

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k063329

B. Purpose for Submission:

New device

C. Measurand:

IgM antibody to hepatitis A virus (Anti-HAV IgM)

D. Type of Test:

Two-step immunoassay, qualitative detection of IgM anti-HAV in human serum and plasma using Chemiluminescent Microparticle Immunoassay (CMIA) technology

E. Applicant:

Abbott Laboratories, Diagnostic Division

F. Proprietary and Established Names:

ARCHITECT® HAVAB®-M

ARCHITECT® HAVAB®-M Calibrator

ARCHITECT® HAVAB®-M Controls

Common Name: Immunoglobulin class M antibody to Hepatitis A Virus (IgM anti-HAV)

IgM anti-HAV Calibrator

IgM anti-HAV Controls

G. Regulatory Information:

1. Regulation section:

866.3310 Hepatitis A virus (HAV) serological assays

2. Classification:

Class II

3. Product code:

LOL, Hepatitis A (antibody and IgM antibody)

4. Panel:

Microbiology (83)

H. Intended Use:

1. Intended use(s):

Reagent Kit:

The ARCHITECT HAVAB-M assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV) in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, and sodium heparin) and neonatal serum. A test for IgM anti-HAV is indicated for testing of specimens from individuals who have signs and symptoms consistent with acute hepatitis. Test results are used in conjunction with other laboratory results and clinical information as an aid in the diagnosis of acute or recent hepatitis A viral infection.

ARCHITECT HAVAB-M Calibrator:

The ARCHITECT HAVAB-M Calibrator is used to calibrate the ARCHITECT *i* System when the system is used for the qualitative detection of IgM antibody to

hepatitis A virus (IgM anti-HAV) using the ARCHITECT HAVAB-M Reagent Kit. The performance of the ARCHITECT HAVAB-M Calibrator has not been established with any other IgM anti-HAV assays.

ARCHITECT HAVAB-M Controls:

The ARCHITECT HAVAB-M Controls are used for monitoring the performance of the ARCHITECT *i* System when used for the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV) using the ARCHITECT HAVAB-M Reagent Kit. The performance of the ARCHITECT HAVAB-M Controls has not been established with any other IgM anti-HAV assays.

2. Indication(s) for use:

The ARCHITECT HAVAB-M assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV) in human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, and sodium heparin) and neonatal serum. A test for IgM anti-HAV is indicated for testing of specimens from individuals who have signs and symptoms consistent with acute hepatitis. Test results are used in conjunction with other laboratory results and clinical information as an aid in the diagnosis of acute or recent hepatitis A viral infection.

Warning: Not intended for use in screening blood, plasma, or tissue donors.

The effectiveness of ARCHITECT HAVAB-M for use in screening blood, plasma, or tissue donors has not been established.

Assay performance characteristics have not been established when the ARCHITECT HAVAB-M assay is used in conjunction with other manufacturers' assays for specific hepatitis markers. Users are responsible for establishing their own performance characteristics.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

The ARCHITECT *i* System (K962919/S1)

I. Device Description:

The ARCHITECT HAVAB-M assay is a two-step immunoassay for the qualitative detection of IgM anti-HAV in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. In the first step, prediluted sample, assay diluent, and hepatitis A virus (human) coated paramagnetic microparticles are combined. IgM anti-HAV present in the sample binds to the hepatitis A virus (human) coated microparticles. After washing, the IgM anti-HAV binds to the anti-human IgM acridinium-labeled conjugate that is added in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of IgM anti-HAV in the sample and the RLUs detected by the ARCHITECT *i* System optics. The presence or absence of IgM anti-HAV in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active ARCHITECT HAVAB-M calibration. The ARCHITECT HAVAB-M assay is calibrated with ARCHITECT HAVAB-M Standard Calibrator. ARCHITECT HAVAB-M Controls are assayed for the verification of the accuracy and precision of

the Abbott ARCHITECT System.

ARCHITECT HAVAB-M Reagent Kit consists of:

- Hepatitis A virus coated microparticles in TRIS buffer, with preservatives and antimicrobial agents;
- Anti-human IgM (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with protein additive, preservatives and other antimicrobial agents; and
- Assay Diluent: TRIS buffer with protein additive, preservatives and other antimicrobial agents.

The ARCHITECT HAVAB-M Controls are:

- Positive control - recalcified anti-HAV positive human plasma in recalcified anti-HAV negative human plasma. Contains Acid Blue No. 9 dye and preservatives. Non-reactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV.
- Negative control - recalcified anti-HAV negative human plasma with preservatives. Non-reactive for anti-HAV, HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV.

The ARCHITECT HAVAB-M Calibrator is recalcified anti-HAV positive human plasma in recalcified anti-HAV negative human plasma. Calibrator 1 is green and contains Acid Yellow No. 23 and Acid Blue No. 9 dyes, and preservatives. The calibrator is reactive for anti-HAV and nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Abbott AxSYM HAVAB-M 2.0 assay
2. Predicate 510(k) number(s):
P790012/S011
3. Comparison with predicate:

| Similarities | | |
|----------------------------------|--|---|
| Item | Device | Predicate |
| Intended Use | For the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV IgM) | Same |
| Methodology | <i>In vitro</i> immunological method using monoclonal antibodies | Same |
| Use of automated instrumentation | Automated analyzer: ARCHITECT <i>i</i> System | Automated analyzer: AxSYM System |
| Intended use population | Individuals with signs and symptoms consistent with acute hepatitis | Persons with signs or symptoms of hepatitis and persons at risk for hepatitis A infection |
| Sample type | Human adult and pediatric serum and plasma (dipotassium EDTA, lithium heparin, sodium heparin) | Human serum and plasma (potassium EDTA, sodium heparin, sodium citrate, lithium heparin) |

| Differences | | |
|--------------------------|---|---|
| Item | Device | Predicate |
| Basic principle | Binding of IgM anti-HAV present in the sample to the hepatitis A virus (human) coated microparticles; followed by IgM anti-HAV binding to the anti-human IgM acridinium-labeled conjugate | Direct binding of the IgM Anti-HAV in the sample to Anti-human IgM Coated on the microparticles; followed by the reaction between Hepatitis A Virus (human) in the HAV solution and the IgM anti-HAV bound to the microparticles. |
| Sample type / population | Human adult and pediatric serum and plasma, neonatal serum | Human serum and plasma |
| Assay type | Two-step Chemiluminescent Microparticle Immunoassay (CMIA) | Three-step Microparticle Enzyme Immunoassay (MEIA) |
| Microparticle coating | Paramagnetic Microparticles Coated With Hepatitis A Virus | Latex Microparticles Coated With Goat Antibodies To Human IgM |
| Detection | anti-human IgM acridinium-labeled conjugate | Anti-HAV (mouse, monoclonal):alkaline phosphatase conjugate |

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

Class II Special Control Guidance Document: Hepatitis A Virus Serological Assays, issued February 9, 2006

L. Test Principle:

The ARCHITECT HAVAB-M assay is a two-step immunoassay for the qualitative detection of IgM anti-HAV in human serum and plasma using CMIA technology.

First step: Sample (pre-diluted), assay diluent, and paramagnetic microparticles coated with HAV (human) are combined. IgM anti-HAV present in the sample binds to the HAV (human) coated microparticles.

Second step: After washing, the IgM anti-HAV binds to the anti-human IgM acridinium-labeled conjugate. Following another wash cycle, pre-trigger and trigger solutions are added, and the resulting chemiluminescent reaction is measured as relative light units (RLUs) detected by the ARCHITECT *i* System optics.

The presence or absence of IgM anti-HAV in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active ARCHITECT HAVAB-M calibration.

Calculations:

- The ARCHITECT *i* System calculates the cutoff RLU from the Calibrator mean RLU. The cutoff RLU is stored for each reagent lot calibration.
Cutoff RLU = 0.375 x (Calibrator mean RLU)
- The ARCHITECT *i* System calculates the S/CO result for each sample as follows:
S/CO = Sample RLU/Cutoff RLU

Interpretation of Results:

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

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

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

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

In addition to the required preclinical studies, the testing scheme was incorporated into the Precision, Calibration Curve Storage, and Instrument Percent Agreement studies. The results from these studies confirm that the ARCHITECT HAVAB-M assay can be used on the ARCHITECT *i* 2000 and *i* 2000SR.

a. Precision/Reproducibility:

Within-laboratory precision:

A 20-day precision study was performed at Abbott Laboratories based on guidance from the CLSI document EP5-A2. ARCHITECT *i* 2000 and *i* 2000_{SR} were used. Testing was performed using 2 instruments (one of each), 3 assay reagent lots, 3 calibrator lots, and one control lot. The ARCHITECT

HAVAB-M Negative Control (NC), Positive Control (PC), high negative panel (targeted to 0.80 S/CO), and low positive panel (targeted to 1.20 S/CO) were tested in replicates of three, two times per day (separated by a minimum of two hours), for total of 20 testing days.

The data presented is a summary of the product performance:

| Instrument | Panel Members/ Controls | Total No. Reps | Mean S/CO | Within-Run | | Between-Run | | Within-Day ^a | | Between-Day | | Between-Lot | | Total ^b | | | |
|---------------------|-------------------------|----------------|-----------|------------|------|-------------|-----|-------------------------|------|-------------|-----|-------------|-----|--------------------|------------------------------|------|-------------------------------|
| | | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | SD Upper 95% CL ^c | %CV | %CV Upper 95% CL ^c |
| i2000 | PC | 356 | 1.88 | 0.100 | 5.3 | 0.033 | 1.7 | 0.106 | 5.6 | 0.052 | 2.8 | 0.026 | 1.4 | 0.118 | 0.127 | 6.3 | 6.7 |
| | Low Positive Panel | 355 | 1.16 | 0.063 | 5.4 | 0.028 | 2.4 | 0.069 | 5.9 | 0.037 | 3.2 | 0.027 | 2.3 | 0.078 | 0.085 | 6.7 | 7.3 |
| | High Negative Panel | 350 | 0.79 | 0.047 | 5.9 | 0.014 | 1.8 | 0.049 | 6.2 | 0.020 | 2.5 | 0.027 | 3.4 | 0.053 | 0.057 | 6.7 | 7.2 |
| | NC | 354 | 0.21 | 0.020 | 9.3 | 0.007 | 3.4 | 0.021 | 9.9 | 0.016 | 7.7 | 0.020 | 9.3 | 0.027 | 0.029 | 12.5 | 13.7 |
| i2000 _{SR} | PC | 350 | 1.85 | 0.125 | 6.8 | 0.000 | 0.0 | 0.125 | 6.8 | 0.031 | 1.7 | 0.047 | 2.5 | 0.129 | 0.138 | 7.0 | 7.5 |
| | Low Positive Panel | 348 | 1.13 | 0.074 | 6.5 | 0.000 | 0.0 | 0.074 | 6.5 | 0.029 | 2.5 | 0.022 | 2.0 | 0.079 | 0.085 | 7.0 | 7.5 |
| | High Negative Panel | 346 | 0.76 | 0.056 | 7.3 | 0.000 | 0.0 | 0.056 | 7.3 | 0.018 | 2.4 | 0.009 | 1.2 | 0.059 | 0.062 | 7.7 | 8.2 |
| | NC | 352 | 0.17 | 0.033 | 18.9 | 0.006 | 3.7 | 0.033 | 19.3 | 0.013 | 7.3 | 0.015 | 8.4 | 0.036 | 0.038 | 20.6 | 22.0 |

^a Within-Day variability contains within-run and between-run variance components.

^b Total variability contains within-run, between-run, and between-day variance components.

^c One-sided 95% confidence limit with degrees of freedom calculated by Satterthwaite's method.

System Reproducibility:

A five-day system reproducibility of the ARCHITECT HAVAB-M assay was performed based on guidance from CLSI document EP15-A2. Testing was conducted at three clinical sites using three master lots each of ARCHITECT HAVAB-M Reagents, Calibrator, and Controls. Two levels of controls and panels were assayed in replicates of four at two separate times of day for five days. The data are summarized in the following table:

| Sample | N | Grand Mean S/CO | Within-Run | | Between-Run | | Between-Day | | Between-Lot | | Between-Site | | Site-Lot Interaction | | Overall ^a | |
|---------------------|-----|-----------------|------------|------|-------------|-----|-------------|-----|-------------|------|--------------|------|----------------------|-----|----------------------|------|
| | | | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Positive Control | 360 | 1.90 | 0.116 | 6.1 | 0.009 | 0.5 | 0.035 | 1.8 | 0.000 | 0.0 | 0.081 | 4.3 | 0.093 | 4.9 | 0.173 | 9.1 |
| Low Positive Panel | 360 | 1.19 | 0.077 | 6.5 | 0.023 | 1.9 | 0.000 | 0.0 | 0.000 | 0.0 | 0.058 | 4.9 | 0.077 | 6.5 | 0.126 | 10.5 |
| High Negative Panel | 360 | 0.81 | 0.053 | 6.5 | 0.023 | 2.8 | 0.004 | 0.5 | 0.000 | 0.0 | 0.053 | 6.5 | 0.035 | 4.4 | 0.086 | 10.6 |
| Negative Control | 360 | 0.22 | 0.046 | 20.7 | 0.021 | 9.4 | 0.000 | 0.0 | 0.026 | 11.6 | 0.041 | 18.5 | 0.018 | 8.0 | 0.072 | 32.5 |

^a Overall variability contains within-run, between-run, between-day, between-lot, between-site and site-lot interaction variance components.

b. Linearity/assay reportable range:

The data provided demonstrate that no high dose hook effect is found for the ARCHITECT HAVAB-M assay.

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

The ranges for the controls are not lot specific and represent the total range of

values which may be generated throughout the life of the product. It is recommended that each laboratory establish its own means and acceptable ranges which should fall within the package insert ranges. Sources of variation that can be expected include: calibration, control lot, instrument, calibrator lot, reagent lot.

The controls must fall within the following ranges:

| Control | Color | Titer | Range (S/CO) |
|------------------|--------------|--------------|---------------------|
| Negative Control | Natural | N/A | ≤ 0.80 |
| Positive Control | Blue | 1:4 | 1.09 - 2.87 |

Control values have not been established for assays other than the ARCHITECT HAVAB-M assay. If the user wishes to use this control material with other assays, it is their responsibility to establish the appropriate ranges. The ARCHITECT HAVAB-M Controls are in a serum matrix made from recalcified plasma. The user should provide alternate control material for plasma when necessary.

Stability: The data demonstrate that human serum (including serum collected in serum separator tubes) or plasma collected in dipotassium EDTA, lithium heparin plasma separator, or sodium heparin tubes may be used with the ARCHITECT HAVAB-M assay when:

- stored at 2 to 8°C for up to 7 days
- stored at room temperature (21-22°C) for up to 3 days
- stored at approximately 30°C for up to 3 days, and
- subjected to up to 3 freeze/thaw cycles.

Sample on board stability: The data support sample storage of up to 3 hours on board the ARCHITECT i System when tested with the ARCHITECT HAVAB-M assay.

d. Detection limit:

N/A

e. Analytical specificity:

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

The data are summarized in the following table.

| Category | n | Comparator IgM Anti-HAV Assay | | | | | | | | |
|-------------------------------------|----------|--------------------------------------|-----------------------|----------------------|--------------------------|-----------------------|----------------------|--------------------------|-----------------------|----------------------|
| | | Nonreactive | | | Grayzone | | | Reactive | | |
| | | ARCHITECT HAVAB-M | | | ARCHITECT HAVAB-M | | | ARCHITECT HAVAB-M | | |
| | | NR^a | GZ^a | R^a | NR^a | GZ^a | R^a | NR^a | GZ^a | R^a |
| Antinuclear Antibody (ANA) positive | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Chronic Lymphocytic Leukemia | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cytomegalovirus (anti-CMV positive) | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Elevated IgG | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| | | | | | | | | | | |
|--|-----|-----|----------------|----------------|---|---|---|----------------|---|---|
| Epstein-Barr Virus (anti-EBV positive) | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hepatitis B Virus (anti-HBV positive) | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hepatitis C Virus (anti-HCV positive) | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Herpes Simplex Virus (HSV) IgG | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Heterophilic Antibodies (Human Anti-Mouse Antibody) positive | 7 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Human Immunodeficiency Virus (anti-HIV-1 positive) | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Human Immunodeficiency Virus (anti-HIV-2 positive) | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IgM monoclonal gammopathies | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Influenza vaccine recipients | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Multiparous female | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Multiple myeloma | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Mumps virus | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non-Hodgkin's Lymphoma ^b | 6 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non-viral liver disease: alcoholic liver disease | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Non-viral liver disease: hepatocellular carcinoma | 8 | 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Rheumatoid factor (RF) positive | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Rubella (anti-Rubella) positive | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Rubeola virus | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Syphilis | 10 | 9 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| Systemic lupus erythematosus (SLE) | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Toxoplasmosis (anti-Toxoplasma positive) | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Varicella Zoster Virus (VZV) positive | 4 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Yeast infection | 7 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| TOTAL | 203 | 198 | 2 ^c | 2 ^c | 0 | 0 | 0 | 1 ^c | 0 | 0 |

^a NR = nonreactive, GZ = grayzone, R = reactive

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

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

Interference:

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

- Bilirubin ≤ 20 mg/dL
- Hemoglobin ≤ 500 mg/dL

- Total Protein ≤ 12 g/dL
- Triglycerides ≤ 3000 mg/dL

f. Assay cut-off:

The presence or absence of IgM antibody to Hepatitis A virus in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff RLU determined from an active ARCHITECT HAVAB-M calibration. The ARCHITECT HAVAB-M results are expressed as the ratio of the sample RLU to the cutoff RLU (S/CO):

$$S/CO = \text{Sample RLU} / \text{Cutoff RLU}$$

where the Cutoff RLU = Calibrator 1 mean RLU x 0.375

where the cutoff multiplier value has been established using a population of specimens, and ROC analysis demonstrated that the optimal sensitivity and specificity is achieved when the cutoff is set using a multiplier of 0.375. 168/173 of true positive specimens were detected, for a sensitivity of 97.11% and specificity of 100.00% (2119/2119) at the lower limit (-20%) of GZ (S/CO = 0.80). The seroconversion sensitivity was verified with this cutoff and found to be acceptable when compared to predicate FDA approved assay, and clinical investigation data support the cutoff calculation.

2. Comparison studies:

a. Method comparison with predicate device:

Of the 658 specimens from the intended use population tested in a prospective multi-center study, 554 specimens (Population 1) were obtained from individuals living in the United States from the following populations: 253 specimens were from individuals at increased risk of HAV infection; 200 specimens were from individuals with signs and symptoms of hepatitis; 1 specimen was from an individual diagnosed with acute HAV infection; and 100 specimens were from pediatric individuals. Additionally, 104 specimens (Population 2) were obtained from individuals living outside the United States diagnosed with acute HAV infection (including one pre-selected IgM anti-HAV positive specimen).

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

| Testing Site | Comparator IgM Anti-HAV Assay | | | | | | | | | | | | | | | | Total | |
|--------------|----------------------------------|---|-----------------|---|-----------------|---|----------------------------------|---|-----------------|---|-----------------|---|----------------------------------|---|-----------------|---|-------|---|
| | Reactive | | | | | | Grayzone | | | | | | Nonreactive | | | | | |
| | ARCHITECT HAVAB-M Interpretation | | | | | | ARCHITECT HAVAB-M Interpretation | | | | | | ARCHITECT HAVAB-M Interpretation | | | | | |
| | R ^a | | GZ ^a | | NR ^a | | R ^a | | GZ ^a | | NR ^a | | R ^a | | GZ ^a | | | |
| | n | % | n | % | n | % | n | % | n | % | n | % | n | % | n | % | n | % |

| | | | | | | | | | | | | | | | | | | | | |
|--------------|---|------|---|------|---|------|---|------|---|------|---|------|---|------|---|------|-----|-------|-----|--------|
| 1 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 260 | 46.93 | 260 | 46.93 |
| 2 | 1 | 0.18 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 155 | 27.98 | 156 | 28.16 |
| 3 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 138 | 24.91 | 138 | 24.91 |
| Total | 1 | 0.18 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 0 | 0.00 | 553 | 99.82 | 554 | 100.00 |

^a NR = nonreactive, GZ = grayzone, R = reactive

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

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

^a NR = nonreactive, GZ = grayzone, R = reactive

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

| Testing Site | Positive Percent Agreement | 95% Exact Confidence Interval | Negative Percent Agreement | 95% Exact Confidence Interval |
|--------------|----------------------------|-------------------------------|----------------------------|-------------------------------|
|--------------|----------------------------|-------------------------------|----------------------------|-------------------------------|

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

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

b. Matrix comparison:

The following tube types are acceptable for use with the ARCHITECT HAVAB-M assay:

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

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

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

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Performance in an Acute HAV Population:

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

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

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

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

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

Performance in a Pediatric Population:

One hundred residual specimens from a pediatric population at low risk for hepatitis were obtained in Fall River, MA.

The negative percent agreement of the ARCHITECT HAVAB-M assay to the comparator assay, and the 95% exact confidence interval is summarized in the table below.

| Agreement of the ARCHITECT HAVAB-M in a Pediatric Population | | |
|---|---|--------------------------------------|
| Population | Negative Percent Agreement % (x/n)^a | 95% Exact Confidence Interval |
| Pediatric | 100.00 (100/100) | 96.38– 100.00 |

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

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

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

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

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

Performance Cord Blood:

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

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

Seroconversion Panels

Three commercially available HAV patient seroconversion panel sets were tested using the ARCHITECT HAVAB-M assay to determine the seroconversion sensitivity of the assay. The ARCHITECT HAVAB-M assay detects the same number of reactive bleeds as the comparator anti-HAV assay. In all seroconversion panels, both the ARCHITECT HAVAB-M assay and the comparator assay detected the first reactive panel bleed. The data are summarized in the following table.

| Panel ID | Comparator IgM anti-HAV Assay | ARCHITECT HAVAB-M Assay | Difference in Days | Difference in Days |
|----------|-------------------------------|-------------------------|--------------------|--------------------|
|----------|-------------------------------|-------------------------|--------------------|--------------------|

| | Days to IgM Anti-HAV First Reactive Result | Days to IgM Anti-HAV Last Reactive Result | Days to IgM Anti-HAV First Reactive Result | Days to IgM Anti-HAV Last Reactive Result | to IgM Anti-HAV First Reactive Result (Comparator - ARCHITECT) | to IgM Anti-HAV Last Reactive Result (Comparator - ARCHITECT) |
|--------|--|---|--|---|--|---|
| RP004 | 7 | 63 | 7 | 63 | 0 | 0 |
| RP013 | 9 | 121 | 9 | 67 | 0 | 54 |
| PHT902 | 16 | 21 | 16 | 21 | 0 | 0 |

NOTE: Only reactive results from both ARCHITECT HAVAB-M and the comparator assay were used. Grayzone results were not used to determine a reactive result.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

HAV Prevalence Population

Of the 1167 specimens tested in the ARCHITECT HAVAB-M clinical study, 862 specimens were from the following populations: 509 specimens were from apparently healthy individuals, 253 specimens were from individuals at increased risk of HAV infection, and 100 specimens were from pediatric individuals.

The 509 specimens from the apparently healthy population from both low prevalence (Port Jefferson, NY and Milwaukee, WI) and high prevalence (Galveston, TX and Phoenix, AZ) areas were obtained from the following collection locations: 145 (28.49%) from Milwaukee, WI; 140 (27.50%) from Galveston, TX; 114 (22.40%) from Phoenix, AZ; and 110 (21.61%) from Port Jefferson, NY. The apparently healthy population (n=509) consisted of the following race/ethnic groups: 269 (52.85%) Caucasian, 175 (34.38%) African-American, 40 (7.86%) Hispanic, 11 (2.16%) Asian, 5 (0.98%) American Indian/Alaska Native, and 9 (1.77%) other. Of the 509 specimens, 358 (70.33%) were female and 151 (29.67%) were male. The mean age was 44 years (age range: 18 to 81 years).

The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results among apparently healthy individuals (n=255) living in **low prevalence** areas for hepatitis A is summarized by age and gender in the table below.

| Age Group (Years) | Gender | ARCHITECT HAVAB-M Result | | | Total |
|-------------------|--------|--------------------------|----------------|-------------------|-------|
| | | Reactive n (%) | Grayzone n (%) | Nonreactive n (%) | |

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

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

| Age Group (Years) | Gender | ARCHITECT HAVAB-M Result | | | Total |
|-------------------|--------|--------------------------|----------------|-------------------|-------|
| | | Reactive n (%) | Grayzone n (%) | Nonreactive n (%) | |
| 10 to 19 | F | 0 (0.00) | 0 (0.00) | 5 (100.00) | 5 |
| | M | 0 (0.00) | 0 (0.00) | 4 (100.00) | 4 |
| 20 to 29 | F | 0 (0.00) | 0 (0.00) | 24 (100.00) | 24 |
| | M | 0 (0.00) | 0 (0.00) | 9 (100.00) | 9 |
| 30 to 39 | F | 0 (0.00) | 0 (0.00) | 36 (100.00) | 36 |
| | M | 0 (0.00) | 0 (0.00) | 7 (100.00) | 7 |
| 40 to 49 | F | 0 (0.00) | 0 (0.00) | 57 (100.00) | 57 |
| | M | 0 (0.00) | 0 (0.00) | 19 (100.00) | 19 |
| 50 to 59 | F | 0 (0.00) | 1 (2.78) | 35 (97.22) | 36 |
| | M | 0 (0.00) | 0 (0.00) | 20 (100.00) | 20 |
| 60 to 69 | F | 0 (0.00) | 0 (0.00) | 20 (100.00) | 20 |
| | M | 0 (0.00) | 0 (0.00) | 12 (100.00) | 12 |

| Age Group (Years) | Gender | ARCHITECT HAVAB-M Result | | | Total |
|----------------------|--------|--------------------------|-------------------|----------------------|-------|
| | | Reactive n (%) | Grayzone n (%) | Nonreactive n (%) | |
| 70 to 79 | F | 0 (0.00) | 0 (0.00) | 3 (100.00) | 3 |
| | M | 0 (0.00) | 0 (0.00) | 2 (100.00) | 2 |
| Overall | F | 0 (0.00) | 1 (0.55) | 180 (99.45) | 181 |
| | M | 0 (0.00) | 0 (0.00) | 73 (100.00) | 73 |
| Total | | 0 (0.00) | 1 (0.39) | 253 (99.61) | 254 |

Population at Increased Risk for HAV Infection

Expected results of asymptomatic individuals from the multi-center study described in “Performance Characteristics” are provided below. The specimens were from 253 individuals at increased risk of HAV infection due to exposure to contaminated food or water, poor sanitary conditions or hygiene, household or sexual contact with an HAV infected individual, recent travel to an HAV endemic area, lifestyle, behavior, or recipients of clotting factor concentrates.

The increased risk population (n=253) consisted of the following race/ethnic groups: 140 (55.34%) Caucasian, 48 (18.97%) African-American, 47 (18.58%) Hispanic, 9 (3.56%) Asian, 3 (1.19%) American Indian/Alaska Native, and 6 (2.37%) other. The 253 specimens from the increased risk population were obtained from the following collection locations: 64 (25.30%) from Galveston, TX; 57 (22.53%) from Dallas, TX; 46 (18.18%) from St. Petersburg, FL; 29 (11.46%) from Denver, CO; 23 (9.09%) from Miami, FL; 23 (9.09%) from Chicago, IL; 7 (2.77%) from Plymouth, MA; and 4 (1.58%) from Colton, CA. Of the 253 specimens, 155 (61.26%) were male and 98 (38.74%) were female. The mean age was 42 years (age range: 18 to 78 years).

The distribution of ARCHITECT HAVAB-M reactive, grayzone, and nonreactive results among individuals with increased risk for HAV (n=253) is summarized by age and gender in the table below.

| Age Group (Years) | Gender | ARCHITECT HAVAB-M Result | | | Total |
|----------------------|--------|--------------------------|-------------------|----------------------|-------|
| | | Reactive n (%) | Grayzone n (%) | Nonreactive n (%) | |

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

Pediatric Population at Low Risk for Hepatitis

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

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

| Age Group (years) | Gender | ARCHITECT HAVAB-M Result | | | Total |
|-------------------|--------|--------------------------|----------------|-------------------|-------|
| | | Reactive n (%) | Grayzone n (%) | Nonreactive n (%) | |

| | | | | | |
|--------------|---|----------|----------|--------------|-----|
| 2-12 | F | 0 (0.00) | 0 (0.00) | 25 (100.00) | 25 |
| | M | 0 (0.00) | 0 (0.00) | 24 (100.00) | 24 |
| 13-18 | F | 0 (0.00) | 0 (0.00) | 41 (100.00) | 41 |
| | M | 0 (0.00) | 0 (0.00) | 10 (100.00) | 10 |
| Overall | F | 0 (0.00) | 0 (0.00) | 66 (100.00) | 66 |
| | M | 0 (0.00) | 0 (0.00) | 34 (100.00) | 34 |
| Total | | 0 (0.00) | 0 (0.00) | 100 (100.00) | 100 |

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.

