K082049

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5.0 510(k) SUMMARY

SUBMITTED BY:

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NAME OF DEVICE:

Trade Name:	LIAISON® Anti-HAV LIAISON® Control Anti-HAV
Common Names/Descriptions:	Hepatitis A Virus (HAV Serological Reagents)
Classification Names:	Hepatitis A Test (Antibody and IgM Antibody)
Product Code:	LOL, JJX
PREDICATE DEVICES	DiaSorin Inc. ETI-AB-HAVK Plus assay (PMA #P890019/S05)

DEVICE DESCRIPTION:

INTENDED USE: The LIAISON® Anti-HAV assay is an *in vitro* chemiluminescent immunoassay intended for the qualitative detection of total antibodies to hepatitis A (anti-HAV) in human serum and sodium heparinized plasma samples using the automated LIAISON® Analyzer. The assay is indicated as an aid in the laboratory diagnosis of current or previous HAV Infections in conjunction with other serological and clinical information and to determine the presence of an antibody response to HAV in vaccine recipients.
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 Anti-HAV (negative and positive) is intended for use as assayed quality control samples to monitor the performance of the LIAISON® Anti-HAV assay.

KIT DESCRIPTION: The method for qualitative determination of anti-HAV is a competitive sandwich chemiluminescence immunoassay (CLIA) based on neutralization. The assay uses magnetic particles (solid phase) coated with IgG antibodies to HAV (mouse monoclonal), and a mouse monoclonal anti- HAV

antibody conjugate linked to an isoluminol derivative (isoluminol-antibody conjugate).

The first incubation step consists of adding the HAV antigen to calibrators, samples or controls, during which anti-HAV present in calibrators, samples or controls binds to a fixed and limited amount of HAV, thus forming an HAV-anti-HAV immune complex.

After this step the second incubation follows and it involves addition of magnetic microparticles and conjugate into the reaction module, during which the antibody conjugate and the solid-phase antibody compete with anti-HAV present in the specimen for HAV. This allows the conjugate to bind to the solid phase and to form a sandwich. If all HAV added is sequestered in an HAV-anti-HAV immune complex during the first incubation, no sandwich is formed during the second incubation. After the second 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 inversely indicative of anti-HAV present in calibrators, samples or controls.

PERFORMANCE DATA:
COMPARATIVE TESTING: Prospective and Retrospective studies were performed to evaluate the performance of the LIAISON® Anti-HAV 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 739 samples from individuals who were sent to the lab for HAV testing or at risk for viral hepatitis, 108 samples from a pediatric population and 73 individuals who participated in a vaccine study. The retrospective study consisted of 109 samples from adults with a current or previous hepatitis A infection and 42 pediatric patients with current hepatitis A infection.

Prospective
HAV Testing and At Risk Populations
Of the 739 samples in this study 500 were excess serum samples from individuals in the Northeastern U.S. sent to the laboratory for HAV testing. In this group 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. The remaining 239 samples were from individuals at risk for viral hepatitis due to lifestyle, behaviour or occupation. This group consisted of the following: 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 these subjects 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).
Two samples were Equivocal by the Comparator ELISA assay after repeat testing per the Instructions for use.

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

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

LIAISON® Anti-HAV	Comparator ELISA			Total
	Positive	Borderline	Negative	
Positive	230	0	3	233
Equivocal	1**	1	2	4*
Negative	7	1	494	502
Total	238	2*	499	739

* Repeat equivocal or borderline results
**sample not retested

	Percent Agreement		Exact 95% Confidence Interval
Positive	230/239	96.6%	93.5 – 98.0%
Negative	494/499	99.0%	97.9 – 99.6%

- Specimens that were Borderline with the comparison method and Negative with the LIAISON® Anti-HAV assay were considered to be False Negative on the LIAISON® Anti-HAV assay.

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

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

LIAISON® Anti-HAV	Comparator ELISA			Total
	Positive	Equivocal	Negative	
Positive	11	0	2	13
Equivocal	1	0	1	2*
Negative	1	1	91	93
Total	13	1*	94	108

* Repeat equivocal or borderline results

	Percent Agreement		Exact 95% Confidence Interval
Positive	11/14	78.6%	49.2 – 95.3%
Negative	91/94	96.8%	92.0 – 99.1%

- Specimens that were Borderline with the comparison method and Negative with the LIAISON® Anti-HAV assay were considered to be False Negative on the LIAISON® Anti-HAV assay.

Retrospective
Current/Previous HAV Infection;
Of the 151 retrospective samples 109 were from adults with a current or previous hepatitis A infection collected in Eastern U.S. and Egypt. They consisted of 31.2% females (n=34) 35.8% males (n=39) ranging in age from 18 to 51. For 32.1% (n=35) of the samples gender and age were unknown. One sample (0.9%) was from an individual18 years of age and gender unknown. The other 42 samples were from pediatric patients with current hepatitis A infection collected in Eqypt. They consisted of 31% female (n=13) and 69% male (n=29), ranging in age from 4-17 years.

Table 3: "Current/Previous" HAV Infection Comparison of LIAISON® Anti-HAV and the Comparator ELISA

LIAISON® Anti-HAV	Comparator ELISA			Total
	Positive	Equivocal	Negative	
Positive	109	0	0	109
Equivocal	0	0	0	0
Negative	0	0	0	0
Total	109	0	0	109

	Percent Agreement		Exact 95% Confidence Interval
Positive	109/109	100.0%	98.0 – 100%

Table 4: "Current/Previous" HAV Infection Pediatric Population Comparison with the LIAISON® Anti-HAV and the Comparator ELISA

LIAISON® Anti-HAV	Comparator ELISA			Total
	Positive	Equivocal	Negative	
Positive	42	0	0	42
Equivocal	0	0	0	0
Negative	0	0	0	0
Total	42	0	0	42

	Percent Agreement		Exact 95% Confidence Interval
Positive	42/42	100.0%	98.0 – 100%

Vaccine study
The HAV antibody response to vaccination was evaluated with the three different vaccines currently licensed in the United States: TWINRIX® (Hepatitis A, Inactivated and Hepatitis B (recombinant)), HAVRIX® (Hepatitis A, Inactivated) both manufactured by GlaxoSmithKline Biologicals and VAQTA® (Hepatitis A, Inactivated) manufactured by MERCK & CO., INC.

For TWINRIX® vaccine, 9 matched sets of pre- and post- vaccine samples were available.
For HAVRIX® vaccine, 32 matched sets of pre- and post- vaccine samples were available.
For VAQTA® vaccine, 32 matched sets of pre- and post- vaccine samples were available.

The data are shown in the table below.

Table 5: Comparison of Vaccine samples on the LIAISON® Anti-HAV and Comparator assay

		Comparator			LIAISON® Anti-HAV		
		Pos	Eqv	Neg	Pos	Eqv	Neg
TWINRIX	Prevaccine	0	0	9	0	0	9
	Post 2nd dose	9	0	0	9	0	0
	Post 3rd dose	9	0	0	9	0	0
HAVRIX	Pre-vaccine	0	0	32	0	0	32
	4wk Post vaccine	31	0	1	29	1	2
VAQTA	Pre-vaccine	0	0	32	0	0	32
	4 wk Post vaccine	31	0	1	31	0	1

The LIAISON® Anti-HAV demonstrated agreement with the Comparator ELISA as follows:

Prospective Population
"At Risk" and "HAV Testing"
Positive agreement - 96.6% (95% CI = 93.5-98.0%)
Negative agreement - 99.0% (95% CI = 97.9 – 99.6%)

"Pediatric Population"
Positive agreement - 78.6% (95% CI = 49.2-95.3%)
Negative agreement - 96.8% (95% CI = 92.0 – 99.1%)

Retrospective Population
"Adult and Pediatric Current/Previous HAV Infection"
Positive agreement - 100% (95% CI = 98.0 – 100%)

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

EXPECTED VALUES:

Prevalence

The expected prevalence results of the LIAISON® Anti-HAV assay were determined in 802 apparently healthy adults from the Western and the Eastern 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, 26.3% of the individuals were found to be positive for anti-HAV 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 20% of the individuals were found to be positive for Anti-HAV antibodies.

The Expected results for the Western and Eastern regions of the U.S. are presented in the tables below.

One sample from each of the regions gave an Equivocal result after repeat testing per Instructions for use.

Expected results for the LIAISON® Anti-HAV assay from the Western U.S. (High Prevalence – n=301)

	N	Negative	Equivocal	Positive	Positive Prevalence
Total	301	221	1	79	26.3%
Gender					
Female	162	115	0	47	29.0%
Male	139	106	1	32	23.0%
Age range (years)	N	(-)	(Eqv)	(+)	
≤18	12	9	0	3	25.0%
<10	1	0	0	1	
10 - 19	15	10	0	5	33.3%
20 - 29	81	56	0	25	30.9%
30 - 39	68	47	0	21	30.9%
40 - 49	52	42	1	9	17.3%
50 - 59	48	41	0	7	14.6%
60 - 69	31	22	0	9	29.0%
≥ 70	5	3	0	2	40.0%

Expected results for the LIAISON® Anti-HAV assay from the Eastern U.S. (Low Prevalence – n=501)

	N	Negative	Equivocal	Positive	Positive Prevalence
Total	501	400	1	100	20.0%
Gender					
Female	233	188	1	44	18.9%
Male	268	212	0	56	20.9%
Age range (years)	N	(-)	(Eqv)	(+)	
≤18	46	0	0	0	0.0%
<10	0	NA	NA	NA	NA
10 - 19	49	49	0	0	0.0%
20 - 29	39	33	0	6	15.4%
30 - 39	78	63	1	14	18.0%
40 - 49	107	95	0	12	11.2%
50 - 59	142	101	0	41	28.9%
60 - 69	52	37	0	15	28.9%
≥ 70	34	22	0	12	35.3%

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 positive samples into negative samples to achieve high negative, low positive and high positive results. The two negative panel samples were not spiked. The LIAISON® Control Anti-HAV set was also included in the 5 day study.

The coded panel was tested at all three sites, using four replicates per run in one run per day during five operating days. 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.

Results,
The 5 day Index results are summarized in Table 6 (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.
The result of the LIAISON® Anti-HAV Negative Control read above the reportable range of the assay >>2.7 therefore, SD and %CVs were not able to be calculated and are shown as (NA).

Table 6: Combined Sites

	Site 1			Site 2			Site 3			Overall (3 site)		
		Total			Total			Total			Total	
Sample ID	Mean Index	sd	%CV	Mean Index	sd	%CV	Mean Index	sd	%CV	Mean Index	sd	%CV
NC	>>2.7	NA	NA	>>2.7	NA	NA	>>2.7	NA	NA	>>2.7	NA	NA
PC	0.42	0.03	7.2	0.36	0.03	7.3	0.20	0.07	10.8	0.33	0.10	30.0
HAVu-e1	1.13	0.10	8.9	0.92	0.08	8.9	0.99	0.04	3.9	1.01	0.12	11.5
HAVu-e2	1.14	0.13	11.2	0.93	0.08	8.4	0.98	0.03	3.3	1.01	0.12	12.3
HAVu-e3	1.17	0.11	9.4	0.95	0.08	8.5	0.97	0.05	5.2	1.03	0.13	12.5
HAVu-e4	1.21	0.15	12.4	1.00	0.10	9.8	1.03	0.04	4.1	1.08	0.14	13.2
HAVu-n1	1.47	0.16	11.2	1.29	0.14	11.2	1.20	0.06	4.9	1.33	0.17	12.4
HAVu-n2	1.33	0.21	16.1	1.07	0.08	7.6	1.16	0.06	4.9	1.19	0.17	14.5
HAVu-p1	0.27	0.03	12.4	0.23	0.02	8.6	0.29	0.02	7.4	0.26	0.04	14.5
HAVu-p2	0.16	0.02	11.6	0.10	0.05	45.5	0.16	0.02	9.5	0.14	0.04	28.1
HAVu-p3	0.84	0.10	12.0	0.67	0.08	12.2	0.67	0.03	4.3	0.73	0.11	15.0
HAVu-p4	0.89	0.09	9.9	0.72	0.07	9.4	0.76	0.03	3.6	0.79	0.10	12.5
HAVu-p5	1.00	0.08	8.3	0.80	0.10	12.0	0.84	0.03	3.7	0.88	0.11	12.8
HAVu-p6	0.84	0.09	10.8	0.67	0.08	11.7	0.72	0.03	4.4	0.74	0.11	13.4

CROSS-REACTIVITY: The cross-reactivity study for the LIAISON® Anti-HAV 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).

Organism/Condition	N	Comparator Anti-HAV Assay	LIAISON® Anti-HAV Positive	LIAISON® Anti-HAV Negative	LIAISON® Anti-HAV Equivocal
Anti-VZV (IgG)	22	Negative	0	22	0
Anti-VZV (IgM)	3	Negative	0	3	0
Anti-EBV VCA IgG	21	Negative	0	21	0
Anti-EBV EA IgG	14	Negative	0	14	0
Anti-Toxoplasma IgG	7	Negative	0	7	0
Anti-Toxoplasma IgM	10	Negative	0	10	0
Anti-HBs	11	Negative	0	11	0
Anti-HBc IgM	13	Negative	0	13	0
Anti-HBc	25	Negative	0	25	0
Anti-HBe	3	Negative	0	3	0
HBeAg	23	Negative	0	23	0
HBsAg	27	Negative	0	27	0
Anti-CMV IgG	14	Negative	0	14	0
Anti-Rubella IgG/IgM	29	Negative	0	29	0
Anti-HSV 1 / 2 IgG	25	Negative	0	24	1
Anti-HSV 2 IgG	19	Negative	0	19	0

Organism/Condition	N	Comparator Anti-HAV Assay	LIAISON® Anti-HAV Positive	LIAISON® Anti-HAV Negative	LIAISON® Anti-HAV Equivocal
Anti-HIV 1 / 2	4	Negative	4	0	0
Anti-HCV	5	Negative	0	5	0
Anti-Mumps IgG	8	Negative	0	8	0
Anti-Measles IgG	3	Negative	0	3	0
Anti-Measles IgM	11	Negative	0	11	0
RF+	5	Negative	2	2	1
ANA	24	Negative	2	19	3
ENA	3	Negative	0	2	1
Nucleotides	1	Negative	0	1	0
γ-globulin	6	Negative	0	6	0
HAMA	10	Negative	0	10	0
Total	346		8	332	6

WARNING: Assay interference due to circulating antibodies against HIV 1/2, Anti-nuclear autoantibodies and rheumatoid factor may occur.

POTENTIALLY INTERFERING SUBSTANCES: Twelve samples at different anti-HAV levels (2 positive, 4 borderline, 4 equivocal, 2 high negative) were prepared with and without the potentially interfering substances hemoglobin, triglycerides, bilirubin and albumin. All samples were tested with the LIAISON® anti-HAV assay and results were compared using a paired t-test. The testing showed that the assay performance was not affected by hemolysis at ≤1000 mg/dL hemoglobin (2% change, 100% concordance of results with and without interferent), lipemia at ≤3000 mg/dL triglycerides (7% change, 92% (11/12) concordance of results with and without interferent), icterus at ≤5 mg/dL bilirubin (0% change, 100% concordance of results with and without interferent) and serum albumin at ≤5 g/dL (3% change, 92% (11/12) concordance of results with and without interferent).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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DEC 0 5 2008

Ms. Carol A. DePouw
Regulatory Affairs Specialist
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Re: k082049
Trade/Device Name: LIAISON® Anti-HAV and LIAISON® Control Anti-HAV
Regulation Number: 21 CFR 866.3310
Regulation Name: Hepatitis A Virus Serological Reagents
Regulatory Class: Class II
Product Code: LOL, JJX
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): K082049

Device Name: LIAISON® Anti-HAV and LIAISON® Control Anti-HAV

Indication For Use:

The LIAISON® Anti-HAV assay is an *in vitro* chemiluminescent immunoassay intended for the qualitative detection of total antibodies to hepatitis A (anti-HAV) in human serum and sodium heparinized plasma samples using the automated LIAISON® Analyzer.

The assay is indicated as an aid in the laboratory diagnosis of current or previous HAV infections in conjunction with other serological and clinical information and to determine the presence of an antibody response to HAV in vaccine recipients.

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 Anti-HAV (negative and positive) is intended for use as assayed quality control samples to monitor the performance of the LIAISON® Anti-HAV 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)

Uwe Scherf

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

510(k) k082049