K082050

5.0 510(k) SUMMARY

NOV - 3 2008

SUBMITTED BY:

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NAME OF DEVICE:

Trade Name:	LIAISON® HAV IgM
Common Names/Descriptions:	Hepatitis A Virus (HAV Serological Reagents)
Classification Names:	Hepatitis A Test (Antibody and IgM Antibody)
Product Code:	LOL

PREDICATE DEVICES: DiaSorin Inc. ETI-HA-IGMK Plus Kit (PMA #P890014/S002)

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 sodium heparin plasma 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 Reactive) is 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.

PERFORMANCE DATA:
COMPARATIVE CLINICAL TRIALS: Prospective and Retrospective studies were performed to evaluate the performance of the LIAISON® HAV IgM assay among individuals who were sent to the lab for Hepatitis A testing and those at high risk for viral hepatitis.

The prospective study consisted of 500 samples from Individuals who were sent to the lab for HAV testing, 239 individuals at risk for viral hepatitis, and 108 Pediatric patients. The retrospective study consisted of 123 samples from individuals with an Acute Hepatitis A infection including 42 pediatric patients with an acute infection.

Prospective
Individuals sent to the Lab for HAV testing
A total of 500 samples collected from the Northeastern US were included in this study. Of the samples from individuals sent to the lab for HAV testing, 59.8% were female (n=299) ranging in age from 20 - 101 yrs. and 40.2% were male (n=201) ranging in age from 17 to 89.

Individuals At Risk for Viral Hepatitis
A total of 239 individuals at risk for viral hepatitis due to lifestyle, behavior or occupation were included in this study. The 239 individuals were from the following at risk groups: homosexual males (n=38), healthcare workers (n=10), Commercial sex workers (n=34), drug users (n=77), prison inmates (n=49), dialysis patients (n=25) and hemophiliacs (n=6). Of the at risk individuals, 29.7% were females (n=71), ranging in age from 17 to 79, and 43.1% were males (n=103) ranging in age from 16 to 79. The age and gender were unknown for the remaining 27.2% (n=65).

The data for the combined populations are shown in Table 1.

Table 1: HAV testing population and At risk
population comparison of LIAISON® HAV IgM and the Comparator ELISA

LIAISON® HAV IgM	Comparator ELISA			Total
	Reactive	Equivocal	Negative	
Reactive	0	0	1	1
Equivocal	0	0	0	0
Negative	0	0	738	738
Total	0	0	739	739

	Negative Percent Agreement		Exact 95% Confidence Interval
Negative	738/739	99.9%	99.4 – 100%

Pediatric Population
One hundred eight (108) prospectively collected pediatric samples were tested. The 108 pediatric samples were collected from children in the United States. Of these 108 samples 57.4% were female (n=62) and 42.6% were male (n=46), ranging in age from 2 to 17.

The results are presented in the Table 2.

Table 2: Pediatric Population Comparison of LIAISON® HAV IgM and Comparator ELISA

LIAISON® HAV IgM	Comparator ELISA			Total
	Reactive	Equivocal	Negative	
Reactive	0	0	0	0
Equivocal	0	0	0	0
Negative	0	0	108	108
Total	0	0	108	108

	Negative Percent Agreement		Exact 95% Confidence Interval
Negative	108/108	100%	97.3 – 100%

Acute HAV Infection;
A retrospective population was tested which consisted of 123 samples from individuals who had an (Acute) HAV infection. Of these 123 samples, 42 were acute pediatrics collected from children in Eqypt. There were 32.5% females (n=40) ranging in age from 4 to 51, 51.2% males (n=63) ranging in age from 4 to 51. For 15.5% of the samples gender and age were unknown. One sample (0.8%) age 18, but gender was unknown. The results are presented in the Table 3.

Table 3: Comparison of LIAISON® HAV IgM and the Comparator ELISA

LIAISON® HAV IgM	Comparator ELISA			Total
	Reactive	Borderline	Negative	
Reactive	119	4	0	123
Equivocal	0	0	0	0
Negative	0	0	0	0
Total	119	4	0	123

	Reactive Percent Agreement		Exact 95% Confidence Interval
Reactive	119/123	96.7%	92.7 – 98.9%

Conclusion: The LIAISON® HAV IgM assay showed equivalent performance to the FDA approved comparison method. The LIAISON® HAV IgM demonstrated overall agreement with the Comparator ELISA as follows:

Prospective Population "At Risk" and "HAV Testing" – 99.9% (95% CI = 99.1 – 100%)
Pediatric Population – 100.0% (95% CI = 97.3 – 100%)
Retrospective Population Acute HAV Infection – 96.7% (95% CI = 92.7 – 98.9%)

The results demonstrate that the LIAISON® HAV IgM assay can be used with the LIAISON® Analyzer for the qualitative detection of IgM antibodies to hepatitis A virus.

EXPECTED VALUES :

Prevalence

The expected prevalence results of the LIAISON® HAV IgM assay were determined in 802 apparently healthy adults from the Western (historically high prevalence) and the Eastern (historically lower prevalence) regions of the U.S. Three hundred one (301) samples were from the Western U.S. and 501 were samples from the Eastern U.S.

Of the Western U.S. individuals 53.8% were females (n=162) ranging in age from 9 to 87 and 46.2% were males (n=139) ranging in age from 16 to 76. The majority of the individuals were Caucasian (60.8%), with other ethnic groups represented as follows: Hispanic (17.6%), African Americans (15.3%), Asian (6.0%) and Middle Eastern (0.3%). In the study group from the Western region, none of the individuals were found to be reactive for HAV IgM antibodies.

Of the Eastern U.S. individuals 46.5% were females (n=233) ranging in age from 17 to 83, and 53.5% were males (n=268) ranging in age from 17 to 82. The majority of the individuals were Caucasian (69.9%), with other ethnic groups represented as follows: Hispanic (14.0%), African American (12.1%) and Asian (4.0%).
In the study group from the Eastern region none of the individuals were found to be reactive for HAV IgM antibodies.
The expected results for the Western and Eastern regions of the U.S. are presented in the tables below.

Expected results for the LIAISON® HAV IgM assay from the Western U.S. (n=301)

	N	Negative	Equivocal	Reactive	Reactive Prevalence
Total	301	301	0	0	NA
Gender					
Female	162	162	0	0	NA
Male	139	139	0	0	NA
Age range (years)	N	(-)	(E)	(+)	
≤18	12	12	0	0	NA
<10	1	1	0	0	NA
10 - 19	15	15	0	0	NA
20 - 29	81	81	0	0	NA
30 - 39	68	68	0	0	NA
40 - 49	52	52	0	0	NA
50 - 59	48	48	0	0	NA
60 - 69	31	31	0	0	NA
≥ 70	5	5	0	0	NA

Expected results for the LIAISON® HAV IgM assay from the Eastern U.S. (n=501)

	N	Negative	Equivocal	Reactive	Reactive Prevalence
Total	501	501	0	0	NA
Gender					
Female	233	233	1	44	NA
Male	268	268	0	56	NA
Age range (years)	N	(-)	(E)	(+)	
≤18	46				
<10	0				
10 - 19	49	49	0	0	NA
20 - 29	39	39	0	0	NA
30 - 39	78	78	0	0	NA
40 - 49	107	107	0	0	NA
50 - 59	142	142	0	0	NA
60 - 69	52	52	0	0	NA
≥ 70	34	34	0	0	NA

SEROCONVERSION PANEL:

Analytical Sensitivity as Seroconversion Panel Performance

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

Panel ID	DiaSorin 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	
PHT901 seroconversion	12	17	12	17	0
PHT902 seroconversion	16	21	16	21	0
RP004 seroconversion	6	62	6	62	0
RP013 seroconversion	8	189	8	189	0
HAV01 seroconversion	0	77	0	91	14

* Only reactive results were used; equivocal results were not used to determine a reactive result.

The sensitivity of the LIAISON® HAV IgM was equivalent to or more sensitive than 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-A2 was consulted in the preparation of the testing protocol.
A coded panel comprised of 12 frozen "engineered" serum samples was prepared by DiaSorin S.p.A. and provided to the sites. The coded panel samples were prepared by spiking reactive samples into negative sample to achieve high negative, low reactive and high reactive results. The two negative panel samples were not spiked. The LIAISON® Control HAV IgM set were also included in the 5 day study.

Results
The 5 day Index results are summarized in Table 4 (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 each of the sites.

Table 4: Combined Sites

sample	N	mean	within run		between runs		total (by site)		between sites		Over all	
ID#		Index	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
NC	60	0.15	0.02	14.2	0.08	15.6	0.02	19.6	0.14	63.6	0.08	54.2
PC	60	2.17	0.11	5.2	0.21	4.7	0.10	6.5	0.10	10.3	0.23	10.7
HAMu-e1	60	0.73	0.03	4.4	0.17	9.1	0.07	9.7	0.40	24.9	0.17	23.5
HAMu-e2	60	0.81	0.05	6.9	0.18	9.9	0.08	11.6	0.59	23.2	0.18	22.6
HAMu-n1	60	0.49	0.02	4.9	0.11	7.8	0.04	9.1	0.07	23.8	0.11	22.7
HAMu-n2	60	0.42	0.02	4.4	0.09	7.0	0.03	8.0	0.09	23.3	0.09	21.2
HAMu-P1	60	6.87	0.35	5.2	0.82	7.5	0.52	9.2	3.97	10.3	0.87	12.7
HAMu-P2	60	4.48	0.30	6.7	0.75	9.7	0.44	11.3	0.10	15.8	0.78	17.4
HAMu-P3	60	2.45	0.12	5.3	0.45	6.7	0.18	9.5	2.64	19.4	0.46	18.8
HAMu-P4	60	2.17	0.09	4.1	0.33	7.9	0.18	8.4	0.71	14.6	0.34	15.5
HAMu-P5	60	1.95	0.08	4.0	0.24	8.7	0.17	8.9	0.27	10.4	0.25	12.6
HAMu-P6	60	1.53	0.06	4.0	0.27	7.1	0.11	7.6	0.07	18.9	0.27	17.4
HAMu-P7	60	1.31	0.06	4.8	0.22	9.5	0.13	10.0	0.17	16.2	0.22	16.8
HAMu-P8	60	1.24	0.07	5.6	0.28	12.6	0.15	12.8	0.12	22.4	0.28	22.5

CROSS-REACTIVITY:
The cross-reactivity study for the LIAISON® HAV IgM assay was designed to evaluate potential interference from other viruses that may cause symptoms similar to HAV infection (EBV, CMV, Rubella, Measles, Mumps, HBV, HCV), other organisms that may cause infectious disease (VZV, HSV, HIV, *Toxoplasma gondii*) and from other conditions that may result from atypical immune system activity (i.e. rheumatoid factor, RF, antinuclear autoantibodies, ANA, human anti-mouse antibodies).

Organism/Condition	N	Comparator HAV IgM Assay	LIAISON® HAV IgM Reactive	LIAISON® HAV IgM Negative	LIAISON® HAV IgM Equivocal
IgG anti-Measles	3	Negative	0	3	0
IgG anti-Mumps	8	Negative	0	8	0
IgG anti-VCA	3	Negative	0	3	0
IgG anti-EA	3	Negative	0	3	0
IgG anti-CMV	3	Negative	0	3	0
IgG anti-Rubella	2	Negative	0	2	0
IgG anti-*Toxoplasma*	3	Negative	0	3	0
IgG anti-HSV-1/2	1	Negative	0	1	0
IgG anti-HSV-2	6	Negative	0	6	0
IgG anti-syphilis	4	Negative	0	4	0
Anti-VZV	3	Negative	0	3	0
Anti-HTLV I/II	3	Negative	0	3	0
Anti-HCV	4	Negative	0	4	0
Anti-*Borrelia*	4	Negative	0	4	0
Anti-HBs	3	Negative	0	3	0
Anti-HIV	10	Negative	0	10	0
Anti-Parvovirus B19	4	Negative	0	4	0
IgM anti-HBc	4	Negative	0	4	0
IgM anti-*Borrelia*	5	Negative	0	5	0
IgM anti-CMV	5	Negative	0	5	0
IgM anti-EBV	5	Negative	0	5	0
IgM anti-HSV	7	Negative	0	7	0
IgM anti-Rubella	6	Negative	0	6	0
IgM anti-*Toxoplasma*	5	Negative	0	5	0
IgM anti-VZV	6	Negative	0	6	0
Anti-Influenza virus	3	Negative	0	3	0
HBsAg	3	Negative	0	3	0
HBeAg	6	Negative	0	6	0
Nucleotides	4	Negative	0	4	0
ENA	4	Negative	0	4	0
Rheumatoid Factor	17	Negative	0	17	0
γ-globulin	36	Negative	0	36	0
HAMA	12	Negative	0	12	0
Total	195		0	195	0

POTENTIALLY INTERFERING SUBSTANCES:

Controlled studies were performed to determine whether the presence of hemoglobin, lipemia, bilirubin, serum albumin and gamma globulin affect assay performance. The highest concentrations which were considered not to impact results are as follows: hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides), icterus (at 20 mg/dL bilirubin), serum albumin (at 5 g/dL), γ-Globulin (at 4 g/dL).

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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NOV - 3 2008

Re: K082050
Trade/Device Name: LIAISON® HAV IgM
Regulation Number: 21 CFR 866.3310
Regulation Name: Hepatitis A virus (HAV) serological assays
Regulatory Class: Class II
Product Code: LOL
Dated: October 24, 2008
Received: October 27, 2008

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K082050

Device Name: LIAISON® HAV IgM and LIAISON® Control HAV IgM

Indication For 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 sodium heparin plasma 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 reactive) is intended for use as assayed quality control samples to monitor the performance of the LIAISON® HAV IgM assay.

Prescription Use __X__ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K082050