510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number: K113704

B. Purpose for Submission: New device clearance

C. Measurand: Hepatitis A IgG

D. Type of Test: Chemiluminescent microparticle immunoassay (CMIA)

E. Applicant: Abbott Laboratories

F. Proprietary and Established Names: ARCHITECT HAVAB-G
ARCHITECT HAVAB-G Calibrator
ARCHITECT HAVAB-G Controls

G. Regulatory Information:

1. Regulation section: 21 CFR 866.3310 Hepatitis A Virus Serological Assays
21 CFR 862.1660 Quality control material assayed and unassayed
21CFR 862.1150 Calibrator

2. Classification: Class II, II, I

3. Product Code: LOL, MJY, MJX, JIS

4. Panel: Microbiology (83), Microbiology (83), Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

ARCHITECT HAVAB-G Reagent Kit: 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.

HAVAB-G Calibrator: The ARCHITECT HAVAB-G Calibrator is for the calibration of the ARCHITECT *i* System, when used for the qualitative detection of IgG antibody to hepatitis A virus (IgG anti-HAV) in 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, using the ARCHITECT HAVAB-G Reagent Kit. The performance of the ARCHITECT HAVAB-G Calibrator has not been established with any other IgG anti-HAV assays.

HAVAB-G Controls: The ARCHITECT HAVAB-G Controls are used for monitoring the performance of the ARCHITECT *i* System, when used for the qualitative detection of IgG antibody to hepatitis A virus 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, using the ARCHITECT HAVAB-G Reagent Kit. The performance of the ARCHITECT HAVAB-G Controls have not been established with any other IgG anti-HAV assays

2. Indication(s) for use: Same as Intended Use

3. Special conditions for use statement(s): For prescription use only

4. Special instrument requirements:

   For use with the Abbott ARCHITECT family *i* 1000_{SR}, *i* 2000, *i* 2000_{SR}

I. Device Description:

The ARCHITECT HAVAB-G assay is a two-step immunoassay for the qualitative detection of IgG anti-HAV in human serum using CMIA technology. The presence or absence of IgG anti-HAV in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active ARCHITECT HAVAB-G calibration. Specimens with signal to cutoff (S/CO) values $\geq$ 1.00 are considered reactive for IgG anti-HAV and specimens with S/CO values < 1.00 are considered nonreactive for IgG anti-HAV.

J. Substantial Equivalence Information:

1. Predicate device name(s): ARCHITECT HAVAB-M

2. Predicate 510(k) number(s): K063329

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Patient Population	Adults and pediatric	same
Instrument Platform	ARCHITECT *i* System	same
Technology	CMIA	same

Differences		
Item	Device	Predicate
Intended Use	Chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgG antibody to hepatitis A virus in human adult and pediatric serum from patients with signs and symptoms or at risk for hepatitis. The 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.	Chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgM antibody to hepatitis A virus in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, and sodium heparin) and neonatal serum. A test for IgM anti-HAV is indicated for testing of specimens from individuals who have signs and symptoms consistent with acute hepatitis.
Specimen Type	Serum	Serum or Plasma
Tube Type	Human serum (including serum collected in separator tubes)	Human serum (including serum collected in separator tubes) or plasma (collected in dipotassium EDTA, sodium heparin, or lithium heparin)
Gray zone	No	Yes
Results Interpretation	<1.00 S/CO=Nonreactive ≥1.00 S/CO=Reactive	<0.80 S/CO=Nonreactive 0.80 to <1.21 S/CO=Gray zone ≥1.21 S/CO=Reactive

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP15-A2, "User Verification of Performance for Precision and Trueness"
CLSI EP7-A2, "Interference Testing in Clinical Chemistry"
CLSI EP12-A2, "User Protocol for Evaluation of Qualitative Test Performance"
Guidance for Industry and FDA Staff-Class II Special Controls Guidance Document: Hepatitis A Serological Assays
Guidance for Industry and FDA Staff- Replacement Reagent and Instrument Family Policy
Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s
Points to Consider for Collection of Data in Support of In Vitro Device Submissions for 510(k) Clearance

L. Test Principle:

The ARCHITECT HAVAB-G assay is a two-step immunoassay for the qualitative detection of IgG anti-HAV in human serum using CMIA technology. In the first step, sample, assay diluent, and hepatitis A virus (human) coated paramagnetic microparticles are combined. IgG Anti-HAV present in the sample binds to the hepatitis A virus (human) coated microparticles. After washing, the anti-human IgG acridinium-labeled conjugate that is added in the second step binds to IgG anti-HAV. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). The presence or absence of IgG anti-HAV in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an ARCHITECT HAVAB-G 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Precision was evaluated for 20 days on 4 ARCHITECT instruments (1- *i* 1000_{SR}, 1- *i* 2000, and 2- *i* 2000_{SR} using two controls and three panel members: ARCHITECT HAVAB-G Negative Control (NC), ARCHITECT HAVAB-G Positive Control (PC) with a target S/CO=2.5, high negative (targeted S/CO=0.85), cut-off sample (targeted S/CO=1.00), and a low positive (targeted S/CO=1.15). Two lots each of reagents, calibrators, and controls were used. The test panel member sample order was randomized per run and blinded per operator.

Instrument	Reagent Lot	Control/Panel Member[a]	n	Mean S/CO	Within-Run		Within-Laboratory	
					SD	%CV	SD	%CV
i 2000$_{SR}$ (1)	1	Positive Control	120	2.12	0.069	3.2	0.078	3.7
		High Negative Panel	118	0.81	0.031	3.8	0.031	3.8
		Cut-off Panel	120	0.93	0.030	3.2	0.034	3.6
		Low Positive Panel	120	1.11	0.033	3.0	0.043	3.8
Sample	2	Positive Control	120	2.14	0.068	3.2	0.084	3.9
		High Negative Panel	119	0.91	0.028	3.0	0.039	4.3
		Cut-off Panel	120	1.02	0.030	2.9	0.040	3.9
		Low Positive Panel	120	1.19	0.039	3.3	0.047	3.9
i 2000 $_{SR}$ (2)	1	Positive Control	118	2.01	0.051	2.5	0.065	3.2
		High Negative Panel	120	0.75	0.025	3.3	0.029	3.8
		Cut-off Panel	118	0.87	0.026	3.0	0.031	3.5
		Low Positive Panel	120	1.05	0.031	2.9	0.037	3.6
	2	Positive Control	120	2.14	0.067	3.1	0.077	3.6
		High Negative Panel	119	0.90	0.027	3.0	0.038	4.2
		Cut-off Panel	120	0.99	0.034	3.4	0.040	4.1
i 2000	1	Positive Control	120	2.10	0.065	3.1	0.072	3.4
		High Negative Panel	119	0.79	0.023	2.9	0.030	3.7
		Cut-off Panel	119	0.92	0.031	3.4	0.032	3.4
		Low Positive Panel	120	1.10	0.035	3.2	0.041	3.7
	2	Positive Control	119	2.31	0.075	3.3	0.086	3.7
		High Negative Panel	118	0.97	0.025	2.6	0.039	4.0
		Cut-off Panel	120	1.09	0.030	2.8	0.038	3.5
		Low Positive Panel	120	1.26	0.036	2.9	0.052	4.1
i 1000 $_{SR}$	1	Positive Control	120	2.04	0.070	3.4	0.075	3.7
		High Negative Panel	120	0.79	0.027	3.4	0.031	3.9
		Cut-off Panel	120	0.91	0.031	3.4	0.034	3.7
		Low Positive Panel	120	1.08	0.034	3.2	0.036	3.3
	2	Positive Control	120	2.20	0.074	3.4	0.087	3.9
		High Negative Panel	120	0.99	0.035	3.5	0.050	5.0
		Cut-off Panel	119	1.07	0.036	3.4	0.037	3.5
		Low Positive Panel	120	1.24	0.033	2.7	0.039	3.2
		Low Positive Panel	120	1.16	0.036	3.1	0.042	3.6

[a] represents a single sample

Reproducibility was evaluated by testing 3 lots each of ARCHITECT HAVAB-G reagents, calibrator, and controls at each of 3 clinical sites for 5 days on the ARCHITECT *i* 2000/ *i* 2000 $_{SR}$. Each run consisted of 2 replicates of 2 aliquots of NC, PC, and 2 reproducibility panel members: high negative sample (targeted S/CO=0.85) and a low positive sample (targeted S/CO=1.15)

Sample *i* 1000_{SR}	n	Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)[a]			Reproducibility with Additional Component of Between-Site (Overall)[b]	
			SD	%CV	SD	%CV	SD	%CV	%CV Upper CL[c]	SD	%CV
Negative Control	120	0.24	0.020	8.3	0.020	8.3	0.020	8.3	9.3	0.023	9.4
Positive Control	120	2.20	0.085	3.9	0.102	4.6	0.102	4.6	5.3	0.102	4.6
High Negative	120	0.85	0.030	3.5	0.034	4.0	0.034	4.0	4.5	0.074	8.7
Low Positive	120	1.16	0.046	4.0	0.052	4.5	0.052	4.5	5.0	0.090	7.8

[a] Within-laboratory (total) variability contains within-run, within-day, and between-day variance components.
[b] Overall variability contains within-run, within-day, between-day, and between-site variance components.
[c] One-sided upper 95% confidence limit for %CV with degrees of freedom calculated by Satterthwaite's method.

Additional Reproducibility study on the *i* 1000_{SR}: A 5 day study was conducted by testing 1 lot each of ARCHITECT HAVAB-G reagents, calibrator, and controls at each of 3 clinical testing sites. Each of the sites ran samples identical to those used for the reproducibility study. Each of 3 clinical testing sites ran the ARCHITECT *i* 1000_{SR}. The ARCHITECT *i* 1000_{SR} results were compared to the overall ARCHITECT *i* 2000/ *i* 2000_{SR} results. The following table shows the results for the ARCHITECT *i* 1000_{SR}.

The following table shows the results for all the systems:

Sample	*i* 1000_{SR}						*i* 2000/*i* 2000_{SR}						Within-Run			Within-Lab		
	n	Mean S/CO	Within-Run		Within-Lab		n	Grand Mean S/CO	Within-Run		Within-Lab							
			SD	%CV	SD	%CV			SD	%CV	SD	%CV	SD Ratio[a]	Lower 95% CL	Upper 95% CL	SD Ratio[a]	Lower 95% CL	Upper 95% CL
Negative Control	120	0.24	0.020	8.3	0.020	8.3	360	0.20	0.010	5.3	0.011	5.8	1.937	1.647	2.311	1.748	1.509	2.046
Positive Control	120	2.20	0.085	3.9	0.102	4.6	360	2.08	0.082	4.0	0.099	4.7	1.033	0.879	1.233	1.038	0.877	1.246
High Negative	120	0.85	0.030	3.5	0.034	4.0	360	0.76	0.033	4.3	0.037	4.9	0.912	0.776	1.089	0.909	0.778	1.075
Low Positive	120	1.16	0.046	4.0	0.052	4.5	360	1.05	0.039	3.8	0.045	4.3	1.165	0.991	1.391	1.152	0.987	1.364

[a]SD Ratio = SD *i* 1000 SR / SD *i* 2000/ *i* 2000 SR

b. Linearity/assay reportable range: N/A

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability: This method has been standardized against the "Second International Standard for Anti-Hepatitis A, Immunoglobulin, Human, NIBSC code: 97/646" of the NIBSC (National Institute for Biological Standards and Control).

Controls: Negative Control: nonreactive human plasma with a target S/CO≤0.65. Positive Control: Reactive human plasma with a target range S/CO of 1.25-3.31.

Calibrators: Calibration of the ARCHITECT *i* System is performed using one (1) calibrator. This calibrator is an anti-HAV reactive serum with an antibody concentration of approximately 50 mIU/mL. The system calculates the cutoff RLU from the mean chemiluminescent signal of three architect HAVAB-G calibrator replicates. The acceptability of the calibration is assessed against a parameter. If the calibration is acceptable, the cutoff RLU is calculated where cutoff RLU=Calibrator mean RLU x 0.29. The acceptable calibration is stored by the system for use with any ARCHITECT HAVAB-G reagent kit of that lot. A single sample of each control level must be tested to evaluate the assay calibration. Once the calibration is accepted and stored, all subsequent samples may be tested without further calibration unless a reagent kit with a new lot number is used or the control is out of range.

d. Detection limit: LoD N/A

e. Analytical specificity:

Cross-reactivity: The following sample types were used for this study: serum from patients with conditions unrelated to HAV infection, antibodies against microorganisms, and an HAV nonreactive specimen spiked with HAV IgM. All samples tested negative by the AxSYM HAVAB 2.0, which measures total HAV antibody. Cross-reactivity was seen in samples tested by the ARCHITECT HAVAB-G: 1/19 Anti-*E. coli*, 2/14 Anti-CMV, 1/3 hemodialysis patient serum, and 1/13 human anti-mouse antibodies as shown in the following table:

		AxSYM HAVAB 2.0			
		Nonreactive		**Reactive**	
		ARCHITECT HAVAB-G		**ARCHITECT HAVAB-G**	
Categ	**N**	**Nonreactiv**	**Reactive**	**Nonreactiv**	**Reactive**
Anti-*E. coli*	19	18	1	0	0
Anti-nuclear antibodies	8	8	0	0	0
Cytomegalovirus (anti-CMV)	14	12	2	0	0
Epstein Barr Virus (anti-EBV)	15	15	0	0	0
HAV IgM*	10	10	0	0	0

Hemodialysis patients	3	2	1	0	0
Hepatitis B Virus (anti-HBV)	10	10	0	0	0
Hepatitis C Virus (anti-HCV)	27	27	0	0	0
Human anti-mouse antibodies (HAMA)	13	12	1	0	0
Influenza vaccine recipients	11	11	0	0	0
Lupus (SLE)	18	18	0	0	0
Monoclonal gammopathy, elevated IgG	3	3	0	0	0
Multiparous pregnant women first	14	14	0	0	0
Multiparous pregnant women second	6	6	0	0	0
Multiparous pregnant women third	7	7	0	0	0
Mumps virus	17	17	0	0	0
Non-infectious hepatitis	9	9	0	0	0
Polyclonal gammopathy, elevated IgG	4	4	0	0	0
Rheumatoid factor	20	20	0	0	0
Rubeola virus	10	10	0	0	0
Toxoplasma gondii	11	11	0	0	0
Varicella zoster virus	10	10	0	0	0
Total	259	254	5	0	0

*HAV nonreactive specimens spiked with HAV IgM.

Interference: The impact of endogenous interfering substances on the ARCHITECT HAVAB-G potential interfering substances found in blood was tested in high negative and low positive samples. Each of these samples was then supplemented with unconjugated bilirubin (≤ 20 mg/dL), conjugated bilirubin (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), total protein (≤ 12 g/dL), or triglycerides (≤ 3000 mg/dL). The samples were tested with a minimum of 12 replicates using one lot each of reagents, calibrator, and controls on one instrument. At these concentrations all showed less than 15% interference (+0.15 S/CO) with the ARCHITECT HAVAB-G assay.

f. *Assay cut-off:* The cutoff RLU equation for the ARCHITECT HAVAB-G US assay was based on the cutoff RLU equation for the ARCHITECT HAVAb-IgG non-US assay. Of the 1209 specimens from both presumed positive (patients diagnosed with HAV, HAV vaccine recipients, and intravenous drug users) and presumed negative populations (random blood donors and random diagnostic patients) that were tested by both ARCHITECT HAVAb-IgG non-US assay and the AxSYM HAVAB 2.0, 674 samples were actually positive or negative and used for the ROC analysis. The optimal sensitivity and specificity was achieved when the cut-off was set using a multiplier of 0.29. The ARCHITECT *i* System calculates the S/CO result for each sample where S/CO=Sample RLU/cutoff RLU and the cutoff RLU=Calibrator 1 mean RLU x 0.29.

Reactive for IgG anti-HAV: S/CO values ≥ 1.00

Nonreactive: S/CO values < 1.00

Abbott performed a dilution study of the HAV WHO standard and determined that the cutoff corresponds to an IgG anti-HAV concentration of 16.8 mIU/mL.

2. Comparison studies:

   a. *Method comparison with predicate device: N/A*

   b. *Matrix comparison: N/A*

3. Clinical studies:

   a. *Clinical Sensitivity: N/A*

   b. *Clinical specificity: N/A*

   c. *Other clinical supportive data (when a. and b. are not applicable):*
   The device under review is for the detection of IgG antibodies for hepatitis A virus (HAV). Currently there are no FDA cleared devices that would detect only HAV IgG antibodies. The cleared devices detect only IgM or both IgM and IgG (total) antibodies. The following testing algorithm was used as a comparator algorithm for evaluating the test device performance:

HAV IgG Final Status

ARCHITECT HAVAB-G	AxSYM HAVAB 2.0	ARCHITECT HAVAB-M	Reference Result	IgG Status
+ True Positive	+	-	IgG	Reactive
+ Need Supplemental Testing	+	+	IgM only or IgM/IgG mixture	Nonreactive or Reactive
- True Negative	-	-	No IgM or IgG	Nonreactive
- True Negative	-	+	IgM	Nonreactive
+ False Positive	-	+	IgM	Nonreactive
+ False Positive	-	-	No IgM or IgG	Nonreactive
- Need Supplemental Testing	+	+	IgM only or IgM/IgG mixture	Nonreactive or Reactive
- False Negative	+	-	IgG	Reactive

Note: For the purposes of this clinical investigation, AxSYM HAVAB 2.0 gray zone results were classified as nonreactive (-) and ARCHITECT HAVAB-M gray zone results were

classified as reactive (+) based on how the gray zone is defined in their respective package inserts.

For specimens that had a reference result of "IgM only or IgM/IgG mixture," supplemental processing and testing was performed to determine the final HAV IgG status. The IgG and IgM antibodies were separated from the sample using affinity chromatography. The Abbott Clinical Chemistry Immunoglobulin G and Clinical Chemistry Immunoglobulin M assays were utilized to create the IgM and IgG pooled fractions which were then evaluated with the ARCHITECT HAVAB-G and ARCHITECT HAVAB-M assays

Clinical Study Cohorts:
A prospective study was conducted to evaluate the performance of the ARCHITECT HAVAB-G compared to the result of the composite algorithm at 3 clinical centers in the United States. A total of 775 specimens were obtained from collection centers or vendors, frozen, and distributed among the 3 clinical centers for comparison algorithm testing from the following populations: individuals at increased risk (n=260) and individuals with signs and symptoms (n=515):

Individuals at increased risk of HAV infection 120/127 were positive, 94.49% agreement (95% confidence interval 88.97% and 97.76%) and 7 were reactive by the comparator algorithm but negative by the ARCHITECT HAVAB-G assay. 133/133 were negative, 100.0% agreement (95% confidence interval 97.26% and 100.0%)

ARCHITECT HAVAB-G Interpretation	**Final HAV IgG Status**	
	Reactive	**Nonreactive**
Reactive	120 (A)	0 (B)
Nonreactive	7 (C)	133 (D)

Negative Percent Agreement = (D/(B+D)) × 100% = 100.00%

95% Confidence Interval for Negative Percent Agreement = (97.26%, 100.00%)

Positive Percent Agreement = (A/(A+C)) × 100% = 94.49%

95% Confidence Interval for Positive Percent Agreement = (88.97%, 97.76%)

Individuals with signs and symptoms of hepatitis 265/277 were positive, 95.30% agreement (95% confidence interval 92.55% and 97.74%) and 12 were reactive by the predicate devices but negative by the ARCHITECT HAVAB-G assay. 230/238 were negative, 96.64% agreement (95% confidence interval of 93.48% and 98.54) and 8 were nonreactive by the comparator algorithm but reactive by the ARCHITECT HAVAB-G assay.

ARCHITECT HAVAB-G Interpretation	Final HAV IgG Status	
	Reactive	Nonreactive
Reactive	265 (A)	8 (B)
Nonreactive	12 (C)	230 (D)

Negative Percent Agreement = (D/(B+D)) × 100% = 96.64%

95% Confidence Interval for Negative Percent Agreement = (93.48%, 98.54%)

Positive Percent Agreement = (A/(A+C)) × 100% = 95.67%

95% Confidence Interval for Positive Percent Agreement = (92.55%, 97.74%)

Hepatitis A vaccine recipients (serum collected after vaccination) 48/48 were positive, 100% agreement and 2/2 were negative, 100% agreement => 50 total. The number of samples for each vaccine brand:

43 GlaxoSmithKline Havrix 41/41 were positive, 100% agreement (95% confidence interval 91.40% and 100.0%) and 2/2 were negative.
1 GlaxoSmithKline Twinrix 1/1 was positive, 100% agreement (95% confidence interval 2.5% and 100.0%)
6 Merck and Co, Inc VAQTA 6/6 were positive, 100% agreement (95% confidence interval 54.07% and 100.0%)

Hepatitis A GlaxoSmithKline Havrix vaccine recipients (pre and post specimens) 20/20 were negative, 100% agreement pre-vaccination and 20/20 were positive, and 100% agreement post-vaccination.

Surplus specimens from pediatric population, Originally Abbott tested 110 pediatric specimens: 96/98 were negative with a 97.96% agreement (95% confidence interval 92.82% and 99.75% and 10/12 were positive with an 83.3% agreement (95% confidence interval 51.59% and 97.91%).

Age Group (Years)	Gender	ARCHITECT HAVAB-G Result		Total
		Reactive n (%)	Nonreactive n (%)	
> 2-12	F	3 (11.11)	24 (88.89)	27
	M	4 (13.79)	25 (86.21)	29
>12-21	F	3 (11.11)	24 (88.89)	27
	M	2 (7.41)	25 (92.59)	27

Age Group (Years)	Gender	ARCHITECT HAVAB-G Result		Total
		Reactive n (%)	Nonreactive n (%)	
Overall	F	6 (11.11)	48 (88.89)	54
	M	6 (10.71)	50 (89.29)	56
Total		12 (10.91)	98 (89.09)	110

An additional 202 pediatric specimens were obtained from 4 sites: 72/72 were positive, 100.0% agreement (95% confidence interval 95.01% and 100.0%) and 127/130 were negative, 97.69% agreement (95% confidence interval 93.4% and 99.52%).

Age Group (Years)	Gender	ARCHITECT HAVAB-G Result		Total
		Reactive n (%)	Nonreactive n (%)	
> 2-12	F	16 (39.02)	25 (60.98)	41
	M	13 (25.00)	39 (75.00)	52
>12-21	F	33 (41.25)	47 (58.75)	80
	M	13 (44.83)	16 (55.17)	29
Overall	F	49 (40.50)	72 (59.50)	121
	M	26 (32.10)	55 (67.90)	81
Total		75 (37.13)	127 (62.87)	202

Prospectively collected pediatric samples were from 7 individuals with increased risk of HAV infection and 16 individuals with signs and symptoms of hepatitis. 2/3 were positive, 66.7% agreement (95% confidence interval of 9.43% to 99.16%) and 20/20 were negative, 100% agreement (95% confidence interval of 83.16% to 100.00%).

Prevalence Studies: The ARCHITECT HAVAB-G assay was used to evaluate the prevalence of HAV IgG antibodies in an apparently healthy population and in individuals at increased risk for hepatitis A. The prospective study population consisted of 520 specimens from low prevalence (Milwaukee, WI; Port Jefferson, NY) and high prevalence (Galveston, TX) areas. The prospective study population was 300 (57.69%) females and 220 (42.31%) males including 246 (47.50%) Caucasians, 149 (28.65%) African Americans, 91 (17.50%) Hispanics, 26 (5.00%) Asians, 3 (0.58%) American Indian/Alaska Natives, 1 (0.19%) Native Hawaiian or other Pacific Islander, and 3 (0.58%) Others. The prevalence rate for reactive anti-HAV IgG assay in specimens collected in a low prevalence region was 25.00%, in a

high region was 32.69%, and for individuals with increased risk was 46.15%. The results of the prevalence study are summarized according to age groups and gender.

Expected results for ARCHITECT HAVAB-G assay in subjects from low prevalence areas

Age Group (Years)	Gender	ARCHITECT HAVAB-G		Total
		Reactive n (%)	Nonreactive n (%)	
10-19	F	0 (0.00)	2 (100.00)	2
	M	2 (40.00)	3 (60.00)	5
20-29	F	0 (0.00)	9 (100.00)	9
	M	5 (25.00)	15 (75.00)	20
30-39	F	4 (25.00)	12 (75.00)	16
	M	1 (5.26)	18 (94.74)	19
40-49	F	2 (15.38)	11 (84.62)	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	7 (87.50)	1 (12.50)	8
Overall	F	9 (14.52)	53 (85.48)	62
	M	43 (29.45)	103 (70.55)	146
Total		52 (25.00)	156 (75.00)	208

Expected results for ARCHITECT HAVAB-G assay in subjects from high prevalence areas

Age Group (Years)	Gender	ARCHITECT HAVAB-G		Total
		Reactive n (%)	Nonreactive n (%)	
10-19	F	1 (14.29)	6 (85.71)	7
	M	0 (0.00)	1 (100.00)	1
20-29	F	7 (14.00)	43 (86.00)	50
	M	4 (28.57)	10 (71.43)	14
30-39	F	16 (30.77)	36 (69.23)	52
	M	11 (57.89)	8 (42.11)	19

40-49	F	23 (31.08)	51 (68.92)	74
	M	5 (29.41)	12 (70.59)	17
50-59	F	13 (36.11)	23 (63.89)	36
	M	5 (26.32)	14 (73.68)	19
60-69	F	9 (64.29)	5 (35.71)	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	74 (31.09)	164 (68.91)	238
	M	28 (37.84)	46 (62.16)	74
Total		102 (32.69)	210 (67.31)	312

Expected results for ARCHITECT HAVAB-G assay in subjects from individuals with increased risk of HAV infection

Age Group (Years)	**Gender**	**ARCHITECT HAVAB-G**		**Total**
		Reactive n (%)	**Nonreactive n (%)**	
10-19	F	1 (100.00)	0 (0.00)	1
	M	0 (0.00)	3 (100.00)	3
20-29	F	6 (18.18)	27 (81.82)	33
	M	3 (16.67)	15 (83.33)	18
30-39	F	4 (26.67)	11 (73.33)	15
	M	6 (30.00)	14 (70.00)	20
40-49	F	21 (61.76)	13 (38.24)	34
	M	23 (48.94)	24 (51.06)	47
50-59	F	15 (51.72)	14 (48.28)	29
	M	18 (62.07)	11 (37.93)	29
60-69	F	12 (80.00)	3 (20.00)	15
	M	9 (69.23)	4 (30.77)	13
70-79	F	1 (100.00)	0 (0.00)	1
	M	0 (0.00)	0 (0.00)	0
80-89	F	1 (50.00)	1 (50.00)	2
	M	0 (0.00)	0 (0.00)	0
Overall	F	61 (46.92)	69 (53.08)	130
	M	59 (45.38)	71 (54.62)	130
Total		120 (46.15)	140 (53.85)	260

Seroconversion Sensitivity: Ten seroconversion panel sets were obtained: 3 from patients with naturally occurring HAV infection and 7 from patients immunized with HAV vaccine. The ARCHITECT HAVAB-G detected reactive samples comparable to AxSYM HAVAB 2.0 for the 3 naturally occurring HAV infection panels. The AxSYM HAVAB 2.0 detected reactive samples earlier (as early as day 14) than the ARCHITECT HAVAB-G (day 60) for the 7 HAV vaccine panels.

Method Comparison on three instruments: The percent agreement and system differences in S/CO values between the ARCHITECT systems were evaluated by testing IgG anti-HAV negative and IgG anti-HAV positive specimens using 1 lot each of ARCHITECT HAVAB-G reagents, calibrator, and controls at each of 3 clinical testing sites. An aliquot of each specimen was tested on one ARCHITECT *i* 1000_{SR} instrument at each clinical site (3 instruments total). Site 1 also tested the same aliquot on one ARCHITECT *i* 2000/*i* 2000_{SR} instrument. The panel of specimens consisted of 30-40% high negatives, 30-40% low positives, and 30-40% moderate positive:

Specimen Category	**S/CO Range**
Low and Moderate Negative	< 0.50
High Negative	≥ 0.50 – 0.99
Low Positive	≥ 1.00 – 1.99
Moderate Positive	≥ 2.00 – 4.00
High Positive	≥ 4.00

A total of 208 native and prepared specimens were tested at each site: 106 HAV nonreactive samples (101 native samples and 5 created by negative serum sample pools) and 102 HAV reactive samples (51 native samples and 51 HAV-reactive samples diluted with negative serum specimens or negative serum sample pools). The correlation coefficient and Deming regression along with the corresponding 95% confidence interval were calculated for the ARCHITECT *i* 1000_{SR} and ARCHITECT *i* 2000/*i* 2000_{SR} :

Clinical Testing Site 1			**Clinical Testing Site 2**			**Clinical Testing Site 3**		
ARCHITECT *i* 1000_{SR} HAVAB-G Interpretation	**ARCHITECT *i* 2000/*i* 2000_{SR} HAVAB-G Interpretation**		**ARCHITECT *i* 1000_{SR} HAVAB-G Interpretation**	**ARCHITECT *i* 2000/*i* 2000_{SR} HAVAB-G Interpretation**		**ARCHITECT *i* 1000_{SR} HAVAB-G Interpretation**	**ARCHITECT *i* 2000/*i* 2000_{SR} HAVAB-G Interpretation**	
	Reactive	**Nonreactive**		**Reactive**	**Nonreactive**		**Reactive**	**Nonreactive**
Reactive	102	1	**Reactive**	102	1	**Reactive**	102	4
Nonreactive	0	105	**Nonreactive**	0	105	**Nonreactive**	0	102
NPA = 99.06% (105/106) CI (94.86%, 99.98%) PPA = 100.00% (102/102) CI (96.45%, 100.00%)			NPA = 99.06% (105/106) CI (94.86%, 99.98%) PPA = 100.00% (102/102) CI (96.45%, 100.00%)			NPA = 96.23% (102/106) CI (90.62%, 98.96%) PPA = 100.00% (102/102) CI (96.45%, 100.00%)		
NPA = negative percent agreement, PPA = positive percent agreement, CI = 95% Confidence Interval								

Specimen Category[a] (S/CO Range)	n	*i* 1000$_{SR}$ (Mean S/CO)		*i* 2000/ *i* 2000$_{SR}$ (S/CO)		Correlation Coefficient (r)		Intercept		Slope	
		Min	Max	Min	Max	r	95% CI	Estimate	95% CI[b]	Estimate	95% CI[b]
All	208	0.20	13.03	0.16	13.26	0.998	(0.998, 0.999)	0.01	(-0.02, 0.04)	1.01	(0.99, 1.04)
High Negative, Low Positive and Moderate Positive (≥ 0.50 to 4.00)	103	0.53	4.10	0.50	3.94	0.991	(0.987, 0.994)	0.07	(0.00, 0.09)	0.97	(0.95, 1.01)
Negative (<1.00)	106	0.20	1.09	0.16	0.99	0.965	(0.949, 0.976)	0.02	(-0.04, 0.05)	1.10	(1.02, 1.28)
Positive (≥ 1.00)	102	1.04	13.03	1.08	13.26	0.997	(0.996, 0.998)	-0.07	(-0.15, -0.02)	1.02	(1.00, 1.05)

[a] Specimen category based on instrument *i* 2000/*i* 2000$_{SR}$ S/CO results.

[b] 95% Confidence Interval (CI) based on 2.5th and 97.5th percentiles of 1,000 point estimates using bootstrap method.

4. Clinical cut-off**:**

   Refer to assay cutoff section above for additional details.

5. Expected values/Reference range:

   The Abbott ARCHITECT HAVAB-G assay was used to evaluate the prevalence of HAV IgG antibodies in an apparently healthy population. Specimens were prospectively collected in a low prevalence region (Milwaukee, WI; Port Jefferson, NY) and a high prevalence region (Galveston, TX) in the United States. Expected results from low and high prevalence based on the test device are presented under the prevalence study section. Prevalence rate for reactive anti-HAV IgG assay in specimens collected in a low prevalence region was 25.00%, in a high region was 32.69%, and for individuals with increased risk was 46.15%.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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