Alinity i HAVAb IgM-15

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BIENNIAL REVIEW:

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SUPERSEDES: Procedure titled _____

INTENDED USE

The Alinity i HAVAb IgM assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV) in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, and sodium heparin) and neonatal serum on the Alinity i analyzer.

A test for IgM anti-HAV is indicated for testing of specimens from individuals who have signs and symptoms consistent with acute hepatitis. Test results are used in conjunction with other laboratory results and clinical information as an aid in the diagnosis of acute or recent hepatitis A viral infection.

Warning: Not intended for use in screening blood, plasma, or tissue donors. The effectiveness of the Alinity i HAVAb IgM assay for use in screening blood, plasma, or tissue

donors has not been established. Assay performance characteristics have not been established when the Alinity i HAVAb IgM assay is used in conjunction with other manufacturers' assays for specific hepatitis markers. Users are responsible for establishing their own performance characteristics.

SUMMARY AND EXPLANATION OF THE TEST

The Alinity i HAVAb IgM assay determines the presence of IgM anti-HAV in human serum and plasma. Hepatitis A is typically 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*, *2*, *3*, *4* In most cases, IgM anti-HAV response peaks within the first month of illness and can persist for up to six months.*5*, *6*

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

This assay is a two-step immunoassay for the qualitative detection of IgM anti-HAV in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Prediluted sample, hepatitis A virus (human) coated paramagnetic microparticles, and assay diluent are combined and incubated. The IgM anti-HAV present in the sample binds to the hepatitis A virus (human) coated microparticles. The mixture is washed. Anti-human IgM acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of IgM anti-HAV in the sample and the RLUs detected by the system optics.

The presence or absence of IgM anti-HAV in the sample is determined by comparing the chemiluminescent RLU in the reaction to the cutoff RLU determined from an active calibration.

For additional information on system and assay technology, refer to the Alinity ci-series Operations Manual, Section 3.

REAGENTS

Kit Contents

Alinity i HAVAb IgM Reagent Kit 08P28

Volumes (mL) listed in the table below indicate the volume per cartridge.

REF	08P2821	08P2831
Tests per cartridge	100	500
Number of cartridges per kit	2	2

REF	08P2821	08P2831
Tests per kit	200	1000
MICROPARTICLES	6.6 mL	27.0 mL
CONJUGATE	26.5 mL	26.5 mL
ASSAY DILUENT	10.4 mL	47.1 mL

MICROPARTICLES Hepatitis A virus (human) coated microparticles in TRIS buffer. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and other antimicrobial agents.

CONJUGATE Anti-human IgM (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) additive (2.0%). Minimum concentration: 0.01 µg/mL. Preservatives: ProClin 300 and other antimicrobial agents.

ASSAY DILUENT TRIS buffer with protein (bovine) additive (2.0%). Preservatives: ProClin 300 and other antimicrobial agents.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use
- Rx ONLY

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.[7, 8, 9, 10]

The following warnings and precautions apply to: MICROPARTICLES / CONJUGATE	
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.

The following warnings and precautions apply to: ASSAY DILUENT	
	
WARNING	Contains methylisothiazolones and polyethylene glycol octylphenyl ether (Triton X-405).
H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P264	Wash hands thoroughly after handling.
P272	Contaminated work clothing should not be allowed out of the workplace.
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.

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.

Follow local chemical disposal regulations based on your location along with recommendations and content in the Safety Data Sheet to determine the safe disposal of this product.

For the most current hazard information, see the product Safety Data Sheet.

Safety Data Sheets are available at www.abbottdiagnostics.com or/and SDS folder.

For a detailed discussion of safety precautions during system operation, **refer to the Alinity ci-series Operations Manual, Section 8.**

Reagent Handling

Upon receipt, gently invert the unopened reagent kit by rotating it over and back for a full 180 degrees, 5 times with green label stripe facing up and then 5 times with green label stripe facing down. This ensures that liquid covers all sides of the bottles within the cartridges. During reagent shipment, microparticles can settle on the reagent septum.

- Place a check in the square on the reagent kit to indicate to others that the inversions have been completed.
- After mixing, place reagent cartridges in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- If a reagent cartridge is dropped, place in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.

For a detailed discussion of reagent handling precautions during system operation, **refer to the Alinity ci-series Operations Manual, Section 7.**

Reagent Storage

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright, gently invert the

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
			cartridge 10 times and place in an upright position for 1 hour before use.
Onboard	System Temperature	30 days	
Opened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright during storage, discard the cartridge. Do not reuse original reagent caps or replacement caps due to the risk of contamination and the potential to compromise reagent performance.

Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 2 to 8°C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.

For information on unloading reagents, **refer to the Alinity ci-series Operations Manual, Section 5.**

Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when:

- a calibration error occurs
- a control value is out of the specified range

Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, **refer to the Alinity ci-series Operations Manual, Section 10**.

INSTRUMENT PROCEDURE

The Alinity i HAVAb IgM assay file must be installed on the Alinity i analyzer prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the Alinity ci-series Operations Manual, Section 2.

For information on printing assay parameters, refer to the Alinity ci-series Operations Manual, Section 5.

For a detailed description of system procedures, refer to the Alinity ci-series Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below were verified for use with this assay.

Other specimen types and collection tube types have not been verified with this assay.

Specimen Types	Collection Tubes
Serum	Serum (glass and plastic) Serum separator (glass and plastic)
Plasma	Lithium heparin plasma separator (plastic) Sodium heparin (plastic) Dipotassium EDTA (plastic)

Specimen Conditions

Do not use:

- heat-inactivated specimens
- pooled specimens
- grossly hemolyzed specimens
- specimens with obvious microbial contamination

- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- 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.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

To ensure consistency in results, recentrifuge specimens prior to testing if

- they contain fibrin, red blood cells, or other particulate matter.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low speed

vortex or by inverting 10 times prior to recentrifugation.

Prepare frozen specimens as follows:

- Frozen specimens must be completely thawed before mixing.
- Mix thawed specimens thoroughly by low speed vortex or by inverting 10 times.
- Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous.
- If specimens are not mixed thoroughly, inconsistent results may be obtained.
- Recentrifuge specimens.

Recentrifugation of Specimens

- Transfer specimens to a centrifuge tube and centrifuge at a minimum of 100 000 g-minutes.
- Examples of acceptable time and force ranges that meet this criterion are listed in the table below.

Centrifugation time using alternate RCF values can be calculated using the following formula:

$$\text{Minimum Centrifugation time (minutes)} = \frac{100\,000 \text{ g-minutes}}{\text{RCF}}$$

Recentrifugation Time (Minutes)	RCF (x g)*	g-Minutes
10	10 000	100 000
20	5000	100 000
40	2500	100 000

* To ensure consistency in results, specimens must be centrifuged using an appropriate tube at a minimum of 2500 RCF to obtain a minimum of 100 000 g-minutes.

$RCF = 1.12 \times r_{max} (rpm/1000)^2$

RCF - The relative centrifugal force generated during centrifugation.

rpm - The revolutions per minute of the rotor on which the specimens are being spun (usually the digital readout on the centrifuge will indicate the rpm).

Centrifugation Time - The time should be measured from the time the rotor reaches the required RCF or rpm to the time it begins decelerating.

r_{max} - Radius of the rotor in millimeters. NOTE: If custom tube adapters (i.e., adapters not defined by the centrifuge manufacturer) are used, then the radius (r_{max}) should be manually measured in millimeters and the RCF calculated.

g-minutes - The unit of measure for the product of RCF (× g) and centrifugation time (minutes).

- 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.

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Serum/Plasma	Room temperature (study performed at 21 to 30°C)	3 days	Specimens may be stored on or off the clot, red blood cells, or separator gel.
	2 to 8°C	7 days	Specimens may be stored on or off the clot, red blood cells, or separator gel.

Based on guidance from CLSI GP44-A4*11*, it is recommended that if testing will be delayed longer than the maximum storage time, remove serum or plasma from the clot, red blood cells, or separator gel and store frozen (-20°C or colder).

Avoid more than 3 freeze/thaw cycles.

Specimen Shipping

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

PROCEDURE

Materials Provided

08P28 Alinity i HAVAb IgM Reagent Kit

Materials Required but not Provided

- Alinity i HAVAb IgM assay file
- 08P2801 Alinity i HAVAb IgM Calibrator
- 08P2810 Alinity i HAVAb IgM Controls or other control material
- Alinity Pre-Trigger Solution
- Alinity Trigger Solution
- Alinity i-series Concentrated Wash Buffer

For information on materials required for operation of the instrument, refer to the Alinity ci-series Operations Manual, Section 1.

For information on materials required for maintenance procedures, refer to the Alinity ci-series Operations Manual, Section 9.

Assay Procedure

For a detailed description of how to run an assay, refer to the Alinity ci-series Operations Manual, Section 5.

- If using primary or aliquot tubes, refer to the Alinity ci-series Operations Manual, Section 4 to ensure sufficient specimen is present.
- 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: 70 µL
- Sample volume for each additional test from same sample cup: 20 µL

≤ 3 hours on the reagent and sample manager:

- Sample volume for first test: 150 µL
- Sample volume for each additional test from same sample cup: 20 µL

> 3 hours on the reagent and sample manager:

- Replace with a fresh aliquot of sample.

- Refer to the Alinity i HAVAb IgM calibrator package insert and/or Alinity i HAVAb IgM control package insert for preparation and usage.
- For general operating procedures, refer to the Alinity ci-series Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the Alinity ci-series Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Sample Dilution Procedures

Samples cannot be diluted for the Alinity i HAVAb IgM assay.

Calibration

For instructions on performing a calibration, **refer to the Alinity ci-series Operations Manual, Section 5.**

Each assay control must be tested to evaluate the assay calibration.

Once a calibration is accepted and stored, **it may be used for 14 days**. During this time, all subsequent samples may be tested without further calibration unless:

- A reagent kit with a new lot number is used.
- Daily quality control results are outside of quality control limits used to monitor and

control system performance.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

Quality Control Procedures

The recommended control requirement for the Alinity i HAVAb IgM assay is that a single sample of each control level be tested once every day testing performed.

To establish statistically-based control limits, each laboratory should establish its own concentration target and ranges for new control lots at each clinically relevant control level. This can be accomplished by assaying a minimum of **20 replicates over several (3-5) days** and using the reported results to establish the expected average (target) and variability about this average (range) for the laboratory. Sources of variation that should be included in this study in order to be representative of future system performance include:

- Multiple stored calibrations
- Multiple reagent lots
- Multiple calibrator lots
- Multiple processing modules (if applicable)
- Data points collected at different times of the day

Refer to published guidelines for information or general control recommendation, for example Clinical and Laboratory Standards Institute (CLSI) Document C24-A3 or other published guidelines, for general quality control recommendations.*12*

- If quality control results do not meet the acceptance criteria defined by laboratory procedure, sample results may be suspect. Follow the established quality control procedures to troubleshoot. Recalibration may be necessary. For troubleshooting information, **refer to the Alinity ci-series Operations Manual, Section 10**.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Quality Control Guidance

Refer to “Basic QC Practices” by James O Westgard, Ph.D. for guidance on laboratory quality control practices.*13*

Verification of Assay Claims

For protocols to verify package insert claims, refer to Verification of Assay Claims in the Alinity ci-series Operations Manual.

RESULTS

Calculation

The Alinity i analyzer calculates results for the Alinity i HAVAb IgM assay using the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

Cutoff RLU = Calibrator 1 Mean RLU x 0.375

The cutoff RLU is stored for each reagent lot calibration.

S/CO = Sample RLU/Cutoff RLU

Interpretation of Results

Result (S/CO)	Instrument Interpretation	Interpretation
< 0.80	Nonreactive (NR)	IgM anti-HAV not detected. Does not exclude the possibility of exposure to or infection with HAV. Levels of IgM anti-HAV may be below the cutoff in early infection.
0.80 to < 1.21	Grayzone (GZ)	IgM antibodies to HAV may or may not be present. Patients exhibiting grayzone test results should be closely monitored by redrawing and retesting at approximately one week intervals.[a]
≥ 1.21	Reactive (R)	IgM anti-HAV detected. Presumptive evidence of HAV infection. A reactive IgM anti-HAV result does not rule out other hepatitis infections.

[a] Monitoring the level of IgM anti-HAV by redrawing and retesting at approximately one week intervals will distinguish rapidly rising IgM anti-HAV levels associated with early acute hepatitis A infection from gradually decreasing or unchanging IgM anti-HAV levels often associated with late acute stage of HAV infection.

For details on configuring the Alinity i analyzer to use grayzone interpretations, refer to the Alinity ci-series Operations Manual, Section 2.

It is recommended that the number of decimal places for reported results be set at 2 (x.xx). For more information on editing the decimal places of reported results, refer to the Alinity ci-series Operations Manual, Section 2.

Assay results should be interpreted only in the context of other clinical laboratory findings and the total clinical status of the individual. It has been shown that a viremic window exists with individuals infected with HAV where the individual may be symptomatic for hepatitis but IgM anti-HAV nonreactive.[14]

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 Alinity ci-series 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).[15, 16] Such specimens may show either falsely elevated or depressed values when tested with assay kits (such as Alinity i HAVAb IgM) that employ mouse monoclonal antibodies.[15] Alinity i 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.
- A reactive IgM anti-HAV result does not necessarily rule out other hepatitis infections.
- The results from this or any other diagnostic kit should be used and interpreted only in the context of the overall clinical picture. A negative test result does not exclude the possibility of exposure to hepatitis A virus. Levels of IgM anti-HAV may be below the cutoff in early infection and late acute infection.
- 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.
- Specimens from individuals with Non-Hodgkin's Lymphoma may cross-react with this assay.

Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section of this package insert for specimen limitations.

EXPECTED VALUES

This study was performed on the ARCHITECT i System.

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics.

Due to geographic locations or demographics, assay results obtained in individual laboratories may vary from data presented. Of the 1167 specimens tested in the ARCHITECT HAVAB-M clinical study, 862 specimens were from the following populations: 509 specimens were from apparently healthy individuals, 253 specimens were from individuals at increased risk of HAV infection, and 100 specimens were from pediatric individuals.

HAV Prevalence Population

The apparently healthy population (n=509) consisted of the following race/ethnic groups:

- 269 (52.85%) Caucasian
- 175 (34.38%) African-American
- 40 (7.86%) Hispanic

- 11 (2.16%) Asian
- 5 (0.98%) American Indian/Alaska Native
- 9 (1.77%) Other

The 509 specimens from the apparently healthy population from both low prevalence (Port Jefferson, NY, and Milwaukee, WI) and high prevalence (Galveston, TX, and Phoenix, AZ) areas were obtained from the following collection locations:

- 145 (28.49%) from Milwaukee, WI
- 140 (27.50%) from Galveston, TX
- 114 (22.40%) from Phoenix, AZ
- 110 (21.61%) from Port Jefferson, NY

Of the 509 specimens, 358 (70.33%) were female and 151 (29.67%) were male. The mean age was 44 years (age range: 18 to 81 years). The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results among apparently healthy individuals (n=255) living in low prevalence areas for hepatitis A is summarized by age and gender in the following table.

		ARCHITECT HAVAB-M Result			
Age Group (Years)	**Gender**	**Reactive n (%)**	**Grayzone n (%)**	**Nonreactive n (%)**	**Total**
10-19	F	0 (0.00)	1 (10.00)	9 (90.00)	10
	M	0 (0.00)	0 (0.00)	6 (100.00)	6
20-29	F	0 (0.00)	0 (0.00)	32 (100.00)	32
	M	0 (0.00)	0 (0.00)	16 (100.00)	16
30-39	F	0 (0.00)	0 (0.00)	28 (100.00)	28
	M	0 (0.00)	0 (0.00)	12 (100.00)	12
40-49	F	0 (0.00)	0 (0.00)	40 (100.00)	40
	M	0 (0.00)	0 (0.00)	8 (100.00)	8
50-59	F	0 (0.00)	0 (0.00)	38 (100.00)	38
	M	0 (0.00)	0 (0.00)	19 (100.00)	19
60-69	F	0 (0.00)	0 (0.00)	23 (100.00)	23
	M	0 (0.00)	0 (0.00)	12 (100.00)	12
70-79	F	0 (0.00)	0 (0.00)	5 (100.00)	5
	M	0 (0.00)	0 (0.00)	3 (100.00)	3
80-89	F	0 (0.00)	0 (0.00)	1 (100.00)	1
	M	0 (0.00)	0 (0.00)	2 (100.00)	2
Overall	F	0 (0.00)	1 (0.56)	176 (99.44)	177
	M	0 (0.00)	0 (0.00)	78 (100.00)	78
Total		**0 (0.00)**	**1 (0.39)**	**254 (99.61)**	**255**

The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results among apparently healthy individuals (n=254) living in high prevalence areas for hepatitis A is summarized by age and gender in the following table.

Age Group (Years)	Gender	ARCHITECT HAVAB-M Result			Total
		Reactive n (%)	Grayzone n (%)	Nonreactive n (%)	
10-19	F	0 (0.00)	0 (0.00)	5 (100.00)	5
	M	0 (0.00)	0 (0.00)	4 (100.00)	4
20-29	F	0 (0.00)	0 (0.00)	24 (100.00)	24
	M	0 (0.00)	0 (0.00)	9 (100.00)	9
30-39	F	0 (0.00)	0 (0.00)	36 (100.00)	36
	M	0 (0.00)	0 (0.00)	7 (100.00)	7
40-49	F	0 (0.00)	0 (0.00)	57 (100.00)	57
	M	0 (0.00)	0 (0.00)	19 (100.00)	19
50-59	F	0 (0.00)	1 (2.78)	35 (97.22)	36
	M	0 (0.00)	0 (0.00)	20 (100.00)	20
60-69	F	0 (0.00)	0 (0.00)	20 (100.00)	20
	M	0 (0.00)	0 (0.00)	12 (100.00)	12
70-79	F	0 (0.00)	0 (0.00)	3 (100.00)	3
	M	0 (0.00)	0 (0.00)	2 (100.00)	2
Overall	F	0 (0.00)	1 (0.55)	180 (99.45)	181
	M	0 (0.00)	0 (0.00)	73 (100.00)	73
Total		**0 (0.00)**	**1 (0.39)**	**253 (99.61)**	**254**

Increased Risk Population for HAV Infection

The specimens were from 253 individuals at increased risk of HAV infection due to exposure to contaminated food or water, poor sanitary conditions or hygiene, household or sexual contact with an HAV-infected individual, recent travel to an HAV endemic area, lifestyle, behavior, or recipients of clotting factor concentrates.

The increased risk population (n=253) consisted of the following race/ethnic groups:

- 140 (55.34%) Caucasian
- 48 (18.97%) African-American
- 47 (18.58%) Hispanic

- 9 (3.56%) Asian
- 3 (1.19%) American Indian/Alaska Native
- 6 (2.37%) Other

The 253 specimens from the increased risk population were obtained from the following collection locations:

- 64 (25.30%) from Galveston, TX
- 57 (22.53%) from Dallas, TX
- 46 (18.18%) from St. Petersburg, FL
- 29 (11.46%) from Denver, CO
- 23 (9.09%) from Miami, FL
- 23 (9.09%) from Chicago, IL
- 7 (2.77%) from Plymouth, MA
- 4 (1.58%) from Colton, CA

Of the 253 specimens, 155 (61.26%) were male and 98 (38.74%) were female. The mean age was 42 years (age range: 18 to 78 years). The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results among individuals with increased risk for HAV (n=253) is summarized by age and gender in the following table.

		ARCHITECT HAVAB-M Result			
Age Group (Years)	**Gender**	**Reactive n (%)**	**Grayzone n (%)**	**Nonreactive n (%)**	**Total**
10-19	F	0 (0.00)	0 (0.00)	1 (100.00)	1
	M	0 (0.00)	0 (0.00)	1 (100.00)	1
20-29	F	0 (0.00)	0 (0.00)	34 (100.00)	34
	M	0 (0.00)	0 (0.00)	18 (100.00)	18
30-39	F	0 (0.00)	0 (0.00)	15 (100.00)	15
	M	0 (0.00)	0 (0.00)	34 (100.00)	34
40-49	F	0 (0.00)	0 (0.00)	21 (100.00)	21
	M	0 (0.00)	0 (0.00)	59 (100.00)	59
50-59	F	0 (0.00)	0 (0.00)	21 (100.00)	21
	M	0 (0.00)	0 (0.00)	31 (100.00)	31
60-69	F	0 (0.00)	0 (0.00)	5 (100.00)	5
	M	0 (0.00)	0 (0.00)	9 (100.00)	9
70-79	F	0 (0.00)	0 (0.00)	1 (100.00)	1
	M	0 (0.00)	0 (0.00)	3 (100.00)	3
Overall	F	0 (0.00)	0 (0.00)	98 (100.00)	98
	M	0 (0.00)	0 (0.00)	155 (100.00)	155
Total		**0 (0.00)**	**0 (0.00)**	**253 (100.00)**	**253**

Pediatric Population at Low Risk for Hepatitis

One hundred residual specimens from a pediatric population at low risk for hepatitis were obtained in Fall River, MA. Of the 100 specimens, 66 (66.00%) were female and 34 (34.00%) were male. The mean age was 12 years (age range: 2 to 18 years).

The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results among pediatric individuals at low risk for hepatitis (n=100) is summarized in the following table.

Age Group (Years)	Gender	ARCHITECT HAVAB-M Result			Total
		Reactive n (%)	Grayzone n (%)	Nonreactive n (%)	
2-12	F	0 (0.00)	0 (0.00)	25 (100.00)	25
	M	0 (0.00)	0 (0.00)	24 (100.00)	24
13-18	F	0 (0.00)	0 (0.00)	41 (100.00)	41
	M	0 (0.00)	0 (0.00)	10 (100.00)	10
Overall	F	0 (0.00)	0 (0.00)	66 (100.00)	66
	M	0 (0.00)	0 (0.00)	34 (100.00)	34
Total		**0 (0.00)**	**0 (0.00)**	**100 (100.00)**	**100**

The ARCHITECT HAVAB-M assay results were in agreement with the comparator IgM anti-HAV assay results.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

The Alinity i analyzer and the ARCHITECT i System utilize the same reagents and sample/reagent ratios.

Alinity i Analyzer Specific Studies

The following results were generated using the Alinity i analyzer.

Precision

Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A2.*18* Testing was conducted using 1 lot of the Alinity i HAVAb IgM Reagent Kit, 1 lot of the Alinity i HAVAb IgM Calibrator, and 1 lot of the Alinity i HAVAb IgM Controls and 1 instrument. Two controls and 2 human plasma panels were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.

Sample	n	Mean (S/CO)	Within-Run (Repeatability)		Within-Instrument (Total)[a]	
			SD	%CV	SD	%CV
Negative Control	120	0.16	0.019	N/A[b]	0.038	N/A[b]
Positive Control	120	1.86	0.101	5.4	0.113	6.1
High Negative Panel	120	0.75	0.042	5.7	0.062	8.2
Low Positive Panel	120	1.42	0.074	5.2	0.093	6.6

[a] Includes within-run, between-run, and between-day variability.

[b] Not applicable

System Reproducibility

A study was performed based on guidance from CLSI EP05-A2 and CLSI EP15-A2.[18, 19] Testing was conducted at 3 clinical sites using 1 lot of the Alinity i HAVAb IgM Reagent Kit,
1 lot of the Alinity i HAVAb IgM Calibrator, and 1 lot of the Alinity i HAVAb IgM Controls and 1 instrument per site. Two controls and 2 human plasma panels were assayed in replicates of 4 at 2 separate times per day for 5 days.

Sample	n	Mean (S/CO)	Within-Run (Repeatability)		Within-Laboratory Precision (Total)[a]		Reproducibility[b]	
			SD	%CV	SD	%CV	SD	%CV
Negative Control	120	0.19	0.041	N/A[c]	0.042	N/A[c]	0.048	N/A[c]
Positive Control	120	1.84	0.105	5.7	0.114	6.2	0.116	6.3
High Negative Panel	120	0.69	0.045	6.5	0.045	6.6	0.048	7.0
Low Positive Panel	120	1.53	0.081	5.2	0.087	5.7	0.089	5.8

[a] Includes within-run, between-run, and between-day variability.

[b] Includes within-run, between-run, between-day and between-site variance components.

[c] Not applicable

Seroconversion Sensitivity

To determine the seroconversion sensitivity, 3 seroconversion panels obtained from commercial vendors were tested on the Alinity i analyzer using the Alinity i HAVAb IgM assay. The panel results were evaluated against a comparator assay (ARCHITECT HAVAB-M) and showed equivalent performance. Data are summarized in the following table.

	Days to Anti-HAV First Reactive Result from Initial Draw Date		Difference in Days to Anti-HAV First Reactive Result (Alinity - ARCHITECT)
Panel ID	Alinity i HAVAb IgM	ARCHITECT HAVAB-M	
PHT903	38	38	0
SCP-HAV-001	6	6	0
SCP-HAV-002	8	8	0

Percent Agreement

A study was performed to compare the Alinity i HAVAb IgM and the ARCHITECT HAVAB-M assays on the Alinity i analyzer and the ARCHITECT i2000SR system using 1 lot each of the Alinity i HAVAb IgM Reagent Kit, Alinity i HAVAb IgM Calibrator, Alinity i HAVAb IgM Controls, ARCHITECT HAVAB-M Reagent Kit, ARCHITECT HAVAB-M Calibrator, and ARCHITECT HAVAB-M Controls. Of the 219 specimens tested, 97 were nonreactive, 12 were in the grayzone, and 110 were reactive, based on the ARCHITECT HAVAB-M results on the ARCHITECT i2000SR instrument. An aliquot of each specimen was tested on 1 Alinity i analyzer at each of the 3 clinical testing sites and on 1 ARCHITECT i2000SR instrument at
1 clinical testing site.

The concordance analysis for the Alinity i analyzer and the ARCHITECT system are summarized in the table below, per site and across sites:

		ARCHITECT HAVAB-M			Negative % Agreement	Positive % Agreement
Site	Alinity i HAVAb IgM	Reactive	Grayzone	Nonreactive	(95% Confidence Interval)[a]	(95% Confidence Interval)[a]
1	Reactive	110	2	0	97.94	100.00
	Grayzone	0	8	2	(95/97)	(110/110)
	Nonreactive	0	2	95	(92.79,99.43)	(96.63,100.00)
2	Reactive	109	3	0	98.97	99.09
	Grayzone	1	4	1	(96/97)	(109/110)

Site	Alinity i HAVAb IgM	ARCHITECT HAVAB-M			Negative % Agreement (95% Confidence Interval)[a]	Positive % Agreement (95% Confidence Interval)[a]
		Reactive	Grayzone	Nonreactive		
	Nonreactive	0	5	96	(94.39,99.82)	(95.03,99.84)
3	Reactive	109	0	0	100.00	99.09
	Grayzone	1	7	0	(97/97)	(109/110)
	Nonreactive	0	5	97	(96.19,100.00)	(95.03,99.84)
All	Reactive	328	5	0	98.97	99.39
	Grayzone	2	19	3	(288/291)	(328/330)
	Nonreactive	0	12	288	(97.01,99.65)	(97.82,99.83)

[a] The 95% confidence intervals for negative percent agreement and positive percent agreement were estimated using Wilson Score method.

$$\text{Positive Percent Agreement} = \frac{\text{[Number of reactive Alinity i results in agreement with ARCHITECT i2000SR results]}}{\text{[Total number of reactive ARCHITECT i2000SR results]}} \times 100\%$$

$$\text{Negative Percent Agreement} = \frac{\text{[Number of nonreactive Alinity i results in agreement with ARCHITECT i2000SR results]}}{\text{[Total number of nonreactive ARCHITECT i2000SR results]}} \times 100\%$$

ARCHITECT i2000 / i2000SR System Specific Studies

The following results were generated using the ARCHITECT i2000 / i2000SR System.

Clinical Performance

A prospective multi-center study was conducted to evaluate the ability of the ARCHITECT HAVAB-M assay to detect IgM anti-HAV antibodies in a group of individuals with signs and symptoms of hepatitis, individuals at risk of HAV infection due to exposure to contaminated food or water, poor sanitary conditions or hygiene, household or sexual contact with an HAV-infected individual, recent travel to an HAV endemic area, lifestyle, behavior, or recipients of clotting factor concentrates, and individuals diagnosed with HAV infection (based on acute signs and symptoms and a positive IgM anti-HAV test result). Of the 1167 specimens tested in the ARCHITECT HAVAB-M clinical study, 658 specimens were from: individuals at increased risk of HAV infection, individuals with signs and symptoms of hepatitis, individuals diagnosed with acute HAV infection (including one pre-selected IgM anti-HAV positive specimen), and from pediatric individuals.

Of the 658 specimens, 554 specimens (Population 1) were obtained from individuals living in the United States from the following populations: 253 specimens were from individuals at increased risk of HAV infection; 200 specimens were from individuals with signs and symptoms of hepatitis; 1 specimen was from an individual diagnosed with acute HAV infection; and
100 specimens were from pediatric individuals.

The specimens in Population 1 (n=554) consisted of the following race/ethnic groups:

- 259 (46.75%) Caucasian
- 92 (16.61%) Hispanic
- 74 (13.36%) African-American
- 12 (2.17%) Asian
- 3 (0.54%) American Indian/Alaska Native
- 14 (2.53%) Other
- 100 (18.05%) Unknown

The specimens in Population 1 (n=554) were obtained from the following collection locations:

- 92 (16.61%) from Galveston, TX
- 100 (18.05%) from Fall River, MA
- 84 (15.16%) from Dallas, TX
- 76 (13.72%) from Denver, CO
- 74 (13.36%) from St. Petersburg, FL
- 53 (9.57%) from Miami, FL
- 46 (8.30%) from Chicago, IL
- 20 (3.61%) from Plymouth, MA
- 9 (1.62%) from Colton, CA

Of the 554 specimens in Population 1, 309 (55.78%) were male and 245 (44.22%) were female. The mean age was 39 years (age range: 2 to 78 years).

Of the 658 specimens, 104 specimens (Population 2) were obtained from individuals living outside the United States diagnosed with acute HAV infection (including one pre-selected IgM anti-HAV positive specimen).

The specimens in Population 2 (n=104) consisted of the following race/ethnic groups:

- 103 (99.04%) Arab
- 1 (0.96%) Other

The specimens in Population 2 (n=104) were obtained from the following collection locations:

- 61 (58.65%) from Cairo, Egypt

- 42 (40.38%) from Minia, Egypt
- 1 (0.96%) from Hue City, Vietnam

Of the 104 specimens in Population 2, 82 (78.85%) were male and 22 (21.15%) were female. The mean age was 13 years (age range: 1 to 32 years).

Each specimen from Populations 1 and 2 was tested using a comparator IgM anti-HAV assay. The comparator assay was performed following the manufacturer's instructions. Each specimen was also tested at one of three clinical sites located in Galveston, TX; Hershey, PA; or Milwaukee, WI, using the ARCHITECT HAVAB-M assay.

Comparison of Results and Percent Agreement

The comparison of the ARCHITECT HAVAB-M results to the comparator IgM anti-HAV results and associated percent agreement (including 95% exact confidence intervals) for Population 1 are summarized in the following tables.

	Comparator IgM Anti-HAV Assay																			
	Reactive						**Grayzone**						**Nonreactive**							
	ARCHITECT HAVAB-M Interpretation						**ARCHITECT HAVAB-M Interpretation**						**ARCHITECT HAVAB-M Interpretation**							
	R[a]		**GZ[a]**		**NR[a]**		**R[a]**		**GZ[a]**		**NR[a]**		**R[a]**		**GZ[a]**		**NR[a]**		**Total**	
Testing Site	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	260	46.93	260	46.93
2	1	0.18	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	155	27.98	156	28.16
3	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	138	24.91	138	24.91
Total	**1**	**0.18**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**553**	**99.82**	**554**	**100.00**

[a] NR = nonreactive, GZ = grayzone, R = reactive

Testing Site	**Positive Percent Agreement**	**95% Exact Confidence Interval**	**Negative Percent Agreement**	**95% Exact Confidence Interval**
1	NA (0/0)	NA	100.00 (260/260)	98.59-100.00
2	100.00 (1/1)	2.50-100.00	100.00 (155/155)	97.65-100.00
3	NA (0/0)	NA	100.00 (138/138)	97.36-100.00
Overall	**100.00 (1/1)**	**2.50-100.00**	**100.00 (553/553)**	**99.34-100.00**

The comparison of the ARCHITECT HAVAB-M results to the comparator IgM anti-HAV results and associated percent agreement (including 95% exact confidence intervals) for Population 2 are summarized in the following tables.

Testing Site	Comparator IgM Anti-HAV Assay																			
	Reactive						Grayzone						Nonreactive							
	ARCHITECT HAVAB-M Interpretation						ARCHITECT HAVAB-M Interpretation						ARCHITECT HAVAB-M Interpretation							
	R[a]		GZ[a]		NR[a]		R[a]		GZ[a]		NR[a]		R[a]		GZ[a]		NR[a]		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2	0	0.00	0	0.00	1	0.96	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	0.96
3	102	98.08	0	0.00	1	0.96	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	103	99.04
Total	**102**	**98.08**	**0**	**0.00**	**2**[b]	**1.92**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**104**	**100.00**

[a] NR = nonreactive, GZ = grayzone, R = reactive

[b] Two specimens from the Acute population were nonreactive by ARCHITECT HAVAB-M and reactive by the comparator assay.

Testing Site	Positive Percent Agreement	95% Exact Confidence Interval	Negative Percent Agreement	95% Exact Confidence Interval
2	0.00 (0/1)	0.00-97.50	NA (0/0)	NA
3	99.03 (102/103)	94.71-99.98	NA (0/0)	NA
Overall	**98.08 (102/104)**	**93.23-99.77**	**NA (0/0)**	**NA**

The positive percent agreement of the ARCHITECT HAVAB-M assay with the comparator assay for Populations 1 and 2 (n=658) was 98.10% (103/105), with a 95% confidence interval of 93.29% to 99.77%. The negative percent agreement of the ARCHITECT HAVAB-M assay with the comparator assay for Populations 1 and 2 was 100.00% (553/553), with a 95% confidence interval of 99.34% to 100.00%.

Clinical Performance in an Acute HAV Population

The specimens were from 104 individuals diagnosed with acute HAV infection (based on acute signs and symptoms and a positive IgM anti-HAV test result) and one pre-selected IgM anti-HAV positive specimen. The acute HAV population (n=105) was obtained from the following collection locations: 1 (0.95%) from St. Petersburg, FL, 1 (0.95%) from Vietnam, and
103 (98.10%) from Egypt. The positive percent agreement of the ARCHITECT HAVAB-M assay to the comparator assay and the 95% exact confidence interval are summarized in the following table.

Agreement of the ARCHITECT HAVAB-M Assay in an Acute HAV Population		
Population	**Positive Percent Agreement % (x/n)[a]**	**95% Exact Confidence Interval**
Individuals Diagnosed with Acute HAV Infection (including one pre-selected IgM anti-HAV positive specimen)	98.10 (103[b]/105)	93.29-99.77

[a] x = the number of reactive ARCHITECT HAVAB-M results that were in agreement with the comparator assay results

n = the total number of comparator assay results that were reactive

[b] Two specimens were nonreactive by ARCHITECT HAVAB-M and reactive by the comparator assay. These two specimens were previously identified in the Comparison of Results and Percent Agreement subsection footnote.

Clinical Performance in a Pediatric Population

One hundred residual specimens from a pediatric population at low risk for hepatitis were obtained in Fall River, MA. The negative percent agreement of the ARCHITECT HAVAB-M assay to the comparator assay and the 95% exact confidence interval are summarized in the following table.

Agreement of the ARCHITECT HAVAB-M Assay in a Pediatric Population		
Population	**Negative Percent Agreement % (x/n)[a]**	**95% Exact Confidence Interval**
Pediatric	100.00 (100/100)	96.38-100.00

[a] x = the number of reactive ARCHITECT HAVAB-M results that were in agreement with the comparator assay results

n = the total number of comparator assay results that were reactive

One hundred and two prospectively collected pediatric specimens from Populations 1 and 2 were from the following individuals: 11 specimens were from individuals with increased risk of HAV infection, 2 specimens were from individuals with signs and symptoms of hepatitis, and 89 specimens were from individuals diagnosed with acute HAV infection. Positive percent agreement and negative percent agreement between the ARCHITECT HAVAB-M assay and the comparator assay were calculated. Positive percent agreement was 98.88% (88/89) with a 95% confidence interval of 93.90% to 99.97% and negative percent agreement was 100.00% (13/13) with a 95% confidence interval of 75.29% to 100.00%. The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results in the prospectively collected pediatric population (n=102) is summarized by age and gender in the following

table.

Age Group (Years)	Gender	ARCHITECT HAVAB-M Result			Total
		Reactive n (%)	Grayzone n (%)	Nonreactive n (%)	
0-1	F	0 (0.00)	0 (0.00)	0 (0.00)	0
	M	1 (100.00)	0 (0.00)	0 (0.00)	1
2-12	F	14 (100.00)	0 (0.00)	0 (0.00)	14
	M	32 (96.97)	0 (0.00)	1 (3.03)	33
13-18	F	3 (75.00)	0 (0.00)	1 (25.00)	4
	M	34 (97.14)	0 (0.00)	1 (2.86)	35
19-21	F	1 (16.67)	0 (0.00)	5 (83.33)	6
	M	3 (33.33)	0 (0.00)	6 (66.67)	9
Overall	F	18 (75.00)	0 (0.00)	6 (25.00)	24
	M	70 (89.74)	0 (0.00)	8 (10.26)	78
Total		**88 (86.27)**	**0 (0.00)**	**14[a] (13.73)**	**102**

[a] One specimen was nonreactive by ARCHITECT HAVAB-M and reactive by the comparator assay. This is one of the two specimens previously identified in the Comparison of Results and Percent Agreement subsection footnote.

Analytical Specificity

The ARCHITECT HAVAB-M assay was evaluated for potential cross-reactivity for specimens from individuals with medical conditions unrelated to HAV infection and specimens containing potentially interfering substances. The data are summarized in the following table.

		Comparator IgM Anti-HAV Assay								
		Nonreactive			Grayzone			Reactive		
		ARCHITECT HAVAB-M			ARCHITECT HAVAB-M			ARCHITECT HAVAB-M		
Category	**n**	**NR[a]**	**GZ[a]**	**R[a]**	**NR[a]**	**GZ[a]**	**R[a]**	**NR[a]**	**GZ[a]**	**R[a]**
Antinuclear Antibody (ANA)	10	10	0	0	0	0	0	0	0	0

		Comparator IgM Anti-HAV Assay								
		Nonreactive			Grayzone			Reactive		
		ARCHITECT HAVAB-M			ARCHITECT HAVAB-M			ARCHITECT HAVAB-M		
Category	**n**	**NR[a]**	**GZ[a]**	**R[a]**	**NR[a]**	**GZ[a]**	**R[a]**	**NR[a]**	**GZ[a]**	**R[a]**
positive										
Chronic Lymphocytic Leukemia	1	1	0	0	0	0	0	0	0	0
Cytomegalovirus (anti-CMV positive)	10	10	0	0	0	0	0	0	0	0
Elevated IgG	10	10	0	0	0	0	0	0	0	0
Epstein-Barr Virus (anti-EBV positive)	10	10	0	0	0	0	0	0	0	0
Hepatitis B Virus (anti-HBV positive)	10	10	0	0	0	0	0	0	0	0
Hepatitis C Virus (anti-HCV positive)	10	10	0	0	0	0	0	0	0	0
Herpes Simplex Virus (HSV) IgG	3	3	0	0	0	0	0	0	0	0
Heterophilic Antibodies (Human Anti-Mouse Antibody) positive	7	7	0	0	0	0	0	0	0	0
Human Immunodeficiency Virus (anti-HIV-1 positive)	10	10	0	0	0	0	0	0	0	0
Human Immunodeficiency Virus (anti-HIV-2 positive)	10	10	0	0	0	0	0	0	0	0
IgM monoclonal gammopathies	1	1	0	0	0	0	0	0	0	0
Influenza vaccine recipients	10	10	0	0	0	0	0	0	0	0

		Comparator IgM Anti-HAV Assay								
		Nonreactive			Grayzone			Reactive		
		ARCHITECT HAVAB-M			ARCHITECT HAVAB-M			ARCHITECT HAVAB-M		
Category	**n**	**NR[a]**	**GZ[a]**	**R[a]**	**NR[a]**	**GZ[a]**	**R[a]**	**NR[a]**	**GZ[a]**	**R[a]**
Multiparous female	10	10	0	0	0	0	0	0	0	0
Multiple myeloma	2	2	0	0	0	0	0	0	0	0
Mumps virus	10	10	0	0	0	0	0	0	0	0
Non-Hodgkin's Lymphoma[b]	6	2	2	2	0	0	0	0	0	0
Non-viral liver disease: alcoholic liver disease	1	1	0	0	0	0	0	0	0	0
Non-viral liver disease: hepatocellular carcinoma	8	8	0	0	0	0	0	0	0	0
Rheumatoid factor (RF) positive	10	10	0	0	0	0	0	0	0	0
Rubella (anti-Rubella) positive	10	10	0	0	0	0	0	0	0	0
Rubeola virus	9	9	0	0	0	0	0	0	0	0
Syphilis	10	9	0	0	0	0	0	1	0	0
Systemic lupus erythematosus (SLE)	5	5	0	0	0	0	0	0	0	0
Toxoplasmosis (anti-Toxoplasma positive)	9	9	0	0	0	0	0	0	0	0
Varicella Zoster Virus (VZV) positive	4	4	0	0	0	0	0	0	0	0
Yeast infection	7	7	0	0	0	0	0	0	0	0
Total	**203**	**198**	**2[c]**	**2[c]**	**0**	**0**	**0**	**1[c]**	**0**	**0**

[a] NR = nonreactive, GZ = grayzone, R = reactive

[b] Specimens from individuals with Non-Hodgkin's Lymphoma may cross-react with this assay.

[c] Of the 203 specimens tested, five were observed to be discordant with the comparator IgM anti-HAV assay.

Interference

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07-A2.*20*

At the concentrations listed below, bilirubin (conjugated and unconjugated), hemoglobin, total protein, and triglycerides showed less than 10% interference in the ARCHITECT HAVAB-M assay for high negative samples targeted to 0.80 S/CO and low positive samples targeted to
1.20 S/CO:

Potentially Interfering Substance	**Interferent Level**
Bilirubin	≤ 20 mg/dL
Hemoglobin	≤ 500 mg/dL
Total Protein	≤ 12 g/dL
Triglycerides	≤ 3000 mg/dL

Tube Type Matrix Comparison

The following tube types are acceptable for use:

- Glass: serum and serum separator
- Plastic: serum, serum separator, lithium heparin plasma separator, sodium heparin, and dipotassium EDTA

On average, the tube types evaluated below showed less than 10% difference when compared to the control tube type (plastic serum). The distribution of the percent differences per tube type is listed in the following table.

	Distribution of the Differences		
Tube Type	**< 10%**	**≥ 10% to ≤ 20%**	**> 20%**
Glass Serum	95.1% (39/41)	4.9% (2/41)	0.0% (0/41)
Glass Serum Separator	92.5% (37/40)	7.5% (3/40)	0.0% (0/40)
Plastic Serum Separator	97.6% (40/41)	2.4% (1/41)	0.0% (0/41)
Plastic Lithium Heparin Plasma Separator	92.7% (38/41)	7.3% (3/41)	0.0% (0/41)
Plastic Sodium Heparin	92.5% (37/40)	7.5% (3/40)	0.0% (0/40)
Plastic Dipotassium EDTA	97.6% (40/41)	2.4% (1/41)	0.0% (0/41)

Neonate Serum

A study was conducted to evaluate whether neonate samples may be tested with the ARCHITECT HAVAB-M assay. Cord blood was used as a surrogate for neonate serum. Twenty-six matched cord blood and maternal serum samples were spiked with IgM HAV positive stock to yield a high negative sample (target S/CO 0.80) and a low positive sample (target S/CO 1.20). None of the samples were initially reactive. The data obtained upon spiking are summarized in the following table, showing the amount of bias for the cord blood samples from the matched maternal serum samples. All individual samples listed as having ≥ 10% bias observed with the cord blood exhibited negative bias when compared to matched maternal serum sample.

Analyte Level S/CO	**Distribution of % Bias**					
	< 10%	**≥ 10% to < 20%**	**≥ 20% to < 30%**	**≥ 30% to < 40%**	**≥ 40% to < 50%**	**≥ 50%**
0.80	50.0% (13/26)	30.8% (8/26)	11.5% (3/26)	0.0% (0/26)	7.7% (2/26)	0.0% (0/26)
1.20	57.7% (15/26)	26.9% (7/26)	11.5% (3/26)	0.0% (0/26)	3.8% (1/26)	0.0% (0/26)

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