfect all spills of specimens or reagents using a tuberculocidal disinfectant such as 0.5% sodium hypochlorite, or other suitable disinfectant.^{11,12}
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.^{13,14}
- ARCHITECT HAVAb-IgM reagents contain a mixture of: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (3:1), which is a component of ProClin and is 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. |

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



- | | |
|--------|---|
| R41 | Risk of serious damage to eyes. |
| S25 | Avoid contact with eyes. |
| S26 | In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. |
| S35 | This material and its container must be disposed of in a safe way. |
| S36/39 | Wear suitable protective clothing and eye/face protection. |
| S46 | If swallowed, seek medical advice immediately and show this container or label. |

- **Information for European customers: For product not classified as dangerous per European Directive 1999/45/EC - Safety data sheet available for professional user on request.**


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

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Prior to loading the ARCHITECT HAVAb-IgM Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.

- **Septums MUST be used to prevent reagent evaporation and contamination, and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- **To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.**
- When handling conjugate vials, change gloves that have contacted human serum or plasma, since introduction of human IgM will result in a neutralized conjugate.
- Prior to placing the septum on an uncapped reagent bottle, squeeze the septum in half to confirm that the slits are open. If the slits appear sealed, continue to gently squeeze the septum to open the slits.
- Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts, which 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 HAVAb-IgM Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT HAVAb-IgM 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 reagents must be discarded.** After reagents are removed from the system, you must initiate a scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and 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 HAVAb-IgM assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM prior to performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
 - NOTE:** For details on defining a grayzone interpretation on the ARCHITECT *i* System, refer to the ARCHITECT System Operations Manual, Section 2.
 - NOTE:** It is recommended to set the number of decimal places for reported results at 2 (x.xx). If the number of decimal places is set higher than 2, there may be a greater incidence of grayzone reactive results reported for the ARCHITECT HAVAb-IgM assay. For more information on editing the decimal places of reported results, 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, sodium citrate, sodium heparin, ACD, CPDA-1, and CPD may be used in the ARCHITECT HAVAb-IgM assay. Other anticoagulants have not been validated for use with the ARCHITECT HAVAb-IgM assay. Follow the manufacturer's instructions for processing 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 that the correct specimen types are used in the ARCHITECT HAVAb-IgM assay.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- This assay was designed and validated for use with human serum or plasma from individual patient and donor specimens. Pooled specimens must not be used since the accuracy of their test results has not been validated.
- Do not use heat-inactivated specimens.
- Do not use grossly hemolyzed specimens.
- Specimens with obvious microbial contamination should not be used.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results or aspiration errors.
- Specimens from heparinized patients may be partially coagulated and erroneous results could occur due to the presence of fibrin. To prevent this phenomenon, draw the specimen prior to heparin therapy.
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter.
- Gravity separation is not sufficient for specimen preparation. Specimens must be separated from clots or red blood cells using centrifugation, as recommended by the tube manufacturer.
- After specimens have been processed according to the collection tube manufacturer's instructions, they must be transferred to a centrifuge tube and centrifuged at $\geq 10,000$ RCF (Relative Centrifugal Force) for 10 minutes, if one or more of the following occurs:
 - they contain red blood cells, clots, or particulate matter
 - they require repeat testing
 Transfer clarified specimens to a sample cup or secondary tube for testing.
- Multiple freeze/thaw cycles of specimens should be avoided. **Mix thawed specimens by inverting tubes 180° from upright and returning, 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 $\geq 10,000$ RCF for 10 minutes to remove particulate matter and ensure consistency in the results.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.
- Specimens may be stored on or off the clot or red blood cells for up to 7 days at 2-8°C. If testing will be delayed more than 7 days, remove serum or plasma from the clot, serum separator, or red blood cells and store frozen at -10°C or colder.
- No qualitative performance differences were observed between experimental controls and 26 nonreactive or 26 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 21 nonreactive or 21 spiked reactive specimens tested with elevated levels of bilirubin (≤ 20 mg/dL), triglycerides ($\leq 3,000$ mg/dL), protein (≤ 12 g/dL), or hemoglobin (≤ 500 mg/dL).
- No qualitative performance differences were observed between experimental controls and 25 nonreactive or 25 spiked reactive specimens tested with elevated levels of red blood cells ($\leq 0.4\%$ v/v).
- When shipped, specimens must be packaged and labeled in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances. Specimens may be shipped at 2-8°C (wet ice) or at -10°C or colder (dry ice). Do not exceed the storage time limitations identified in this section of the package insert. Prior to shipment, it is recommended that specimens be removed from the clot, serum separator, or red blood cells.

PROCEDURE

Materials Provided:

- 6C30 ARCHITECT HAVAb-IgM Reagent Kit

Materials Required but not Provided:

- ARCHITECT *i* System
- ARCHITECT *i* **ASSAY CD-ROM**
- 6C30-01 ARCHITECT HAVAb-IgM Calibrator
- 6C30-10 ARCHITECT HAVAb-IgM Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.
- For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT HAVAb-IgM Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that 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 inverting the bottle until the microparticles have been completely resuspended.
 - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott Laboratories representative.**
 - Once the microparticles have been resuspended, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Squeeze the septum in half to confirm that the slits are open. Carefully snap the septum onto the top of the bottle.
- Order calibration, if necessary.
 - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
 - For information on ordering patient specimens and controls and general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Load the ARCHITECT HAVAb-IgM Reagent Kit on the ARCHITECT *i* System.
 - Verify that all necessary reagents are present. Ensure that septums are present on all reagent bottles.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
 - Priority: 70 µL for the first ARCHITECT HAVAb-IgM test plus 20 µL for each additional ARCHITECT HAVAb-IgM test from the same sample cup.
 - ≤ 3 hours on board: 150 µL for the first ARCHITECT HAVAb-IgM test plus 20 µL for each additional ARCHITECT HAVAb-IgM test from the sample cup.
 - > 3 hours on board: 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 sample volume is present.
- Prepare calibrator and controls.
 - ARCHITECT HAVAb-IgM Calibrator 1 and Controls should be mixed by gentle inversion 5-10 times prior to use.
 - To obtain the recommended volume requirements for the ARCHITECT HAVAb-IgM Calibrator 1 and Controls, hold the bottles **vertically** and dispense 4 drops of calibrator or 4 drops of each control into each respective sample cup.

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

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

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT HAVAb-IgM assay.

Calibration

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

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT HAVAb-IgM assay is that a single sample of each control 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 HAVAb-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 HAVAb-IgM assay belongs to method group 5.

RESULTS

Calculation

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

- $\text{Cutoff RLU} = \text{Calibrator 1 mean RLU Value} \times 0.375$
- The cutoff RLU is stored for each reagent lot calibration.

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

- $S/CO = \text{sample RLU}/\text{cutoff RLU}$
- Example If the sample RLU = 2161 and the Cutoff RLU = 512.25
 $2161/512.25 = 4.22$
 $S/CO = 4.22$

Interpretation of Results

Initial ARCHITECT HAVAb-IgM Results

Initial Results (S/CO)	Interpretation
< 0.80	Nonreactive (NR)
0.80 to 1.20	Grayzone Reactive (GZ)
> 1.20	Reactive (R)

It is recommended that patients exhibiting grayzone reactive ARCHITECT HAVAb-IgM results be closely monitored at approximately one week intervals. This monitoring will distinguish rising IgM anti-HAV levels associated with acute hepatitis A infection from decreasing or unchanging IgM anti-HAV levels often associated with recovery.

NOTE: For details on defining a grayzone interpretation on the ARCHITECT *i* System, refer to the ARCHITECT System Operations Manual, Section 2.

NOTE: It is recommended to set the number of decimal places for reported results at 2 (x.xx). If the number of decimal places is set higher than 2, there may be a greater incidence of grayzone reactive results reported for the ARCHITECT HAVAb-IgM assay. For more information on editing the decimal places of reported results, 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

- If the IgM anti-HAV 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 must be centrifuged prior to running the assay if one or more of the following has occurred:
 - they contain red blood cells, clots, or particulate matter
 - they require repeat testing
- Do not use heat-inactivated specimens.
- Do not use grossly hemolyzed specimens.
- Specimens with obvious microbial contamination should not be used.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- 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.
- 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.^{15,16} ARCHITECT HAVAb IgM 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.¹⁷ 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.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT HAVAb-IgM assay demonstrated imprecision of $\leq 10\%$ for the Calibrator 1 and Positive Control in a study where a panel, consisting of one diluted IgM anti-HAV reactive specimen, three control lots, and three calibrator lots, was tested. The study was performed at one external site, running one ARCHITECT *i* System, and one internal site, running two ARCHITECT *i* Systems. Both sites tested all panel members with three reagent lots and evaluated them with each calibrator lot. Each combination of instruments, control lots, calibrator lots, and reagent lots was tested in four runs. The controls and calibrator were tested in replicates of three on each run. The diluted IgM anti-HAV reactive specimen was tested in replicates of four on each run. The intra-run and inter-run standard deviation (SD) and percent coefficient of variation (%CV) were analyzed with a variance components analysis¹⁸ using a mixed analysis of variance model.¹⁹ The data from this study are summarized in Table 1.*

Table 1
ARCHITECT HAVAb-IgM Precision

Panel Member	n	Mean	Intra-assay		Inter-assay ^a	
			SD	%CV	SD	%CV
Calibrator 1	324	1337 RLU	86.9	6.5	88.6	6.6
Negative Control	972	0.23 S/CO	0.026	11.33	0.030	13.10
Positive Control	972	1.89 S/CO	0.113	5.98	0.127	6.72
Diluted Specimen	432	1.16 S/CO	0.068	5.90	0.086	7.42

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

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

Specificity

The ARCHITECT HAVAb-IgM assay demonstrated an overall specificity of $\geq 99.0\%$ in a study testing serum and plasma specimens from the following populations:

- Randomly selected blood donors (BD)
- Randomly selected hospitalized patients (HP)
- Potentially interfering substances (IS)^b

The testing was performed at one clinical site and one internal site. Of the 2126 specimens initially tested, seven specimens were determined to be either reactive or grayzone reactive by ARCHITECT HAVAb-IgM. Five of these seven specimens were also reactive by supplemental testing. The remaining two specimens were concordant reactive or grayzone reactive by ARCHITECT HAVAb-IgM and AxSYM[®] HAVAb-M[™] 2.0. Therefore, these seven specimens were considered true anti-HAV IgM reactives and were excluded from the specificity calculation. The data from this study are summarized in Table 2.*

Table 2
ARCHITECT HAVAb-IgM Specificity Results

Population	n	Initial Reactive/GZ	Repeat Reactive/GZ
BD	724	0/0	--
HP	1312	0/1	0/0
IS ^b	83	0/0	--
Total	2119	0/1	0/0

^b Specimens containing the following potentially interfering substances were evaluated for cross-reactivity by ARCHITECT HAVAb-IgM:

- CMV-IgG
- HBV
- HIV-1
- Flu vaccines
- Alcoholic cirrhosis
- Elevated IgG
- Elevated IgM
- CMV-IgM
- HCV
- HSV
- Autoimmune antibodies (ANA)
- Rheumatoid factor
- HAMA

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

Sensitivity

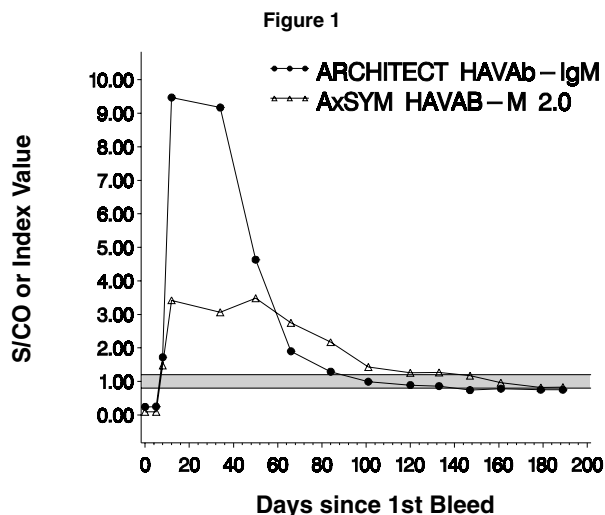
- The ARCHITECT HAVAb-IgM assay demonstrated a sensitivity of $\geq 95.0\%$ in a study testing serum and plasma specimens precharacterized as anti-HAV IgM reactive. Specimens were drawn from patients diagnosed with acute HAV infection and were collected within two months after the onset of symptoms. The data from this study are summarized in Table 3.*

Table 3
ARCHITECT HAVAb-IgM Sensitivity Results

Population	n	Reactive	GZ	Nonreactive	Sensitivity
Acute HAV Infection	141	135	4	2	98.58% (139/141)

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

- Testing by ARCHITECT HAVAb-IgM was performed on 120 specimens from patients who had recovered from hepatitis A. Two of these specimens, which were reactive by ARCHITECT HAVAb-IgM, were also reactive by supplemental testing. The remaining 118 specimens were nonreactive by ARCHITECT HAVAb-IgM.
- Testing by ARCHITECT HAVAb-IgM and AxSYM HAVAB-M 2.0 was performed on serial bleed panels. The results demonstrate that the ARCHITECT HAVAb-IgM assay's sensitivity is such that a reactive result implies acute hepatitis A viral infection (up to two months after the onset of symptoms). Representative data for one of the panels is provided in Figure 1.



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