



August 25, 2016

Food and Drug Administration  
10903 New Hampshire Avenue  
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Silver Spring, MD 20993-0002

DiaSorin, Inc.  
Carol A. DePouw  
Regulatory Affairs Specialist  
1951 Northwestern Avenue  
Stillwater, MN 55082-0285

Re: K160650

Trade/Device Name: LIAISON<sup>®</sup> HAV IgM and LIAISON<sup>®</sup> Control HAV IgM  
Regulation Number: 21 CFR 866.3310  
Regulation Name: Hepatitis A virus (HAV) serological assays  
Regulatory Class: II  
Product Code: LOL, JJX  
Dated: July 27, 2016  
Received: July 28, 2016

Dear Ms. DePouw:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

**Steven R. Gitterman -S**

for Uwe Scherf M. Sc., Ph.D.  
Director  
Division of Microbiology Devices  
Office of In Vitro Diagnostics and Radiological  
Health  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)  
K160650

Device Name  
LIAISON® HAV IgM Assay  
LIAISON® Control HAV IgM

### Indications for Use (Describe)

The LIAISON® HAV IgM assay is an in vitro chemiluminescent immunoassay intended for the qualitative detection of IgM antibodies to hepatitis A virus (IgM anti-HAV) in human serum and plasma (sodium citrate, potassium EDTA, lithium and sodium heparin, and citrate dextrose (ACD)) using the LIAISON® Analyzer. Assay results, in conjunction with other serological and clinical information, may be used for testing specimens from individuals who have signs and symptoms consistent with acute hepatitis as an aid in the laboratory diagnosis of acute or recent HAV infection. This assay is not intended for screening blood or solid or soft tissue donors. Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients. The user is responsible for establishing their own assay performance characteristics in these populations.

The LIAISON® Control HAV IgM (negative and positive) are intended for use as assayed quality control samples to monitor the performance of the LIAISON® HAV IgM assay.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

### CONTINUE ON A SEPARATE PAGE IF NEEDED.

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## **5.0 510(k) SUMMARY**

**SUBMITTED BY:**

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**NAME OF DEVICE:**

Trade Name: LIAISON® HAV IgM,  
LIAISON® Control HAV IgM

Common Names/Descriptions: Hepatitis A Test (Antibody and IgM Antibody)  
and Controls

Classification Names: Hepatitis A Virus (HAV) Serological assays  
21 CFR 866.3310 Class II Special Controls;  
Microbiology  
Single (Specified) analyte controls (assayed  
and unassayed); Class I reserved;  
21 CFR 862.1660: Clinical Chemistry

Product Code: LOL, JJX

**PREDICATE DEVICES**

DiaSorin Inc. ETI-HA-IGMK Plus Kit  
(PMA #P890014)

**DEVICE DESCRIPTION:**

**INTENDED USE:**

The LIAISON® HAV IgM assay is an *in vitro* chemiluminescent immunoassay intended for the qualitative detection of IgM antibodies to hepatitis A virus (IgM anti-HAV) in human serum and plasma (sodium citrate, potassium EDTA, lithium and sodium heparin and citrate dextrose (ACD)) using the LIAISON® Analyzer. Assay results, in conjunction with other serological and clinical information, may be used for testing specimens from individuals who have signs and symptoms consistent with acute hepatitis as an aid in the laboratory diagnosis of acute or recent HAV infection.

This assay is not intended for screening blood or solid or soft tissue donors. Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients. The user is responsible for establishing their own assay performance characteristics in these populations.

The LIAISON® Control HAV IgM (negative and positive) are intended for use as assayed quality control samples to monitor the performance of the LIAISON® HAV IgM assay.

**KIT DESCRIPTION:** The method for qualitative determination of HAV IgM is an antibody capture chemiluminescence immunoassay (CLIA). IgG to human IgM (mouse monoclonal) is used for coating magnetic particles (solid phase) and a mouse monoclonal antibody to HAV is linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, IgM antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugate reacts with HAV antigen just added and the immune complex thus formed reacts with IgM already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle.

Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of anti-HAV IgM present in calibrators, samples or controls.

**REASON FOR SUBMISSION:**

The purpose of this 510(k) Submission is to present the proposed modifications to the DiaSorin LIAISON® HAV IgM and the LIAISON® Control HAV IgM (K082050).

Description of modifications to the LIAISON® HAV IgM and the LIAISON® Control HAV IgM:

1. Proprietary changes to the monoclonal antibodies and conjugate.
2. Extension of stability claims for the calibration curve, on-board and open use storage.
3. Addition of sample types and sample stabilities.
4. Change from buffer based controls to serum based controls.

**PERFORMANCE DATA:**

The following studies were conducted to demonstrate that the modifications to the LIAISON® HAV IgM assay confirm the substantial equivalence to the predicate device and raise no new questions of safety and effectiveness. Studies not pertaining to the modifications may be found in the original 510(k) K082050.

**COMPARATIVE STUDIES:**

Five commercially available HAV seroconversion panels were tested using the LIAISON® HAV IgM and the FDA-approved comparator assay to determine sensitivity of the assay. The results are summarized in Table 1.

Table 1

Panel ID	LIAISON® HAV IgM		Comparator Assay		Difference in days from last reactive result
	Post-bleed day of earliest reactive result	Post-bleed day of last reactive result	Post-bleed day of earliest reactive result	Post-bleed day of last reactive result	
0615-0026 seroconversion	14	27	14	27	0
PHT902 seroconversion	16	21	16	21	0
PHT903 seroconversion	38	108	38	108	0
RP004 seroconversion	6	62	6	62	0
RP013 seroconversion	8	189	8	189	0

The sensitivity of the LIAISON® HAV IgM was equivalent to the comparator assay in the five seroconversion panels tested.

#### REPRODUCIBILITY:

A 5 day reproducibility/precision study was conducted at three external laboratories. The CLSI document EP15-A3 was consulted in the preparation of the testing protocol. A coded panel comprised of 6 frozen serum samples was prepared by DiaSorin S.p.A. The coded panel was prepared by either spiking or diluting samples as necessary to contain negative, low positive and mid positive samples.

The LIAISON® Control HAV IgM (negative and positive) were also included in the 5 day study. The LIAISON® HAV IgM Negative Control as well as negative panel sample (HAVM-P00) read below the detectable limit of the curve  $<<0.10$ ; therefore, standard deviation (SD) and %CVs were calculated using the Relative Light Units (RLU's) for each respective sample

#### Results

The 5 day results are summarized in Table 2 (combined sites). The mean Index value, standard deviation, and coefficient of variation (%CV) of the results were computed for each of the tested specimens for intra- run, run to run, between site, and Total across sites.

Table 2: Combined Sites

Sample ID	mean	Intra-Run		Run to Run		Between Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
HAVM Negative*	334	18.70	5.6	7.45	2.2%	8.28	2.5	21.80	6.5%
HAVM Positive	2.22	0.26	11.7%	0.05	2.2%	0.05	2.3%	0.26	11.8%
HAVM-P00	535	20.50	3.8%	16.10	3.0%	0.00	0.0%	26.00	4.9%
HAVM-P01*	1.48	0.12	8.4%	0.01	0.7%	0.03	2.1%	0.13	8.6%
HAVM-P04	0.60	0.07	11.0%	0.01	1.7%	0.01	1.2%	0.07	11.2%
HAVM-P14	1.18	0.08	6.6%	0.02	1.9%	0.02	1.3%	0.08	6.7%
HAVM-P15	2.42	0.21	8.6%	0.03	1.3%	0.03	1.2%	0.21	8.8%
HAVM-P16	5.62	0.48	8.5%	0.00	0.0%	0.31	5.5%	0.57	10.1%

\*RLU used in calculations

**STABILITY STUDIES: REAGENTS**

<u>LIAISON® HAV IgM</u>	
<u>Study</u>	<u>Stability</u>
<u>Calibration Curve</u>	<u>4 weeks</u>
<u>Open Use storage On-board Analyzer</u>	<u>8 weeks</u>
<u>Open Use storage at 2-8°C</u>	<u>8 weeks</u>

  

<u>LIAISON® Control HAV IgM</u>	
<u>Study</u>	<u>Stability</u>
<u>Open Use storage at 2-8°C</u>	<u>4 weeks</u>

**SAMPLE EQUIVALENCY AND STABILITY STUDIES:**

Sample sets of matched serum/multiple plasma were used in the study to evaluate the risk of potential unspecific reaction related to the use of different sample matrix.

Forty (40) matched sets of samples were assayed. The samples were collected as serum, serum in serum separator tubes, and plasma in anticoagulants Sodium Citrate, Potassium EDTA, Lithium and Sodium heparin and Citrate Dextrose (ACD). The serum specimen in the set was assumed as the reference. Samples belonging to each set were tested in triplicate with one LIAISON® HAV IgM reagent lot on one instrument in a single run.

Results of the SST tube and all plasma samples were compared to serum by Passing and Bablok regression and Bland Altman agreement. All slopes were between 0.90-1.10, and the bias was within  $\pm 10\%$ .

Human serum, SST serum, Sodium Citrate Plasma, Potassium EDTA Plasma, Lithium Heparin Plasma, Sodium Heparin Plasma, or ACD Plasma are acceptable sample types for use in the LIAISON® HAV IgM assay.

**SAMPLE STABILITY:**

Studies were performed to evaluate the stability of samples at different sample storage conditions. The results are provided in the table below.

<u>Specimen</u>	
<u>Study</u>	<u>Stability</u>
<u>Room Temperature (15-30°C)</u>	<u>2 days</u>
<u>Refrigerated (2-8°C)</u>	<u>7 days</u>
<u>Freeze/Thaw Cycles</u>	<u>5 cycles</u>

**CUT-OFF VERIFICATION:**

A verification study was performed to ensure that the original cut-off values were appropriate for the modified LIAISON® HAV IgM.

The user may continue to use the following cut-off values for interpretation of patient results.

Index	Results	Interpretation
< 0.90	Negative (No further testing)	No detectable IgM antibodies to HAV were found. A negative result generally indicates that the patient has not been infected. If clinical exposure to HAV is suspected despite a negative finding, a second sample should be collected and tested no less than <b>one to two weeks later</b> .
≥ 0.90 and < 1.10	Equivocal (Retest in duplicate)	Equivocal samples should be retested in duplicate by the LIAISON® HAV IgM assay to confirm the initial result. Samples which are reactive (≥ 1.10) on both repeat tests should be considered reactive. Samples which are negative (< 0.90) on both repeat tests should be considered negative. A second sample should be collected and tested no less than <b>one to two weeks later</b> when at least one of the repeat results is equivocal or if the duplicates of the repeat results are reactive and negative.*
≥ 1.10	Reactive (No further testing)	Indicates the presence of detectable IgM antibodies to HAV. A reactive result generally indicates that the patient has an acute HAV infection. A reactive anti-HAV IgM result does not rule out other hepatitis infections.

**CONCLUSION:**

The material submitted in this premarket notification is complete and supports a substantial equivalence decision. The labeling is sufficient and it satisfies the requirements of 21CFR 809.10.