SIEMENS Healthineers

Hepatitis A Total (aHAVT)

Assay for the Detection of Total Antibodies to Hepatitis A Virus

Current Revision and Date[a]	Rev. 04, 2020-08	
Product Name	Atellica IM Hepatitis A Total (aHAVT)	REF 10995446
Abbreviated Product Name	Atellica IM aHAVT	
Test Name/ID	aHAVT	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM APW1	REF 10995458
Optional Materials	Atellica IM aHAVT QC	REF 10995448
Specimen Types	Serum, EDTA plasma, lithium heparin plasma, sodium heparin plasma	
Sample Volume	20 µL	
Measuring Interval	0.00–100.00 mIU/mL	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

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Intended Use

The Atellica® IM Hepatitis A Total (aHAVT) assay is for *in vitro* diagnostic use in the quantitative determination of total antibodies to hepatitis A virus (anti-HAV) in human serum and plasma (EDTA, lithium heparin, and sodium heparin) using the Atellica® IM Analyzer.

An assay for anti-HAV is indicated as an aid in the diagnosis of previous or ongoing hepatitis A viral infection, or for the detection of anti-HAV after vaccination.

Summary and Explanation

The Atellica IM aHAVT assay is a competitive chemiluminometric immunoassay used for the detection of total antibody to hepatitis A virus in human serum or plasma.

Hepatitis A is caused by infection with the hepatitis A virus. HAV is a 27-nanometer single-stranded, non-enveloped RNA virus that is classified as a picornavirus. Transmission of hepatitis A is via the fecal-oral route and infection occurs mainly as a result of contaminated food or poor sanitary conditions.[1,2]

Hepatitis A virus replicates in the liver. The virus is excreted in the bile and shed in the stool. Only 1 serotype has been observed among HAV isolates collected from various parts of the world. The average incubation period for HAV infection is 30 days with a range of 15–40 days. Chronic infection has not been reported to occur following HAV infection. Symptoms last approximately 2 weeks and include hepatomegaly, jaundice, dark urine, fatigue, and gastrointestinal distress such as anorexia, nausea, vomiting, and abdominal pain. At the onset of symptoms resulting from HAV infection, antibody to HAV is detectable. The early antibody response is largely comprised of the IgM antibody subclass. Anti-HAV IgM is detectable for 3–6 months after the onset of illness, whereas anti-HAV IgG can persist indefinitely. The specific determination of anti-HAV IgM is the most useful serological marker for diagnosing acute HAV infection. Total anti-HAV is used primarily for determination of previous exposure to hepatitis A virus.[1-4]

The Atellica IM aHAVT assay detects all classes of antibodies against hepatitis A virus. The detection of anti-HAV total activity is used to identify susceptible individuals and to determine acquisition of immunity after vaccination.[5-7]

Principles of the Procedure

The Atellica IM aHAVT assay is a fully automated, competitive immunoassay using direct chemiluminescent technology. The assay consists of 3 reagent addition and incubation steps. First, the sample is pretreated with Ancillary Reagent containing cysteine. Next, HAV antigen is added from the ancillary well (Antigen Reagent). Lite Reagent and Solid Phase are then added. The Lite Reagent contains mouse monoclonal antibody to HAV antigen labeled with acridinium ester and biotinylated Fab fragment of a mouse monoclonal antibody to HAV antigen. The Solid Phase contains streptavidin covalently coupled to paramagnetic particles. After the final incubation, the immuno-complex formed is washed with Atellica IM Wash prior to initiation of the chemiluminescent reaction.

An inverse relationship exists between the amount of antibody to HAV present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Reagents

Material Description	Storage	Stability[a]
Atellica IM aHAVT ReadyPack® primary reagent pack **Lite Reagent** 10.0 mL/reagent pack Mouse monoclonal anti-HAV (~1.0 µg/mL) labeled with acridinium ester and biotinylated mouse monoclonal anti-HAV Fab fragment (~0.08 µg/mL) in phosphate buffer; bovine serum albumin; sodium azide (< 0.1%); preservatives **Solid Phase** 17.5 mL/reagent pack Streptavidin coupled to paramagnetic particles in phosphate buffer; bovine serum albumin; sodium azide (< 0.1%); preservatives **Ancillary Well Reagent (Antigen Reagent)** 10.0 mL/reagent pack HAV antigen (~0.06 µg/mL) in tricine buffer; bovine serum albumin; stabilizers; sodium azide (< 0.1%); preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 41 days
Atellica IM aHAVT ReadyPack ancillary reagent pack **Ancillary Reagent** 5.0 mL/reagent pack Cysteine in citrate buffer; EDTA; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 41 days

Material Description	Storage	Stability[a]
Atellica IM aHAVT CAL 2.0 mL/vial Processed human plasma positive for anti-HAV antibodies; sodium azide (< 0.1%)	Unopened at 2–8°C	Until expiration date on product
	Opened at 2–8°C	60 days after opening product
	Onboard at room temperature	8 hours
	Atellica® Sample Handler[b]	
Atellica IM APW1 ReadyPack ancillary reagent pack[c] 25.0 mL/pack 0.4 N sodium hydroxide	Unopened at 2–8°C	Until expiration date on product
	Onboard	14 days

[a] Refer to *Storage and Stability*.

[b] Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

[c] Refer to *Materials Required but Not Provided*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens.com/healthineers.

H290, H319, H315
P280, P264,
P305+P351+P338,
P310, P390, P501

Warning!
May be corrosive to metals. Causes serious eye irritation. Causes skin irritation.
Wear protective gloves/protective clothing/eye protection/face protection. Wash hands thoroughly after handling. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER or doctor/physician. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hydroxide (in Atellica IM APW1)

CAUTION POTENTIAL BIOHAZARD

Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[8-10]

The calibrators contain human plasma that is reactive for anti-HAV total but negative for anti-HAV IgM.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Note For information about calibrator preparation, refer to *Preparing the Calibrators*.

Storage and Stability

Store reagents in an upright position. Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

Store calibrators in an upright position. Protect the product from heat and light sources. Unopened calibrators are stable until the expiration date on the product when stored at 2–8°C. Opened calibrators are stable for 60 days at 2–8°C. Calibrators are stable for 8 hours at room temperature.

Store Atellica IM APW1 in an upright position. Unopened Atellica IM APW1 is stable until the expiration date on the product when stored at 2–8°C.

Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 41 days. Discard reagents at the end of the onboard stability interval.

Atellica IM APW1 is stable onboard the system for 14 days.

Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Serum and plasma (EDTA, lithium heparin, sodium heparin) are the recommended sample types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[10]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[11]
- Follow the instructions provided with your specimen collection device for use and processing.[12]
- Allow blood specimens to clot completely before centrifugation.[9]
- Keep tubes capped at all times.[9]

- Samples are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post-draw. When testing 7 samples where the centrifugation step was varied up to 24 hours post-draw, no clinically significant differences were observed.
- Test samples as soon as possible after collecting. Store samples at 2–8°C if not tested immediately.

Storing the Specimen

- Store primary tube samples at 2–8°C for up to 7 days. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel barrier blood collection tubes. When 10 samples in these primary tubes were tested for up to 7 days at 2–8°C, no clinically significant differences were observed.
- Store samples capped and upright at all times at 2–8°C for up to 7 days.
- Freeze samples, devoid of red blood cells, at ≤ -20°C for up to 30 days. Do not store in a frost-free freezer. When 10 samples were subjected to 2 freeze-thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge them before using.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Samples maintained at room temperature for up to 12 hours or refrigerated for up to 7 days demonstrated no qualitative differences; however, good laboratory practice indicates that samples should be stored refrigerated. Store samples capped and upright at 2–8°C upon arrival. If shipment is expected to exceed 7 days, ship specimens frozen.

Preparing the Samples

This assay requires 20 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

Note Do not use specimens with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[9]

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10995446	1 ReadyPack primary reagent pack containing Atellica IM aHAVT Lite Reagent, Solid Phase, and Ancillary Well Reagent (Antigen Reagent) 1 ReadyPack ancillary reagent pack containing Atellica IM aHAVT Ancillary Reagent ANC Atellica IM aHAVT master curve and test definition MC TDEF 1 vial Atellica IM aHAVT CAL low calibrator CAL L 1 vial Atellica IM aHAVT CAL high calibrator CAL H Atellica IM aHAVT calibrator lot-specific value sheet CAL LOT VAL	100

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description	
	Atellica IM Analyzer[a]	
10995458	Atellica IM APW1 (probe wash)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Optional Materials

The following materials may be used to perform this assay, but are not provided:

REF	Description	
10995448	Atellica IM aHAVT QC (quality control material)	2 x 7.0 mL negative quality control CONTROL – 2 x 7.0 mL positive quality control CONTROL + Quality control lot-specific value sheet CONTROL LOT VAL

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 20 µL of sample and 50 µL of Ancillary Reagent into a cuvette, then incubates for 3 minutes at 37°C.
2. Dispenses 100 µL of Ancillary Well Reagent (Antigen Reagent), then incubates for 29 minutes at 37°C.
3. Dispenses 100 µL of Lite Reagent and 175 µL of Solid Phase, then incubates for 20 minutes at 37°C.
4. Separates, aspirates, and washes the cuvettes with Atellica IM Wash.
5. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
6. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading primary reagent packs onto the system, mix them by hand and visually inspect the bottom of the reagent pack to ensure that all particles are resuspended. For information about preparing the reagents for use, refer to the online help.

Note The Ancillary Reagent provided in this kit is matched to the Solid Phase, Lite Reagent, and Ancillary Well Reagent. Do not mix Ancillary Reagent lots with different lots of Solid Phase, Lite Reagent, and Ancillary Well Reagent.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. The system automatically mixes reagent packs to maintain homogeneous suspension of the reagents. For information about loading reagent packs, refer to the online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, load the assay master curve and test definition values by scanning the MC TDEF 2D barcodes. For loading instructions, refer to the online help.

Performing Calibration

For calibration of the Atellica IM aHAVT assay, use the calibrators provided with each kit.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	41
Pack Calibration	28
Reagent Onboard Stability	41

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Preparing the Calibrators

Calibrators are liquid and ready to use. Gently mix and invert the vials to ensure homogeneity of the material.

Note Use calibrator material within the stability limits specified in *Storage and Stability* and discard any remaining material.

Calibration Procedure

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the online help.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet MC TDEF provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the lot-specific value sheet CAL LOT VAL provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the online help.

Performing Quality Control

For quality control of the Atellica IM aHAVT assay, use the Atellica IM aHAVT QC or an equivalent product at least once during each work shift that samples are analyzed. Use the quality control material in accordance with the quality control instructions for use.

For the assigned values, refer to the lot-specific value sheet CONTROL LOT VAL provided. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Test quality control samples after a successful calibration.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help.

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Interpretation of Results

The system reports Atellica IM aHAVT assay results in mIU/mL and as Nonreactive or Reactive:

- **Nonreactive:** Samples with a value < 20 mIU/mL are considered nonreactive for antibodies to hepatitis A virus.
- **Reactive:** Samples with a value ≥ 20 mIU/mL are considered reactive for antibodies to hepatitis A virus.

The cut-off value for the Atellica IM aHAVT assay was verified based on results of clinical agreement generated from clinical studies.

Note If the controls are out of range, the sample results are invalid. Repeat the assay.

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

The following information pertains to limitations of the assay:

- The Atellica IM aHAVT assay is limited to the detection of total antibodies to hepatitis A antigen in human serum and plasma (EDTA, lithium heparin, and sodium heparin).
- The Atellica IM aHAVT assay does not distinguish among different classes of antibodies. The assay cannot be used to determine if a reactive sample is the result of an acute infection or is the result of a previous infection. The sample should be tested in a specific HAV IgM assay to determine if there is an ongoing or recent infection.
- The performance of the Atellica IM aHAVT assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- The performance of the assay has not been established for populations of immunocompromised or immunosuppressed patients.
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[13,14] Additional information may be required for diagnosis.

Performance Characteristics

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur® system. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur system.

Performance Characteristics on the ADVIA Centaur System

Specificity

The assay was evaluated for potential cross-reactivity with other viral antibodies and disease state specimens using the ADVIA Centaur system. The anti-HAV total status of each specimen was verified using an anti-HAV total comparative assay. If there was a discrepancy between the ADVIA Centaur assay result and the comparative assay result, the results were verified using the consensus method. The following results were obtained:

		Number of Positive Anti-HAV Total Results	
Clinical Category	**Number Tested**	**ADVIA Centaur Assay**	**Comparative Assay**
Hepatitis C Infection (HCV)	10	4	4
Hepatitis B Infection (HBV)	10	2	2
Autoimmune Disease (Rheumatoid Arthritis, Systemic Lupus)	20	11	11
Epstein-Barr Virus (EBV) IgG	10	3	3
Epstein-Barr Virus (EBV) IgM	10	3	3
Herpes Simplex Virus (HSV) IgG	10	5	5
Herpes Simplex Virus (HSV) IgM	10	3	3
CMV IgG	10	5	5

Clinical Category	Number Tested	Number of Positive Anti-HAV Total Results	
		ADVIA Centaur Assay	Comparative Assay
Toxoplasma IgG	10	2	2
Toxoplasma IgM	10	3	3
Human Immunodeficiency Virus (HIV 1/2)	10	2	2
VZV IgG	10	2	2
Rubeola IgG	10	2	2
Anti-Nuclear Antibody (ANA)	10	2	2
HAMA	10	1	1
Flu Vaccine Recipient	10	6	6
Total Samples Tested	170	56	56

Assay results obtained at individual laboratories may vary from the data presented.

Clinical Sensitivity and Specificity

The performance of the assay was determined by testing a total of 843 samples at 2 sites. The results were compared to test results using a commercially available automated anti-HAV total assay. The samples included the following populations: hospitalized patients, HAV infected and recovered patients, and acute HAV patients. Further evaluation (consensus testing) was performed with the discordant samples using another commercially available assay for anti-HAV total.

The performance of the HAV Total assay using the ADVIA Centaur system for each sample population is shown in the following table:

Patient Group	Number	ADVIA Centaur HAV Total Assay	
		Nonreactive	Reactive
Hospitalized patients	548	545 (99.5%)	3 (0.5%)
Infected/recovered patients	174	0	174 (100%)
Acute HAV patients	71	0	71 (100%)
Pre-Vaccination	25	24 (96%)	1 (4%)
Post-Vaccination	25	0	25 (100%)
Total	843		

The combined results for all samples tested are shown in the following table:

ADVIA Centaur HAV Total Assay	Comparative Anti-HAV Total Assay		
	Reactive	Nonreactive	Total
Reactive	269	5	274
Nonreactive	0	569	569
Total	269	574	843

The initial specificity of the HAV Total assay using the ADVIA Centaur system was 99.13% (569/574) with a 95% confidence interval (CI) of 97.98%–99.72%.

The initial sensitivity of HAV Total assay using the ADVIA Centaur system was 100% (269/269) with 95% confidence interval (CI) of 98.64%–100%.

Further analysis of the 5 specimens with discordant results was performed using an additional commercially available assay for anti-HAV Total. Of the 5 samples that were reactive using the ADVIA Centaur HAV Total assay and nonreactive using the comparative assay, 5 were reactive using the consensus method.

The combined results for all the samples tested using the ADVIA Centaur HAV Total assay and the commercial comparative assay after resolution of discordant results are shown in the following table:

	Consensus Results		
ADVIA Centaur HAV Total Assay	**Reactive**	**Nonreactive**	**Total**
Reactive	274	0	274
Nonreactive	0	569	569
Total	274	569	843

The resolved specificity of the HAV Total assay using the ADVIA Centaur system was 100% (569/569) with a 95% confidence interval (CI) of 99.35%–100%.

The resolved sensitivity of HAV Total assay using the ADVIA Centaur system was 100% (274/274) with 95% confidence interval (CI) of 98.66%–100%.

Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Interference testing was performed in accordance with CLSI Document EP7-A2.[15]

Hemolysis, Icterus, Lipemia (HIL), and Other Interferences

Serum specimens that are or that contain . . .	**Demonstrate ≤ 10% change in results or have an insignificant effect on the assay up to . . .**
hemolyzed	up to 500 mg/dL of hemoglobin
icteric	up to 60 mg/dL of conjugated bilirubin
icteric	up to 40 mg/dL of unconjugated bilirubin
lipemic	up to 3000 mg/dL of triglycerides
hypoproteinemic	as low as 3.5 g/dL of protein
hyperproteinemic	up to 12.0 g/dL of protein
hyper IgG	up to 60 mg/mL of immunoglobulin G

	Biotin Test Level (ng/mL)								
	0	**9**	**19**	**38**	**75**	**150**	**300**	**600**	**1200**
Negative Sample									
Index Value	0.68	0.58	0.58	0.63	0.95	1.38	3.32	> MI[a]	> MI
% Bias	N/A[b]	-14	-14	-6	41	104	389	N/A	N/A
Interpretation	NR[c]	NR	NR	NR	NR	FR[d]	FR	N/A	N/A
Positive Sample									
Index Value	1.97	1.78	1.74	1.80	2.26	2.74	> MI	> MI	> MI
% Bias	N/A	-10	-12	-9	15	39	N/A	N/A	N/A
Interpretation	R[e]	R	R	R	R	R	R	R	R

[a] Measuring Interval
[b] Not Applicable
[c] Nonreactive
[d] False Reactive
[e] Reactive

Specimens that contain biotin at a concentration of 38 ng/mL demonstrate no change in interpretation. Biotin concentrations greater than this may lead to a change in interpretation.

The recommended adult daily dietary intake for biotin is 30 µg/day. Over the counter dietary supplements promoted for use in hair, skin and nail health may contain 5–100 mg of biotin, with recommendations to take multiple pills per day. Pharmacokinetic studies in healthy adults have shown that, in subjects ingesting 5 mg, 10 mg, and 20 mg of biotin, serum concentrations of biotin can reach up to 73 ng/mL, 141 ng/mL, and 355 ng/mL, respectively.[16] Subjects who take up to 300 mg of biotin per day may have plasma biotin levels as high as 1160 ng/mL.[17]

Results were established using the ADVIA Centaur system, except for biotin which were established using an Atellica IM Analyzer.

Performance Characteristics on the Atellica IM Analyzer

Measuring Interval

The Atellica IM aHAVT assay provides results from 0.00–100.00 mIU/mL.

Relative Sensitivity

Relative sensitivity was determined by comparing the Atellica IM aHAVT assay using the Atellica IM Analyzer to the ADVIA Centaur aHAVT assay using the ADVIA Centaur XP system. A population of 103 ADVIA Centaur aHAVT reactive samples was tested using the Atellica IM aHAVT assay. The performance of the Atellica IM aHAVT assay is shown in the following table:

Number	Nonreactive	Reactive	Relative Sensitivity (%)
103	1	102	99.0% (102/103)

The relative sensitivity of the Atellica IM aHAVT assay was 99.0% (102/103) with a 95% confidence interval of 94.7%–99.9%.

Assay results obtained at individual laboratories may vary from the data presented.

Relative Specificity

Relative specificity was determined by comparing the Atellica IM aHAVT assay using the Atellica IM Analyzer to the ADVIA Centaur aHAVT assay using the ADVIA Centaur XP system. A population of 106 ADVIA Centaur aHAVT nonreactive samples was tested using the Atellica IM aHAVT assay. The performance of the Atellica IM aHAVT assay is shown in the following table:

Number	Nonreactive	Reactive	Relative Specificity (%)
106	106	0	100.0% (106/106)

The relative specificity of the Atellica IM aHAVT assay was 100.0% (106/106) with a 95% confidence interval of 96.5%–100.0%.

Assay results obtained at individual laboratories may vary from the data presented.

Seroconversion Panels

Commercially available aHAVT patient seroconversion panels were tested using the ADVIA Centaur aHAVT assay and the Atellica IM aHAVT assay. The performance of the Atellica IM aHAVT assay on the seroconversion panels exactly matched the performance of the ADVIA Centaur aHAVT assay. The following results were obtained:

	aHAVT Reactive Result From Initial Draw Date		Atellica IM aHAVT Assay vs ADVIA Centaur aHAVT Assay
Panel ID	ADVIA Centaur Assay (Days)	Atellica IM Assay (Days)	Difference in Bleed Number (Bleeds)
SC6150026	10	10	0
DS1701008	10	10	0
DS1701009	6	6	0

Assay results obtained at individual laboratories may vary from the data presented.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[18] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days. The assay was designed to have within-laboratory precision of ≤ 3.00 SDs for samples ≤ 19.00 mIU/mL and ≤ 10% CV for samples ≥ 20.00 mIU/mL. The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (mIU/mL)	SD[b] (mIU/mL)	CV[c] (%)	SD (mIU/mL)	CV (%)
Plasma A	80	16.17	0.79	4.9	1.06	6.6
Plasma B	80	23.82	0.78	3.3	1.20	5.0
Plasma C	80	32.89	0.84	2.5	1.32	4.0
Plasma D	80	36.75	0.93	2.5	1.30	3.5
Plasma E	80	52.82	1.36	2.6	1.65	3.1
Plasma F	80	80.47	1.32	1.6	1.95	2.4

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean (mIU/mL)	SD[b] (mIU/mL)	CV[c] (%)	SD (mIU/mL)	CV (%)
Negative Control	80	0.00	0.00	N/A	0.00	N/A
Positive Control	80	38.34	0.99	2.6	1.19	3.1

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.

Assay results obtained at individual laboratories may vary from the data presented.

Standardization

The Atellica IM aHAVT assay is standardized to the WHO Second International Standard for Anti-Hepatitis A Immunoglobulin (97/646).

Assigned values for calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens.com/healthineers

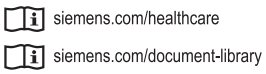
References

1. Hollinger FB, Ticehurst JR. Hepatitis A virus. In: Fields BN, Knipe DM, Howley PM, eds. *Fields Virology*, 3rd ed. Philadelphia, PA: Lippincott-Raven Publishers; 1996:735–782.
2. Stapleton JT. Hepatitis A virus: biology, pathogenesis, epidemiology, clinical description, and diagnosis. In: Specter S, ed. *Viral Hepatitis: Diagnosis, Therapy, and Prevention*. Totowa, NJ: Humana Press Inc.; 1999:7–33.
3. Cuthbert JA. Hepatitis A: old and new. *Clin Microbiol Rev*. 2001;14(1):38–58.
4. Bower WA, Nainan OV, Han X, Margolis HS. Duration of viremia in hepatitis A virus infection. *J Infect Dis*. 2000;182(1):12–17.
5. Siegl G, Lemon SM. Recent advances in hepatitis A vaccine development. *Virus Res*. 1990:17:75–92.
6. Maiwald H, Jilg W, Bock HL, Loscher T, Sonnenburg F. Long-term persistence of anti-HAV antibodies following active immunization with hepatitis A vaccine. *Vaccine*. 1997:15:346–348.
7. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Prevention of hepatitis A through active or passive immunization. *MMWR*. 1996:45: (RR-15).
8. Centers for Disease Control. Perspectives in disease prevention and health promotion update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR*. 1988;37(24):377–382, 387–388.
9. Clinical and Laboratory Standards Institute. *Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP44-A4.
10. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document M29-A4.

11. Clinical and Laboratory Standards Institute. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2007. CLSI Document GP41-A6.
12. Clinical and Laboratory Standards Institute. *Tubes and Additives for Venous and Capillary Blood Specimen Collection; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP39-A6.
13. Kricka LJ. Human anti-animal antibody interferences in immunological assays. *Clin Chem*. 1999;45(7):942–956.
14. Vaidya HC, Beatty BG. Eliminating interference from heterophilic antibodies in a two-site immunoassay for creatine kinase MB by using F(ab')2 conjugate and polyclonal mouse IgG. *Clin Chem*. 1992;38(9):1737–1742.
15. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP7-A2.
16. Grimsey P, Frey N, Bendig G, et al. Population pharmacokinetics of exogenous biotin and the relationship between biotin serum levels and *in vitro* immunoassay interference. *Int. J. Pharmacokinet*. 2017;2(4):247–256.
17. Piketty ML, Prie D, Sedel F, et al. High-dose biotin therapy leading to false biochemical endocrine profiles: validation of a simple method to overcome biotin interference. *Clin Chem Lab Med*. 2017;55(6):817-825.
18. Clinical and Laboratory Standards Institute. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document EP05-A3.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
	Revision
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.
	Corrosive

Symbol	Symbol Title and Description
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner
IVD	*In vitro* diagnostic medical device
Σ (n)	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Symbol	Symbol Title and Description
	Mixing of substances Mix product before use.
	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
	Printed with soy ink
CE	CE Mark
CE 0088	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year-month-day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
UNITS C	Common Units
UNITS SI	International System of Units
MATERIAL	Material
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens.com/healthineers

Siemens Healthineers Headquarters
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens.com/healthineers