ATTACHMENT 1

SEP 11 2012

PREMARKET NOTIFICATION
510(K)
SAFETY AND EFFECTIVENESS SUMMARY
(as required by 21 CFR § 807.92)

A. 510(k)Number:
K112221

B. Purpose for Submission:
New device

C. Measurand:
Anti-SLA/LP autoantibodies

D. Type of Test:
Qualitative enzyme immunoassay

E. Applicant:
EUROIMMUN US INC.

F. Proprietary and Established Names:
EUROIMMUN Anti-SLA/LP ELISA (IgG)

G. Regulatory Information:

1. Regulation:
   21 CFR 866.5660 - Multiple autoantibodies immunological test system
2. Classification:
   Class II
3. Product code:
   NIY
4. Panel:
   Immunology

H. Intended Use:

1. Intended use(s):
   The EUROIMMUN Anti-SLA/LP ELISA (IgG) test kit is intended for the qualitative detection of IgG class autoantibodies against SLA/LP in human serum and plasma. It is used as an aid in the diagnosis of autoimmune hepatitis, type 1, in conjunction with other laboratory and clinical findings.
2. Indication(s) for use:
   Same as intended use.
3. Special conditions for the use statement(s):
   For prescription use only.
4. Special instrument requirements:
   Microwell plate reader capable of measuring OD at 450nm and at 620nm for dual wavelength readings.

I. Device Description:
The EUROIMMUN Anti-SLA/LP ELISA (IgG) consists of a microwell ELISA plate coated with SLA/LP antigen, calibrator, positive and negative control, peroxidase-labelled anti-human IgG conjugate, sample buffer, wash buffer concentrate, TMB chromogen/substrate solution and stop solution.

J. Substantial Equivalence Information:

1. Predicate device name (s):
   Inova Quanta Lite SLA ELISA
2. Predicate 510(k) number(s):
   K021482
3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to SLA/LP* as an aid in diagnosis of autoimmune hepatitis.	Detection of IgG antibodies to SLA* as an aid in diagnosis of autoimmune hepatitis.
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Assay format	Qualitative	Same
Calibration	Relative	Same
Antigen	Recombinant SLA/LP* antigen	Recombinant SLA* antigen
Substrate	TMB	Same
Reagent preparation	All reagents, calibrator and controls are ready to use, except for the wash buffer.	Same
Procedure	Sample incubation with micro-well antigen coated plate, followed by a wash step, incubation with an anti-human IgG enzyme conjugate; wash step, incubation with substrate; then the addition of a stop solution and reading at 450nm.	Same
Differences		
Item	**New Device**	**Predicate Device**
Conjugate	Rabbit anti-human IgG labeled with horseradish peroxidase	Goat anti-human IgG labeled with horseradish peroxidase
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive, 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types and dilution	Serum or plasma 1:101 dilution	Serum 1:101 dilution
Reported results	Ratio	Units
Cut off level	Ratio 1.0	25 Units

* Although named differently, the antigen used by the new and predicate device is not different. Wies et al. have found that the antigens soluble liver antigen (SLA) and liver-pancreas antigen (LP) are the same and suggested to use the combined name "SLA/LP". Inova does not follow this recommendation.

Wies I, Brunner S, Henninger J, et al. Identification of target antigen for SLA/LP autoantibodies in autoimmune hepatitis. Lancet 2000; 355: 1510-15.

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

None referenced.

L. Test Principle:

Patient samples are diluted 1:101 in sample buffer, 100 µl of each diluted patient sample and pre-diluted controls and calibrator are added to the antigen coated microtiter wells and incubated for 30 minutes at room temperature. After incubation the microtiter well strips are washed with wash buffer to remove unbound antibodies and 100 µl of the anti-human IgG enzyme conjugate reagent is added to each microtiter well. After an additional 30-minutes incubation at room temperature, the microtiter wells are again washed 3 times with 300 µl of wash buffer to remove any unbound enzyme conjugate and 100 µl of the chromogen substrate is added. The strips are incubated for 15 minutes at room temperature and 100 µl stop solution is added. The microtiter plates are placed in an ELISA reader and read at a wavelength of 450 nm and a reference wavelength of between 620 nm and 650 nm within 30 minutes.

M. Performance Characteristics (where applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The reproducibility of the test was investigated with samples at different points on the calibration curve. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 24 determinations performed in 6 different runs (days) according to the package insert. Both intra-assay and inter-assay reproducibility were found to be sufficient as no positive sample was found negative and vice versa. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-SLA/LP ELISA (IgG) Ratio							
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8
Mean value (x):	0.2	0.4	0.9	1.1	1.3	1.6	3.6	4.9
Range of values:	0.2 - 0.2	0.4 - 0.4	0.8 - 0.9	1.1 - 1.2	1.1 - 1.4	1.5 - 1.7	3.4- 3.7	4.6 - 5.3
Expected result:	neg	neg	neg	pos	pos	pos	pos	pos
% positive:	0%	0%	0%	100%	100%	100%	100%	100%
% negative:	100%	100%	100%	0%	0%	0%	0%	0%

Inter-assay reproducibility

n = 24	Anti-SLA/LP ELISA (IgG) Ratio							
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	Sample 8
Mean value (x):	0.2	0.4	0.8	1.2	1.2	1.7	3.9	5.4
Range of values:	0.2 - 0.3	0.3 - 0.4	0.8 - 0.9	1.0 - 1.3	1.0 - 1.3	1.6 - 1.8	3.4 - 4.2	4.7 - 5.8
Expected result:	neg	neg	neg	pos	pos	pos	pos	pos
% positive:	0%	0%	0%	100%	100%	100%	100%	100%
% negative:	100%	100%	100%	0%	0%	0%	0%	0%

The Lot to Lot reproducibility was investigated during the validaton and quality control of the kit using different lots with QC samples distributed over the measurement range. Lot to lot reproducibility was found to be sufficient as no positive sample was found negative and vice versa. The following results were obtained:

Lot to lot reproducibility

	Anti-SLA/LP ELISA (IgG) Ratio			
	Sample 1	Sample 2	Sample 3	Sample 4
n	6*	6*	6*	6*
Mean value (x):	5.6	7.6	9.7	0.9
Range of values:	5.4 – 6.0	7.3 – 8.0	9.5 – 9.9	0.9 – 0.9
Expected result:	pos	pos	pos	pos
% positive:	100%	100%	100%	100%
% negative:	0%	0%	0%	0%

	Anti-SLA/LP ELISA (IgG) Ratio				
	Sample 5	Sample 6	Sample 7	Sample 8	Sample 9
n	38**	38**	16**	10**	10**
Mean value (x):	3.1	3.9	0.1	0.1	0.1
Range of values:	2.1 – 4.1	3.2 – 4.6	0.1 – 0.2	0.1 – 0.2	0.1 – 0.2
Expected result:	pos	pos	neg	neg	neg
% positive:	100%	100%	0%	0%	0%
% negative:	0%	0%	100%	100%	100%

*3 lots x 2 runs ** n lots x 1 run

b. Linearity/assay reportable range:

Not applicable.

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

There is no recognized standard or reference material for anti-SLA/LP antibodies. Results are given as ratios.

d. *Limit of detection:*

Not applicable.

e. *Analytical specificity:*

Cross-reactivity: The quality of the antigen used and the antigen source ensure a high specificity of the ELISA. Cross reactivity was investigated using a panel of 18 sera serologically positive for antibodies against LKM. All 18 sera were negative in the Anti-SLA/LP ELISA (IgG), so no cross reactivity is expected.

Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different specimens at different anti-SLA/LP concentrations (ratio 0.4 – 10.0) were spiked with potential interfering substances and were incubated with the test system. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 90 – 119%. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride and 40 mg/dl for bilirubin.

f. *Assay cut-off:*

Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*

A study was performed in cooperation with a university clinical hospital comparing the performance of the EUROIMMUN Anti- SLA/LP ELISA (IgG) and an FDA released predicate device. 167 samples were investigated (58 from AIH patients, 66 from PBC patients, 15 from patients with AIH/PBC overlap syndrome and 28 from patients with viral hepatitis). The panel consisted of 30 men and 137 women. Age ranged from 1 to 87 years with an average age of 50 years. To cover the lower range with more samples, additional 23 samples were created by mixing of positive and negative samples. Borderline samples were considered for positive agreement.

n = 190		Predicate ELISA		
		positive	borderline	negative
EUROIMMUN Anti-SLA/LP ELISA (IgG)	positive	30	1	5
	negative	0	0	154

Negative agreement	154	/	159	=	96.9%	95% C.I.:	92.8%	-	99.0%
Positive agreement	31	/	31	=	100.0%	95% C.I.:	88.8%	-	100.0%
Overall agreement	185	/	190	=	97.4%	95% C.I.:	94.0%	-	99.1%

b. *Matrix comparison:*

The usability of plasma was investigated using 16 sample pairs each of serum and corresponding plasma. The samples cover concentrations in the diagnostically important range and the cut-off. Passing-Bablok regression was calculated for the comparison of serum to plasma. The results are shown in the table below.

	EDTA plasma	Heparin plasma	Citrate plasma
Regression equation (y = plasma, x = serum)	y = -0.02 + 1.00 x	y = 0.02 + 1.00 x	y = 0.04 + 0.99 x
95% C.I. of intercept	-0.14 to 0.18	-0.06 to 0.21	-0.18 to 0.16
95% C.I. of slope	0.94 to 1.06	0.94 to 1.03	0.94 to 1.05

A comparison in which the 95% C.I. of the slope contains 1.0 and the 95% C.I. of the intercept contains 0 indicates equivalence of concentration between serum and the corresponding plasma matrices. The comparisons above satisfy this condition.

Coefficients of determination were found to be above 0.99 and %BIAS from serum was in the range of 88 to 120 % (serum = 100 %).

3. Clinical studies:

In a clinical study, performed in cooperation with several university, hospital and private laboratories, in total 515 clinically characterized samples (65 from AIH-1 patients, 68 from AIH-2 patients, 15 from patiens with AIH/PBC overlap syndrome and 367 from other control groups) were investigated for anti-SLA/LP antibodies (IgG). The EUROIMMUN Anti-SLA/LP ELISA (IgG) showed a sensitivity for AIH type 1 of 27.7% (95% C.I.: 17.3 – 40.2%). The specificity was 100.0% (95% C.I.: 99.2 – 100.0%) without the AIH/PBC overlap samples; specificity was 99.3% (95% C.I.: 98.1 – 100%) when these samples were included.

a. Clinical sensitivity:

No.	Panel	n	Anti-SLA/LP ELISA (IgG)		
			positive	%	95% C.I.
1	Autoimmune hepatitis type 1 (AIH-1)	65	18	27.7%	17.3 – 40.2%

b. Clinical specificity:

No.	Panel	n	Anti-SLA/LP ELISA (IgG)		
			negative	%	95% C.I.
2	AIH/PBC overlap syndrome	15	12	80.0%	51.9 – 95.7%
3	Autoimmune hepatitis type 2 (AIH-2)	68	68	100.0%	91.0 – 100.0%
4	Viral hepatitis	118	118	100.0%	96.9 – 100.0%
5	Toxic liver damages	14	14	100.0%	76.8 – 100.0%
6	Steatohepatitis	24	24	100.0%	85.8 – 100.0%
7	Primary biliary liver cirrhosis (PBC)	111	111	100.0%	96.7 – 100.0%
8	Primary sclerosing cholangiitis (PSC)	19	19	100.0%	82.4 – 100.0%
9	Other autoimmune diseases*	81	81	100.0%	95.5 – 100.0%
	Total (without panel 2)	435	435	100.0%	99.2 – 100.0%
	Total (including panel 2)	450	447	99.3%	98.1 – 99.9%

c. *from the following groups: MCTD (n = 20), celiac disease (n = 11), Diabetes Type I (n = 12), Hashimoto (n = 11), Grave's disease (n = 12), ulcerative colitis (n = 15)

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

Not applicable.

4. Clinical cut-off:

See Assay cut-off.

5. Expected values/Reference range:

The levels of anti-SLA/LP antibodies (IgG) were analyzed with the EUROIMMUN Anti-SLA/LP ELISA (IgG) in a panel of 150 apparently healthy blood donors (mixed age and sex). With a cut-off of ratio 1.0, all blood donors were found negative.

Positives	0
Negatives	150
Lowest value	Ratio 0.0
Highest value	Ratio 0.8
Mean value	Ratio 0.1
Std dev. (SD)	Ratio 0.11
95th percentile	0.3
99th percentile	0.6

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.

Date

Signature

Kathryn Kohl, Managing Director
Typed Name, Title

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

SEP 11 2012

EUROIMMUN US, Inc.
c/o Ms. Kathryn Kohl
Managing Director
1100 The American Road
Morris Plains, NJ 07950

Re: k112221
Trade/Device Name: EUROIMMUN Anti-SLA/LP (IgG)
Regulation Number: 21 CFR §866.5660
Regulation Name: Multiple autoantibodies immunological test system
Regulatory Class: II
Product Code: NIY
Dated: September 5, 2012
Received: September 7, 2012

Dear Ms. Kohl:

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 class II (Special Controls), 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); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); 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 Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

for Maria Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K112221

Device Name: Anti-SLA/LP ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-SLA/LP ELISA (IgG) test kit is intended for the qualitative detection of IgG class autoantibodies against SLA/LP (soluble liver antigen/liver-pancreas antigen) in human serum and plasma. It is used as an aid in the diagnosis of autoimmune hepatitis, type 1, in conjunction with other laboratory and clinical findings.

Prescription Use ____X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510K K112221