APR 0 9 2013

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

A. 510(k)Number:
K112996

B. Purpose for Submission:
New device

C. Measurand:
Anti-nuclear antibodies

D. Type of Test:
Qualitative enzyme immunoassay

E. Applicant:
EUROIMMUN US INC.

F. Proprietary and Established Names:
EUROIMMUN Anti-ENA Pool ELISA (IgG)

G. Regulatory Information:

1. Regulation:
   21 CFR 866.5100 - Antinuclear antibody immunological test system
2. Classification:
   Class II
3. Product code:
   LJM
4. Panel:
   Immunology

H. Intended Use:

1. Intended use(s):
   The EUROIMMUN Anti-ENA Pool ELISA (IgG) is intended for the qualitative determination of IgG class antibodies against nuclear antigens (mixture of nRNP/Sm, Sm, SS-A (SS-A 60/Ro-52), SS-B, Scl-70 and ribosomal P proteins) in human serum. It is used as an aid in the diagnosis of mixed connective tissue diseases (MCTD), systemic lupus erythematosus, Sjögren's syndrome and progressive systemic sclerosis, 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-ENA Pool Screen ELISA (IgG) consists of a microwell ELISA plate coated with a mixture of nRNP/Sm, Sm, SS-A (SS-A 60/Ro-52), SS-B, Scl-70 and ribosomal P proteins and antigens, 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):
   Aesku Aeskulisa ANA Hep-2
2. Predicate 510(k) number(s):
   K081104
3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to nuclear antigens	Same
Assay format	Qualitative	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative evaluation	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
Substrate	TMB	Same
Sample types	Serum	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
Reported results	OD Ratio	Same
Cut off level	Ratio 1.0	Same

Differences		
Item	**New Device**	**Predicate Device**
Antigen mixture	nRNP/Sm, Sm, SS-A (SS-A 60/Ro-52), SS-B, Scl-70 and ribosomal P proteins	dsDNA, histones, SS-A (Ro), SS-B (La), Sm, snRNP/Sm, Scl-70, Jo-1 and centromeric antigens and lysed HEp-2 cells
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 positive, 1 cut-off (used for calculation of results), 1 negative
Sample buffer	Ready for use	5x concentrate
Wash buffer	10x concentrate	50x concentrate
Stop solution	0.5 M sulphuric acid	1 M hydrochloric acid
Sample dilution	1:201	1:101

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

Guidance for Industry and FDA Staff: Recommendations for Anti-Nuclear Antibody (ANA) Test System Premarket (510(k)) Submissions (January 22, 2009)

L. Test Principle:

Patient samples are diluted 1:201 in sample buffer, 100 µl of each diluted patient sample and pre-diluted controls and calibrator are added to the antigen mixture 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 30 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed with 3 replicates according to the package insert. The following results were obtained:

Intra-Assay Reproducibility

n = 20	Anti-ENA Pool ELISA (IgG) *Ratio*							
	Sample 1	**Sample 2**	**Sample 3**	**Sample 4**	**Sample 5**	**Sample 6**	**Sample 7**	**Sample 8**
Mean Value (x):	0.4	0.8	1.4	2.4	5.7	8.3	0.1	7.4
Range of Values:	0.3 – 0.4	0.7 – 0.8	1.3 – 1.4	2.2 – 2.6	5.4 – 6.0	7.8 – 9.0	0.1	6.8 – 7.6
Expected Result:	negative	negative	positive	positive	positive	positive	negative	positive
% positive:	0%	0%	100%	100%	100%	100%	0%	100%
% negative:	100%	100%	0%	0%	0%	0%	100%	0%
	Sample 9	**Sample 10**	**Sample 11**	**Sample 12**	**Sample 13**	**Sample 14**	**Sample 15**	**Sample 16**
Mean Value (x):	2.8	4.9	2.5	8.3	10.3	2.1	5.6	2.8
Range of Values:	2.5 – 3.0	4.7 – 5.2	2.1 – 2.7	8.0 – 8.6	9.5 – 11.1	2.0 – 2.3	4.9 – 6.2	2.5 – 3.0
Expected Result:	positive	positive	positive	positive	positive	positive	positive	positive
% positive:	100%	100%	100%	100%	100%	100%	100%	100%
% negative:	0%	0%	0%	0%	0%	0%	0%	0%

Table 5.1.1.2 Inter-assay reproducibility

n = 30	Anti-ENA Pool ELISA (IgG) *Ratio*						
	Sample 1	**Sample 2**	**Sample 3**	**Sample 4**	**Sample 5**	**Sample 6**	**Sample 7**
Mean Value (x):	0.4	0.8	1.3	2.7	5.6	8.4	0.2
Range of Values:	0.3 – 0.5	0.7 – 0.9	1.2 – 1.4	2.5 – 3.0	4.9 – 6.1	7.6 – 9.1	0.2 – 0.3
Expected Result:	negative	negative	positive	positive	positive	positive	negative
% positive:	0%	0%	100%	100%	100%	100%	0%
% negative:	100%	100%	0%	0%	0%	0%	100%
	Sample 8	**Sample 9**	**Sample 10**	**Sample 11**	**Sample 12**	**Sample 13**	**Sample 14**
Mean Value (x):	6.5	2.0	3.5	1.8	6.8	7.1	2.0
Range of Values:	5.3 – 7.3	1.5 – 2.8	2.6 – 4.9	1.1 – 2.1	5.4 – 8.9	4.5 – 9.8	1.6 – 2.4
Expected Result:	positive	positive	positive	positive	positive	positive	positive
% positive:	100%	100%	100%	100%	100%	100%	100%
% negative:	0%	0%	0%	0%	0%	0%	0%

The Lot to lot reproducibility was investigated during the validation and quality control of the kit using different lots with QC samples distributed over the measurement range. The following results were obtained:

Lot to Lot Reproducibility

Anti-ENA Pool ELISA (IgG)

	Sample 1 *Ratio*	Sample 2 *Ratio*	Sample 3 *Ratio*	Sample 4 *Ratio*	Sample 5 *Ratio*	Sample 6 *Ratio*	Sample 7 *Ratio*	Sample 8 *Ratio*
n:	6*	6*	11**	////	9**	11**	11**	9**
Mean Value (x):	1.1	0.9	0.1	////	2.7	3.6	5.0	8.5
Range of Values:	1.1 – 1.2	0.8 – 0.9	0.1 – 0.2	////	2.5 – 3.3	3.0 – 4.2	4.1 – 5.7	7.0 – 9.8
Expected Result:	positive	negative	negative	////	positive	positive	positive	positive
% positive:	100%	0%	0%	////	100%	100%	100%	100%
% negative:	0%	100%	100%	////	0%	0%	0%	0%

//// *Omitte, Replaced by Sample 14*

Anti-ENA Pool ELISA (IgG)

	Sample 9 *Ratio*	Sample 10 *Ratio*	Sample 11 *Ratio*	Sample 12 *Ratio*	Sample 13 *Ratio*	Sample 14 *Ratio*	Sample 15 *Ratio*	Sample 16 *Ratio*
n:	6*	6*	6*	6*	6*	6*	6*	6*
Mean Value (x):	0.2	6.3	2.4	3.9	2.2	6.8	8.2	2.0
Range of Values:	0.1 – 0.3	5.5 – 7.6	1.9 – 3.0	2.9 – 5.2	1.9 – 2.7	5.9 – 8.2	7.0 – 9.7	1.8 – 2.3
Expected Result:	negative	positive	positive	positive	positive	positive	positive	positive
% positive:	0%	100%	100%	100%	100%	100%	100%	100%
% negative:	100%	0%	0%	0%	0%	0%	0%	0%

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

■ *Additional Samples Run*

No.	Lot	Test	Sample 9 *Ratio*	Sample 10 *Ratio*	Sample 11 *Ratio*	Sample 12 *Ratio*
1	1	1	0.1	7.6	3.0	5.2
2	2	2	0.1	7.5	2.9	5.0
3	3	3	0.3	5.8	2.1	3.4
4	4	4	0.3	6.0	2.2	3.4
5	5	5	0.3	5.5	1.9	3.2
6	6	6	0.3	5.5	2.0	2.9

No.	Lot	Test	Sample 13 *Ratio*	Sample 14 *Ratio*	Sample 15 *Ratio*	Sample 16 *Ratio*
1	1	1	2.7	8.1	9.7	2.3
2	2	2	2.7	8.2	9.7	2.2
3	3	3	2.0	6.1	7.9	1.8
4	4	4	2.0	6.4	7.4	1.8
5	5	5	1.9	5.9	7.4	1.9
6	6	6	2.0	6.2	7.0	1.8

b. *Linearity/assay reportable range:*
Not applicable.

c. *High dose Hook effect*
Potential for a high dose Hook effect is a phenomenon that is inherent with one step "sandwich" assay designs: Very high concentrations of antigen in the patient sample bind to all available sites - saturating them - on both the antibody-solid phase and the antibody-labeled conjugate and thereby prevent the "sandwich" formation. Under these conditions, the measured level of analyte may be significantly lower than the actual level present in the sample. The two-step immunoassay design of the Anti-ENA Pool ELISA (IgG) eliminates the adverse contribution of binding proteins, endogenous interfering substances and general matrix effects due to the extra wash step.

d. *Traceability, Stability, Expected values (controls, calibrators or methods):*
A recognized standard or reference material for anti-nuclear antibodies is not available. Results of this assay are given in ratios. The reactivity of the Anti-ENA Pool ELISA (IgG) was verified using the CDC ANA reference panel.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen mixture coated on the plates, containing the antigens nRNP/Sm, Sm, SS-A (SS-A 60/Ro-52), SS-B, Scl-70 and ribosomal P-proteins, ensures a high specificity of the ELISA. The reactivity of the assay was confirmed using the CDC ANA reference panel. CDC sample No. 10, characterized as anti-Jo-1 positive, was found positive due to Ro-52 antibodies which commonly occur in anti-Jo-1 positive samples. As the definition of CDC sample No. 10 did not include a check for Ro-52 antibodies, anti-Jo-1 positive samples that were negative for anti-Ro-52 were tested and found negative, while samples positive for both anti-Jo-1 and anti-Ro-52 were found positive, so no cross-reactivity to Jo-1 is expected. Cross reactivity was investigated using a total of 82 clinically and serologically characterized samples (10 celiac disease for antibodies against gliadin and tissue transglutaminase, 17 Wegener's granulomatosis for ANCA, 39 rheumatoid arthritis for antibodies against CCP and 16 infectious diseases antibody positive samples). All except of 2 samples were negative in the Anti-ENA Pool ELISA (IgG), so no cross reactivity is expected.

Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 4 different specimens at different ANA concentrations (ratio 0.7 – 8.4) 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 of the positive or borderline samples was within the range of 91 – 105 %. 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. Furthermore, the influence from rheumatoid factor was investigated by spiking of 6 different speciments with a rheumatoid factor positive material (characterized nephelometrically). The recovery in relation to the original sample (not spiked) was calculated. The recoveries were found within 96 - 106%. No interference was observed with rheumatoid factor at 500 IU/ml.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 278 clinically characterized samples from patients and control groups (49 mixed connective tissue diseases, 26 systemic lupus erythematosus, 29 Sjögren's syndrome, 22 systemic sclerosis, 20 polymyositis/dermatomyositis, 10 celiac disease, 17 Wegener's granulomatosis, 39 rheumatoid arthritis, 16 infectious disease and 50 healthy), obtained from different sources. The panel consisted of 100 men and 164 women with 14 unknown. Age ranged from 7 to 87 years with an average age of 46 years (15 unknown). The samples were tested with the EUROIMMUN Anti-ENA Pool ELISA (IgG) and with the Aesku Aeskulisa ANA Hep-2 as the predicate device. The results are shown in the table below. All discrepant samples were from controls.

n = 278		Predicate ELISA	
		positive	negative
EUROIMMUN Anti-ENA Pool ELISA (IgG)	positive	135	1
	negative	3	139

Negative agreement	139	/	140	=	99.3%	95% C.I.:	96.1%	- 100.0%
Positive agreement	135	/	138	=	97.8%	95% C.I.:	93.8%	- 99.5%
Overall agreement	274	/	278	=	98.6%	95% C.I.:	96.4%	- 99.6%

b. Matrix comparison:
Not applicable.

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 432 clinically characterized samples were investigated for ENA antibodies (IgG). The EUROIMMUN Anti-ENA Pool ELISA (IgG) showed an overall sensitivity of 60.9% (95% C.I.: 54.7 – 66.9%) and a specificity of 96.5% (95% C.I.: 92.5 – 98.7%). The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-ENA Pool ELISA (IgG)		
			positive	%	95% C.I.
1	Mixed connective tissue disease	44	44	100.0%	92.0 – 100.0%
2	Systemic lupus erythematosus	85	47	55.3%	44.1 – 66.1%
3	Systemic sclerosis	66	30	45.5%	33.1 – 58.2%
4	Sjögren's syndrome	66	48	72.7%	60.4 – 83.0%
	Total	261	159	60.9%	54.7 – 66.9%

b. Clinical specificity:

No.	Panel	n	Anti-ENA Pool ELISA (IgG)		
			negative	%	95% C.I.
5	Polymyositis/dermatomyositis	26	22	84.6%	65.1 – 95.6%
6	Celiac disease	21	21	100.0%	83.9 – 100.0%
7	Wegener's granulomatosis	17	15	88.2%	63.6 – 98.5%
8	Rheumatoid arthritis	39	39	100.0%	91.0 – 100.0%
9	Other autoimmune diseases*	52	52	100.0%	93.2 – 100.0%
10	Bacterial/viral infections	16	16	100.0%	79.4 – 100.0%
	Total	171	165	96.5%	92.5 – 98.7%

* from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), Diabetes Type I (n = 12)

c. 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 ANA (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (mixed age and sex). The results are shown in the table below.

n	200
Positives	3
Negatives	197
Prevalence	1.5%
	Ratio
Lowest value	0.0
Highest value	5.0
Mean value	0.2
Std deviation	0.37

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.

03.2013 Michael Locke

Date Signature

Michael Locke, Dir. Of Regulatory Affairs
Typed Name, Title

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

April 9, 2013

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

Re: k112996
Trade/Device Name: EUROIMMUN Anti-ENA Pool ELISA (IgG)
Regulation Number: 21 CFR §866.5100
Regulation Name: Antinuclear Antibody Immunological Test System
Regulatory Class: Class II
Product Code: LLL
Dated: March 28, 2013
Received: April 3, 2013

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. 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 Part 801); 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 regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Indications for Use

510(k) Number (if known): k112996

Device Name: EUROIMMUN Anti-ENA Pool ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-ENA Pool ELISA (IgG) is intended for the qualitative determination of IgG class antibodies against nuclear antigens (mixture of nRNA/Sm, Sm, SS-A (SS-A 60/Ro-52), SS-B, Scl-70, and ribosomal P proteins) in human serum. It is used as an aid in the diagnosis of mixed connective tissue disease (MCTD), systemic lupus erythematosus, Sjögren's syndrome and progressive systemic sclerosis, 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 Diagnostics and Radiological Health (OIR)

Maria M. Chan -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k) k112996