510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K222850

B Applicant

Abbott Laboratories

C Proprietary and Established Names

HAVAb IgG II

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LOL	Class II	21 CFR 866.3310 - Hepatitis A Virus (HAV) Serological Assays	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

Market clearance of HAVAb IgG II assay for the detection of anti-IgG Hepatitis A Virus in human adult and pediatric (4 through 21 years) serum (collected in serum and serum separator) and plasma (collected in sodium heparin, lithium heparin, lithium heparin separator, dipotassium EDTA, and tripotassium EDTA tubes) samples using the Alinity i system.

B Measurand:

IgG antibodies to Hepatitis A Virus

C Type of Test:

A chemiluminescent microparticle immunoassay (CMIA)

III Intended Use/Indications for Use:

A Intended Use(s):

The HAVAb IgG II assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibody to hepatitis A virus (IgG anti-HAV) in human adult and pediatric (4 throught 21 years) serum (collected in serum and serum separator tubes) and plasma (collected in sodium heparin, lithium heparin, lithium heparin separator, dipotassium EDTA, and tripotassium EDTA tubes) from patients with signs and symptoms or at risk for hepatitis A on the Alinity i system.

The HAVAb IgG II assay is used to determine the immune status of individuals to hepatitis A virus (HAV) infection.

Warning: This assay has not been cleared for use in screening blood, plasma, or tissue donors. This assay cannot be used for the diagnosis of acute HAV infection.

Assay performance characteristics have not been established when the HAVAb IgG II assay is used in conjunction with other hepatitis assays.

B Indication(s) for Use:

Same as Intended Use

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

For use with the Alinity i system instrument from Abbott Laboratories Inc.

IV Device/System Characteristics:

A Device Description:

The HAVAb IgG II assay is an automated two-step immunoassay for the qualitative detection of IgG anti-HAV in human adult and pediatric serum and plasma from patients with signs and symptoms or at risk for hepatitis A, using chemiluminescent microparticle immunoassay (CMIA) technology.

B Principle of Operation:

The HAVAb IgG II assay is a fully automated chemiluminescent microparticle immunoassay (CMIA). In the first step of the assay, sample, HAV (human) coated paramagnetic microparticles, and assay diluent are combined and incubated. The IgG anti-HAV present in the sample binds to the HAV (human) coated microparticles. The mixture is then washed. In the second step, Anti-human IgG acridinium-labeled conjugate is added to create a reaction mixture and incubated. The mixture is then washed again. In the third step of the assay, the Pre-Trigger and Trigger Solutions are added. The resulting chemiluminescent reaction is measured as a relative light unit (RLU). The presence or absence of IgG anti-HAV in the sample is determined

by the Alinity i system, which calculates results by comparing the chemiluminescent RLU in the reaction to the cutoff RLU determined from an active calibration. Specimens with signal to cutoff (S/CO) values ≥ 1.00 are considered reactive for IgG anti-HAV, and specimens with S/CO values < 1.00 are considered nonreactive for IgG anti-HAV.

S/CO	Interpretation
< 1.00	Nonreactive
≥ 1.00	Reactive

C Instrument Description Information:

1. Instrument Name:
   Alinity i system

2. Specimen Identification:
   A barcode reader reads the barcodes assigned to the specimen

3. Specimen Sampling and Handling:
   Sample presence, sample type (calibrator, control, specimen), rack ID/ position number, and processing completion are tracked by operating software and sample barcode.

4. Calibration:
   Calibration for the Alinity i system is performed using one (1) calibrator. The calibrator is an anti-HAV IgG reactive recalcified human plasma with an antibody concentration of approximately 50 mIU/mL. The calibrator is traceable to the WHO 2nd International Standard for anti-hepatitis A Immunoglobulin, Human (NIBSC Code 97/646).

5. Quality Control:
   The HAVAb IgG II Controls:
   The negative control contains recalcified human plasma with protein (bovine) stabilizer negative for anti-HAV with a target concentration of ≤ 0.56 S/CO.

   The positive control contains recalcified human plasma reactive for IgG anti-HAV with a target concentration of 1.03 - 3.53 S/CO.

V Substantial Equivalence Information:

A Predicate Device Name(s):
ARCHITECT HAVAB-G assay

B Predicate 510(k) Number(s):
K113704

C Comparison with Predicate(s):

Device & Predicate Device(s):	K222850	K113704
Device Trade Name	**HAVAb IgG II (Candidate)**	**ARCHITECT HAVAB-G (Predicate)**
General Device Characteristic Similarities		
Intended Use/Indications For Use	The HAVAb IgG II assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibody to hepatitis A virus (IgG anti-HAV) in human adult and pediatric (4 through 21) serum (collected in serum and serum separator tubes) and plasma (collected in sodium heparin, lithium heparin, lithium heparin separator, dipotassium EDTA, and tripotassium EDTA tubes) from patients with signs and symptoms or at risk for hepatitis on the Alinity i system. The HAVAb IgG II assay is used to determine the immune status of individuals to hepatitis A virus (HAV) infection. Warning: This assay has not been cleared for use in screening blood, plasma, or tissue donors. This assay cannot be used for the diagnosis of acute HAV infection. Assay performance characteristics have not been established when the HAVAb IgG II assay is used in conjunction with other hepatitis assays.	The ARCHITECT HAVAB-G assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG antibody to hepatitis A virus (IgG anti-HAV) in human adult and pediatric serum from patients with signs and symptoms or at risk for hepatitis. The ARCHITECT HAVAB-G assay is used to determine the immune status of individuals to hepatitis A virus infection. **Warning: This assay has not been FDA cleared or approved for the screening of blood or plasma donors. This assay cannot be used for the diagnosis of acute HAV infection.** Assay performance characteristics have not been established when the ARCHITECT HAVAB-G assay is used in conjunction with other hepatitis assays.
Methodology	same	Chemiluminescent Microparticle Immunoassay
Antigen Used	same	HAV (Strain pHM175)
Interpretation of Results	same	Nonreactive: < 1.00 S/CO Reactive: ≥ 1.00 S/CO
Calibrator	same	1 Calibrator
Controls	same	2 (Negative and Positive)

General Device Characteristic Differences		
Type of Specimen	Serum and Plasma	Serum
Platform	Alinity i system	ARCHITECT i System
Components	**Microparticles** – HAV (human) coated microparticles in MOPS / potassium chloride buffer. Minimum concentration: 0.08% solids. Preservative: ProClin 300. **Conjugate** – Anti-human IgG (mouse, monoclonal) acridinium-labeled conjugate in MES / sodium chloride buffer with protein (bovine) stabilizer and surfactants. Minimum concentration: 0.01 µg/mL. Preservatives: ProClin 300 and ProClin 950. **Assay Diluent** – Assay diluent containing protein (goat, mouse, and bovine) stabilizers in TRIS buffer and surfactant. Preservatives: ProClin 300 and ProClin 950.	**Microparticles** – HAV (human) coated microparticles in TRIS buffer. Minimum concentration: 0.08% solids. Preservatives: ProClin 300 and antimicrobial agents. **Conjugate** – Anti-human IgG (mouse monoclonal) acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 0.01 µg/mL. Preservatives: sodium azide and antimicrobial agents. **Assay Diluent** – Protein (goat) stabilizer in TRIS buffer. Preservatives: ProClin 300 and antimicrobial agents.

VI Standards/Guidance Documents Referenced:

1. Class II Special Controls Guidance Document: Hepatitis A Virus Serological Assays, Feb. 9, 2006. http://www.fda.gov/cdrh/ode/guidance/1536.pdf

2. CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; 2014

3. CLSI EP07-A3, Interference Testing in Clinical Chemistry; 2018

4. CLSI EP15-A2E, User Verification of Performance for Precision and Trueness, 2006

5. CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; 2012

6. CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; 2009

7. CLSI EP35, Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures, 2019

8. CLSI EP37, Supplemental Tables for Interference Testing in Clinical Chemistry, 2018

9. CDRH guidance document. *Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable,* April 25, 2006.

10. CDRH guidance document. *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)],* July 28, 2014.

11. CDRH guidance document. *Format for Traditional and Abbreviated 510(k)s,* September 13, 2019.

12. CDRH guidance document. *eCopy Program for Medical Device Submissions,* April 27, 2020.

13. CDRH guidance document. *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices,* May 11, 2005.

14. CDRH guidance document. *General Principles of Software Validation,* January 11, 2002.

15. CDRH guidance document. *Content of Premarket Submissions for Management of Cybersecurity in Medical Devices*, October 2, 2014.

16. CDRH guidance document. *Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software*, January 14, 2005.

17. CDRH guidance document. *Postmarket Management of Cybersecurity in Medical Devices,* December 28, 2016.

18. CDRH guidance document. *Off-the-Shelf Software Use in Medical Devices,* September 27, 2019.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Within-laboratory Precision (20 days):

   Within- laboratory Precision was evaluated for 20 days on two Alinity i instruments at one internal site. Two plasma control members- a negative (mean 0.10 S/CO) and positive (mean 2.20 S/CO) HAVAb controls, and two serum member panels- one high negative (mean 0.73 S/CO), and one low positive (mean 1.27 S/CO), were tested. Each sample was tested in duplicate, in two runs per day, for 20 days, with one control lot, two reagent lots, and two calibrator lots. Calibration was conducted at the beginning of the study by testing the

calibrator in triplicates. The mean S/CO and standard deviation (SD) was calculated for each sample, and the coefficient of variation (%CV) was calculated for positive samples. Within-laboratory precision study results are shown in the following table.

Within-laboratory precision study results

			Within-Run (Repeatability)		Within-Laboratory[a]	
Sample	**n**	**Mean (S/CO)**	**SD**	**%CV**	**SD (Range[b])**	**%CV (Range[b])**
High Negative Panel 1	80	0.71	0.025	NA	0.028 (0.026-0.045)	NA
Low Positive Panel 2	80	1.25	0.040	3.2	0.040 (0.036-0.078)	3.2 (2.9-5.8)
Negative Control	80	0.09	0.011	NA	0.015 (0.011-0.035)	NA
Positive Control	80	2.19	0.053	2.4	0.063 (0.055-0.090)	2.9 (2.5-4.0)

NA = Not applicable
[a] Includes within-run, between-run, and between-day variability.
[b] Minimum and maximum SD or %CV across 4 reagent lot/calibrator lot/instrument combinations.

2. Reproducibility (Multi-site):

A 5-day multi-site reproducibility study at 3 testing sites evaluated samples with 3 different reagent lots for each site, 2 lots of the calibrators, and 2 lots of the controls tested on the Alinity i system. Samples consisted of a negative (<0.56 S/CO) and positive (1.03-3.53 S/CO) control, one high negative (0.60-0.80 S/CO) sample, and one low positive (1.24- 1.52 S/CO) sample. Testing was performed at 2 runs per day (separated by two hours between runs), in duplicates. Calibration was performed prior to the start of testing, samples were randomized, and study personnel blinded to S/CO values. The mean S/CO value and standard deviation was calculated for each sample, and the coefficient of variation (%CV) calculated for the positive samples.

Reproducibility study results

Sample	n	Mean (S/CO)	Repeatability		Within-Laboratory[a]		Reproducibility[b]	
			SD	%CV	SD	%CV	SD	%CV
High Negative Panel A	360	0.66	0.037	NA	0.042	NA	0.053	NA
Low Positive Panel B	360	1.32	0.044	3.4	0.056	4.3	0.069	5.2
Negative Control	360	0.11	0.039	NA	0.042	NA	0.046	NA
Positive Control	360	2.26	0.066	2.9	0.088	3.9	0.106	4.7

[a] Includes repeatability (within-run), between-run, and between-day variability.
[b] Includes repeatability (within-run), between-run, between-day, and between-instrument variability.

2. Linearity:
Not applicable.

3. Analytical Specificity/Interference:

Cross-reactivity
Serum from patients with conditions unrelated to HAV infection, antibodies against microorganisms, and an HAV non-reactive specimen spiked with HAV IgM were tested for cross-reactivity. Each sample was tested with the candidate device on one Alinity i system and with comparator device ARCHITECT HAVAB-G, using one of each reagent, calibrator and control lots. A total of 241/251 samples tested negative on both candidate and comparator devices. Cross-reactivity was seen in samples that were reactive by the candidate device and non-reactive by the comparator in: 1/15 Anti-CMV, 1/4 Anti-*E. coli*, 2/24 Anti-HBV, 2/20 Anti-*T. gondii*, 1/2 hemodialysis patients, 2/14 hyper IgG, and 1/32 multiparous pregnant women as shown in the below table.

Cross-reactivity of HAVAb IgG II assay on the Alinity i instrument

Category	n	HAVAb IgG II (on Alinity i)	
		Reactive	Nonreactive
Anti-cytomegalovirus (anti-CMV)	15	1	14
Anti-Epstein-Barr virus (anti-EBV)	11	0	11
Anti-*E coli*	4	1	3
Anti-hepatitis B virus (anti-HBV) (*i.e.*, anti-HBc, anti-HBs, and HBsAg)	24	2	22
Anti-hepatitis C virus (anti-HCV)	13	0	13
Anti-mumps virus	12	0	12
Anti-nuclear antibodies (ANA)	13	0	13
Anti-rubeola (measles) virus	14	0	14
Anti-*Toxoplasma gondii* (anti-*T gondii)*	20	2	18
Anti-varicella zoster virus (anti-VZV)	12	0	12

Human anti-mouse antibodies (HAMA)	9	0	9
Hemodialysis patients	2	1	1
Hepatitis (noninfectious; chronic or acute toxic)	10	0	10
Heterophile antibodies (nonspecific)	5	0	5
Hyper IgG (monoclonal)	14	2	12
Hyper IgM (monoclonal)	6	0	6
Hyper IgM (polyclonal)	3	0	3
Influenza vaccine recipients	12	0	12
Lupus	10	0	10
Multiparous pregnant women (all trimesters)	32	1	31
Rheumatoid factor (RF)	10	0	10
Total	**251**	**10**	**241**

Endogenous Interference:
The impact of endogenous interfering substances found in blood was tested in high negative (0.80 S/CO) and low positive (1.2 S/CO) contrived samples prepared by spiking high IgG anti-HAV positive human serum samples into a pool of normal human serum units. Each of these samples was divided in two aliquots, one aliquot was not supplemented with the potential interferents, and a second aliquot was supplemented with the following potential interferents: unconjugated bilirubin (40 mg/dL), conjugated bilirubin (40 mg/dL), biotin (up to 4300 ng/mL), hemoglobin (1000 mg/dL), total protein (15 g/dL), or triglycerides (1500 mg/dL). The samples were tested with a minimum of 12 replicates using one lot each of reagents, calibrator, and controls on one instrument. Interference of <10% for 1.20 S/CO samples or <0.10 S/CO for 0.8 S/CO samples was observed at the following concentrations

	Interferent Level	
Potentially Interfering Substance	**Default Units**	**Alternate Units**
Bilirubin (Conjugated)	40 mg/dL	475 µmol/L
Bilirubin (Unconjugated)	40 mg/dL	684 µmol/L
Biotin	3600 ng/mL	-
Hemoglobin	1000 mg/dL	10 g/L
Total Protein	15 g/dL	150 g/L
Triglycerides	1500 mg/dL	16.94 mmol/L

4. Assay Reportable Range:
Not applicable.

5. Stability (Controls, Calibrators, or Methods):

Controls stability:

Real-time stability studies conducted to date support storage of opened and unopened controls at 2 to 8°C for up to 4 months and In-Use Opened at 2 to 8°C for 3 hours.

Calibrator stability:

Calibrator stability studies conducted to date support storage of opened and unopened calibrator at 2 to 8°C up to 4 months.

Reagent stability:

Real-time stability studies conducted to date support storage of opened and unopened reagent kits at 2 to 8°C for up to 4 months and onboard the Alinity i system up to 30 days.

Specimen stability:

Specimen stability studies conducted to date support stability of specimens stored at room temperature (15 to 25ºC) up to 16 hours, at 2 to 8°C up to 8 days, and at -20ºC up to 30 days.

6. Detection Limit:

Limit of Blank (LoB) was determined with four normal human serum samples tested in 5 replicates, and the Limit of Detection (LoD) was determined with 4 low-level analyte samples (2, 4, 6, 8 mIU/mL) in duplicates and tested in 10 replicates. All samples were tested on two different Alinity i instruments, using two reagent lots, and one lot of each control and calibrator. The LoB was determined to be 0.35 S/CO and the LoD to be 0.40 S/CO.

7. Analytical Sensitivity at the Cut-Off:

The analytical sensitivity of the candidate device at the assay cutoff value of 1.00 S/CO was conducted to determine the relationship between S/CO and the units of the WHO International Standard (WHO IS) for anti-hepatitis A, Immunoglobulin, Human (NIBSC Code: 97/646). The study was performed by diluting the WHO IS with anti-HAV negative recalcified plasma to a concentration of 50 mIU/mL (Intermediate). Recalcified plasma is the same matrix as the calibrator/control material that is tested to be negative for anti-HAV antibodies, which is similar to serum. A panel of five different dilutions was prepared by combining the Intermediate with anti-HAV negative recalcified plasma to a concentration of 10, 12.5, 14.5, 17.5, and 20 mIU/mL. Each dilution was tested in 9 replicates per lot, with 3 reagent lots, on one Alinity i instrument. The calibrators and controls were also tested. For each reagent lot, the least squares linear regression analysis was performed on the mean S/CO for each dilution (mean of 9 replicates each) vs. the target concentration across the dilutions. The analytical sensitivity at 1.0 S/CO was determined to be 15.7 mIU/mL.

8. Accuracy (Instrument):

Not applicable.

9. Carry-Over:

Susceptibility of within-assay sample carryover from very high positive IgG anti-HAV samples (target > 60,000 mIU/mL) to a contrived high negative serum sample (target 0.8

S/CO) was evaluated. A wash buffer sample was tested in three replicates to clear the system. One replicate of the high negative sample was tested to serve as a sample that was not exposed to potential sample carryover (protected negative sample). This was followed by one replicate of the high positive sample that was used to introduce potential carryover effects. Then, one other replicate of the negative sample was tested to serve as a sample exposed to potential sample carryover (unprotected negative sample). This carryover event series was tested 12 times across 5 runs. The mean S/CO value, standard deviation, difference and percent difference of the means between the protected and unprotected samples was evaluated as shown below.

HAVAb IgG II within-assay sample carryover

Protected Sample			Unprotected Sample			Difference[a]		% Difference[b]	
N	Mean S/CO	SD	N	Mean S/CO	SD	Result S/CO	Two-Sided 95% CI	Result S/CO	Two-Sided 95% CI
12	0.75	0.039	12	0.79	0.033	0.04	(0.01, 0.07)	5.7	(1.6, 9.8)

[a] Difference = Unprotected sample mean S/CO - Protected sample mean S/CO
[b] %Difference = Difference S/CO × 100 / Protected sample mean S/CO

B Comparison Studies:

1. Method Comparison with Predicate Device:

A prospective multicenter study was conducted to evaluate the performance of HAVAb IgG II assay evaluated on three Alinity i instruments at three clinical centers in the United States. Samples were tested using three lots of HAVAb IgG II reagent, two lots of HAVAb IgG II calibrator, and two lots of HAVAb IgG II controls. A total of 944 native human serum specimens were tested, consisting of individuals at increased risk of HAV infection, individuals with signs and symptoms of hepatitis infection, HAV vaccine recipients, and pediatric population. Specimens <1.00 S/CO were considered non-reactive, and specimens ≥ 1.0 S/CO were considered reactive. Percent agreement with the results obtained with the ARCHITECT HAVAB-G assay is summarized in the following sections.

Summary of Agreement Rates Across Cohorts

At Increased Risk of HAV Infection

The percent agreement for specimens from individuals at increased risk of HAV infection (n=250) is shown in the following table.

Individuals at Increased Risk of HAV Infection		
	ARCHITECT HAVAB-G	
HAVAb IgG II (on Alinity i)	Reactive	Nonreactive
Reactive	119	2
Nonreactive	4	125

Positive % agreement = 96.75% (119/123), 95% confidence interval (CI) (91.94%- 98.73%)
Negative % agreement = 98.43% (125/127), 95% CI (94.44%-99.57%)

Individuals with Signs and Symptoms of Hepatitis Infection
The percent agreement for specimens from individuals with signs and symptoms of hepatitis infection (n=499) is shown in the following table.

Individuals with Signs and Symptoms of Hepatitis Infection		
	ARCHITECT HAVAB-G	
HAVAb IgG II (on Alinity i)	**Reactive**	**Nonreactive**
Reactive	290	2
Nonreactive	14	193

Positive % agreement = 95.39% (290/304), 95% CI (92.42%-97.24%)
Negative % agreement = 98.97% (193/195), 95% CI (96.34%-99.72%)

Pediatric Population
The percent agreement for specimens from the pediatric population (n=105) is shown in the following table.

Pediatric Population		
	ARCHITECT HAVAB-G	
HAVAb IgG II (on Alinity i)	**Reactive**	**Nonreactive**
Reactive	90	1
Nonreactive	0	14

Positive % agreement = 100.00% (90/90), 95% CI (95.91%-100.00%)
Negative % agreement = 93.33% (14/15), 95% CI (70.18%-98.81%)

2. Matrix Comparison/Tube Type Equivalency
The aim of the matrix equivalency study was to verify the appropriate specimen tube type for use with the HAVAb IgG II assay for serum, serum separator, and plasma (sodium heparin, lithium heparin, lithium heparin separator, dipotassium EDTA, and tripotassium EDTA) samples. A total of 22 sets of matched serum, serum separator, dipotassium EDTA, lithium heparin, sodium heparin, lithium heparin separator, and tripotassium EDTA were used in this study. The study included a total of 22 negative and 20 positive samples. Serum negative donor specimens were spiked with a high positive specimen (at a volume ≤ 5%) to contrive high negative (0.65 to 0.86 S/CO) and low positive (1.2 to 1.5 S/CO) samples. Each sample set was tested in at least 2 replicates, with one reagent, calibrator and control lot, on one instrument. Agreement of performance between the serum control and the evaluated tube type was calculated and supports the use of this assay with the following tube types: dipotassium EDTA, lithium heparin, sodium heparin, lithium heparin separator, serum separator, and tripotassium EDTA.

C. Expected Values/Reference Range

The expected values were calculated based on the clinical study conducted to support the performance of the HAVAb IgG II assay on Alinity i system.

Expected Values from Apparently Healthy Individuals:
Prospectively collected serum samples from apparently healthy individuals (n = 519) were tested with HAVAb IgG II assay on Alinity i system to evaluate the prevalence of hepatitis A virus antibodies (IgG anti-HAV) in an apparently healthy population. Study specimens from the low prevalence areas of Port Jefferson, NY and Milwaukee, WI, and the high prevalence area of Galveston, TX were enrolled in the study. The percentage of previously vaccinated individuals in this group is unknown.

The apparently healthy population consisted of the following race/ ethnic groups:

- 248 (47.78%) White
- 149 (28.71%) Black or African American
- 90 (17.34%) Hispanic or Latino
- 27 (5.20%) Asian
- 3 (0.58%) American Indian or Alaska Native
- 1 (0.19%) Native Hawaiian or Other Pacific Islander
- 1 (0.19%) Hispanic or Latino / American Indian or Alaska Native

Of the 519 specimens, 299 (57.61%) were from females (F) and 220 (42.39%) were from males (M).

Apparently healthy individuals from high prevalent area for HAV (Galveston, TX)

Age Group (Years)	Sex	HAVAb IgG II Result (High Prevalence)		Total
		Reactive n (%)	Nonreactive n (%)	
22-29	F	7 (15.22)	39 (84.78)	46
	M	4 (36.36)	7 (63.64)	11
30-39	F	19 (36.54)	33 (63.46)	52
	M	10 (52.63)	9 (47.37)	19
40-49	F	21 (28.77)	52 (71.23)	73
	M	5 (29.41)	12 (70.59)	17
50-59	F	13 (36.11)	23 (63.89)	36

Age Group (Years)	Sex	HAVAb IgG II Result (High Prevalence)		Total
		Reactive n (%)	Nonreactive n (%)	
	M	5 (26.32)	14 (73.68)	19
60-69	F	10 (71.43)	4 (28.57)	14
	M	3 (75.00)	1 (25.00)	4
70-79	F	4 (100.00)	0 (0.00)	4
	M	0 (0.00)	0 (0.00)	0
80-89	F	1 (100.00)	0 (0.00)	1
	M	0 (0.00)	0 (0.00)	0
Overall	F	75 (33.19)	151 (66.81)	226
	M	27 (38.57)	43 (61.43)	70
Total		**102 (34.46)**	**194 (65.54)**	**296**

Apparently healthy pediatric individuals from high prevalent area for HAV (Galveston, TX)

Age Range (Years)	Sex	HAVAb IgG II Result (High Prevalence)		Total
		Reactive n (%)	Nonreactive n (%)	
16-21	F	2 (18.18)	9 (81.82)	11
	M	0 (0.00)	4 (100.00)	4
Total		**2 (13.33)**	**13 (86.67)**	**15**

Apparently healthy individuals from low prevalent area for HAV (Milwaukee, WI and Port Jefferson, NY)

Age Group (Years)	Sex	HAVAb IgG II Result (Low Prevalence)		Total
		Reactive n (%)	**Nonreactive n (%)**	
22-29	F	1 (16.67)	5 (83.33)	6
	M	5 (33.33)	10 (66.67)	15
30-39	F	2 (12.50)	14 (87.50)	16
	M	1 (5.26)	18 (94.74)	19
40-49	F	3 (23.08)	10 (76.92)	13
	M	6 (24.00)	19 (76.00)	25
50-59	F	0 (0.00)	12 (100.00)	12
	M	11 (40.74)	16 (59.26)	27
60-69	F	0 (0.00)	4 (100.00)	4
	M	7 (31.82)	15 (68.18)	22
70-79	F	1 (25.00)	3 (75.00)	4
	M	4 (20.00)	16 (80.00)	20
80-89	F	2 (100.00)	0 (0.00)	2
	M	5 (62.50)	3 (37.50)	8
Overall	F	9 (15.79)	48 (84.21)	57
	M	39 (28.68)	97 (71.32)	136
Total		**48 (24.87)**	**145 (75.13)**	**193**

Apparently healthy pediatric individuals from low prevalent area for HAV (Milwaukee, WI and Port Jefferson, NY)

Age Range (Years)	Sex	HAVAb IgG II Result (Low Prevalence)		Total
		Reactive n (%)	Nonreactive n (%)	
18-21	F	0 (0.00)	5 (100.00)	5
	M	2 (20.00)	8 (80.00)	10
Total		**2 (13.33)**	**13 (86.67)**	**15**

Expected Values in individuals at Increased Risk for HAV infection, Signs and Symptoms of Hepatitis, and Pediatric Population:

Of the 845 prospective samples analyzed in the intended use population collected via routine physician order, 250 specimens were from individuals with increased risk of HAV infection, 499 from individuals with signs and symptoms of hepatitis infection, and 105 from individuals representing the pediatric population. Specimen collection ages ranged from 10-80 and was geographically diverse across the US with testing across three clinical sites: Temple, Texas; Pompano Beach, Florida; and Dallas, Texas. The percentage of previously vaccinated individuals within these groups is unknown. There was no excluded data from the expected values analysis.

Individuals at Increased Risk of HAV Infection
The increased risk adult population consisted of the following race/ethnic groups:

- 106 (43.09%) Black or African American
- 90 (36.59%) White
- 32 (13.01%) Hispanic or Latino
- 3 (1.22%) Asian
- 1 (0.41%) American Indian or Alaska Native
- 14 (5.69%) Other

The specimens from the increased risk adult population were collected from multiple sites. The percentage of reactive results from each site is as follows:

- 83.33% (5/6) from Chicago, IL
- 75.00% (6/8) from Miami, FL
- 71.43% (5/7) from Denver, CO
- 56.67% (68/120) from Los Angeles, CA
- 58.33% (7/12) from Dallas, TX
- 35.71% (10/28) from High Point, NC; Colton, CA; and Hyannis, MA
- 31.25% (5/16) from St. Petersburg, FL
- 30.61% (15/49) from Galveston, TX

Of the 246 specimens from adults, 88 (35.77%) were from females and 158 (64.23%) were from males. The mean age was 44.9 years (range: 22 to 77 years). The distribution of reactive and nonreactive results among individuals at increased risk of HAV infection is summarized by age and sex in the following table.

Summary of reactive and nonreactive results by age and gender in individuals at increased risk of HAV infection

Age Group (Years)	Sex	HAVAb IgG II Result		Total
		Reactive n (%)	Nonreactive n (%)	
22-29	F	7 (43.75)	9 (56.25)	16
	M	5 (31.25)	11 (68.75)	16
30-39	F	10 (32.26)	21 (67.74)	31
	M	14 (50.00)	14 (50.00)	28
40-49	F	7 (46.67)	8 (53.33)	15
	M	25 (54.35)	21 (45.65)	46
50-59	F	10 (62.50)	6 (37.50)	16
	M	16 (38.10)	26 (61.90)	42
60-69	F	6 (66.67)	3 (33.33)	9
	M	18 (78.26)	5 (21.74)	23
70-79	F	1 (100.00)	0 (0.00)	1
	M	2 (66.67)	1 (33.33)	3
Overall	F	41 (46.59)	47 (53.41)	88
	M	80 (50.63)	78 (49.37)	158
Total		**121 (49.19)**	**125 (50.81)**	**246**

Individuals with Signs and Symptoms of Hepatitis Infection

The individuals with signs and symptoms of hepatitis adult population (n=482) consisted of the following race/ethnic groups:

- 197 (40.87%) White
- 161 (33.40%) Black or African American
- 97 (20.12%) Hispanic or Latino

- 16 (3.32%) Asian
- 3 (0.62%) American Indian or Alaska Native
- 8 (1.66%) Other

The specimens from the signs and symptoms of hepatitis adult population were collected from multiple sites. The percentage of reactive results from each site is as follows:

- 83.33% (100/120) from Chicago, IL
- 62.86% (22/35) from Dallas, TX
- 64.71% (11/17) from Miami, FL
- 59.87% (91/152) from El Monte, CA; Los Angeles, CA; Pico Riveria, CA; Pomona, CA; and South El Monte, CA
- 52.08% (25/48) from St. Petersburg, FL
- 48.72% (19/39) from Denver, CO
- 47.06% (8/17) from Galveston, TX
- 25.93% (14/54) from Colton, CA, and Hyannis, MA

Of the 482 specimens from adults, 162 (33.61%) were from females and 320 (66.39%) were from males. The mean age was 46.2 years (range: 22 to 80 years). The distribution of reactive and nonreactive results among individuals with signs and symptoms of hepatitis infection is summarized by age and sex in the following table.

Summary of reactive and nonreactive results by age group and gender in individuals with signs and symptoms of hepatitis infection

Age Group (Years)	Sex	HAVAb IgG II Result		Total
		Reactive n (%)	Nonreactive n (%)	
22-29	F	10 (55.56)	8 (44.44)	18
	M	19 (59.38)	13 (40.63)	32
30-39	F	16 (59.26)	11 (40.74)	27
	M	22 (48.89)	23 (51.11)	45
40-49	F	38 (71.70)	15 (28.30)	53
	M	57 (50.89)	55 (49.11)	112
50-59	F	30 (71.43)	12 (28.57)	42
	M	60 (61.22)	38 (38.78)	98
60-69	F	13 (72.22)	5 (27.78)	18
	M	19 (65.52)	10 (34.48)	29
70-79	F	3 (75.00)	1 (25.00)	4

Age Group (Years)	Sex	HAVAb IgG II Result		Total
		Reactive n (%)	Nonreactive n (%)	
	M	3 (100.00)	0 (0.00)	3
80-89	F	0 (0.00)	0 (0.00)	0
	M	0 (0.00)	1 (100.00)	1
Overall	F	110 (67.90)	52 (32.10)	162
	M	180 (56.25)	140 (43.75)	320
Total		**290 (60.17)**	**192 (39.83)**	**482**

Pediatric Population

The pediatric population (n=105) consisted of the following race/ ethnic groups:

- 88 (83.81%) Hispanic or Latino
- 2 (1.90%) Black or African American
- 1 (0.95%) Other
- 14 (13.33%) Unknown

The specimens from the pediatric population were collected from multiple sites. The percentage of reactive results from each site is as follows:

- 98.90% (90/91) from Arcadia, CA, and Los Angeles County, CA
- 7.14% (1/14) from Fall River, MA, and Liege, Belgium

Of the 105 specimens, 60 (57.14%) were from females and 45 (42.86%) were from males. The mean age was 12.7 years (range: 4 through 21 years). The distribution of reactive and nonreactive results among the pediatric population is summarized by age and sex in the following table.

Summary of reactive and nonreactive results by age group and gender in a representative pediatric population

Age Group (Years)	Sex	HAVAb IgG II Result		Total
		Reactive n (%)	Nonreactive n (%)	
4-12	F	22 (68.75)	10 (31.25)	32
	M	19 (100.00)	0 (0.00)	19
> 12-21	F	26 (92.86)	2 (7.14)	28

Age Group (Years)	Sex	HAVAb IgG II Result		Total
		Reactive n (%)	Nonreactive n (%)	
Overall	M	24 (92.31)	2 (7.69)	26
	F	48 (80.00)	12 (20.00)	60
	M	43 (95.56)	2 (4.44)	45
Total		**91 (86.67)**	**14 (13.33)**	**105**

In addition, 4 specimens collected from individuals at increased risk of HAV infection and 17 specimens from individuals with signs and symptoms of hepatitis infection were from pediatric subjects. Of the 21 specimens, 7 (33.3%) were from females and 14 (66.7%) were from males. The distribution of reactive and nonreactive results is summarized by age and sex in the following table.

Summary of reactive and nonreactive results by age group and gender of pediatric individuals with increased risk of HAV infection and signs and symptoms of hepatitis infection

Age Group (Years)	Sex	HAVAb IgG II Result		Total
		Reactive n (%)	Nonreactive n (%)	
> 12-21	F	1 (14.29)	6 (85.71)	7
	M	1 (7.14)	13 (92.86)	14
Total		**2 (9.52)**	**19 (90.48)**	**21**

Positive Predictive Value and Negative Predictive Value by Prevalence

The positive predictive value (PPV) and negative predictive value (NPV) at prevalence of 0.5%, 1.0%, 2.0%, 5.0%, 10.0%, and 15.0% for specimens from individuals at increased risk of HAV infection (n=250), individuals with signs and symptoms of hepatitis infection (n=499), and the pediatric population (n=105) were also calculated based on CLSI EP12, 3rd ed. and summarized in the following table.

	Individuals at Increased Risk of HAV Infection		**Individuals with Signs and Symptoms of Hepatitis Infection**		**Pediatric Population**	
Prevalence (%)	**PPV (%) (95% CI)**	**NPV (%) (95% CI)**	**PPV (%) (95% CI)**	**NPV (%) (95% CI)**	**PPV (%) (95% CI)**	**NPV (%) (95% CI)**
0.5	23.59 (8.02, 52.97)	99.98 (99.96, 99.99)	31.85 (11.56, 63.02)	99.98 (99.96, 99.99)	7.01 (1.65, 29.89)	100.00 (99.98, 100.00)
1.0	38.29 (14.92, 69.36)	99.97 (99.92, 99.99)	48.44 (20.81, 77.40)	99.95 (99.92, 99.97)	13.16 (3.26, 46.15)	100.00 (99.96, 100.00)
2.0	55.63 (26.16, 82.06)	99.93 (99.83, 99.97)	65.50 (34.68, 87.37)	99.91 (99.84, 99.94)	23.44 (6.38, 63.39)	100.00 (99.91, 100.00)
5.0	76.38 (47.74, 92.18)	99.83 (99.57, 99.93)	83.04 (57.80, 94.69)	99.76 (99.60, 99.85)	44.12 (14.94, 81.70)	100.00 (99.77, 100.00)
10.0	87.22 (65.86, 96.14)	99.63 (99.10, 99.86)	91.18 (74.30, 97.41)	99.49 (99.16, 99.69)	62.50 (27.05, 90.41)	100.00 (99.51, 100.00)
15.0	91.55 (75.39, 97.53)	99.42 (98.57, 99.77)	94.26 (82.12, 98.36)	99.19 (98.67, 99.51)	72.58 (37.07, 93.74)	100.00 (99.22, 100.00)

D Other Supportive Instrument Performance Characteristics Data:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.