K123261

JUN 1 2 2013

ATTACHMENT 1

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-nRNP/Sm autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-nRNP/Sm ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5110 - Antinuclear antibody immunological test system
2. Classification:
Class II
3. Product code:
LKO
4. Panel:
Immunology

H. **Intended Use:**
1. Intended use(s):
The EUROIMMUN Anti-nRNP/Sm ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against nRNP/Sm in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of mixed connective tissue diseases and systemic lupus erythematosus, 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-nRNP/Sm ELISA (IgG) consists of a microwell ELISA plate coated with nRNP/Sm 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 RNP ELISA
2. Predicate 510(k) number(s):
K922833

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to nRNP/Sm	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative evaluation	Same
Antigen	Purified U1-nRNP complex; U1-nRNP contains RNP as well as Sm reactive proteins	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
Substrate	TMB	Same
Reagent preparation	All reagents, calibrators 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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-nRNP/Sm ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	5.1	3.3	1.9	1.2	0.8	0.4
Range of values:	5.0 – 5.1	3.2 – 3.4	1.8 – 2.0	1.1 – 1.2	0.7 – 0.9	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-nRNP/Sm ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	5.2	3.3	1.8	1.1	0.8	0.4
Range of values:	4.8 – 5.5	3.1 – 3.6	1.6 – 1.9	1.1 – 1.2	0.7 – 0.9	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-nRNP/Sm ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	3.6	2.5	5.4	0.4	0.9	1.1
Range of values:	3.4 – 3.9	2.3 – 2.8	4.8 – 5.7	0.3 – 0.4	0.9 – 0.9	1.1 – 1.1
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-nRNP/Sm ELISA (IgG) Ratio				
	Sample 7	Sample 8	Sample 9	Sample 10	Sample 11
n	11**	11**	11**	11**	11**
Mean value (x):	0.2	3.4	5.2	6.6	8.5
Range of values:	0.1 – 0.3	3.1 – 3.8	4.7 – 5.9	5.7 – 7.2	8.0 – 9.7
Expected result:	negative	positive	positive	positive	positive
% positive:	0%	100%	100%	100%	100%
% negative:	100%	0%	0%	0%	0%

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

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-nRNP/Sm 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-nRNP/Sm ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, SS-A, SS-B, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-nRNP/Sm ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-nRNP/Sm concentrations (ratio 0.9 – 5.6) were spiked with potential interfering substances and were incubated with the test system acording to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 85 – 109 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 287 clinically characterized samples (52 MCTD, 69 SLE, 51 Sjögren's syndrome, 15 systemic sclerosis, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 49 men and 238 women. Age ranged from 14 to 85 years with an average age of 46 years. Anti-nRNP/Sm antibodies are expected in either MCTD or SLE. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-nRNP/Sm ELISA (IgG) and with the Inova Quanta Lite RNP ELISA as the predicate device. Of the 8 discrepant samples, one was from a MCTD patient and the other 7 were from controls.

All samples n = 287		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-nRNP/Sm ELISA (IgG)	positive	83	0
	negative	8	196

Negative agreement	196	/	196	=	100.0%	95% C.I.:	98.1%	- 100.0%
Positive agreement	83	/	91	=	91.2%	95% C.I.:	83.4%	- 96.1%
Overall agreement	279	/	287	=	97.2%	95% C.I.:	94.6%	- 98.8%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. The comparison below satisfies this condition. Coefficients of determination were found to be above 0.99 and %recovery compared toserum was in the range of 91 to 120 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	15	15	15
Regression equation (y = plasma, x = serum)	y = 0.46 + 0.98 x	y = -0.25 + 1.05 x	y = 0.37 + 1.04
95% C.I. of intercept	-0.56 – 2.41	-1.54 – 1.27	-1.72 – 1.82
95% C.I. of slope	0.95 – 1.01	0.97 – 1.09	0.97 – 1.09
Coefficient of determination R^2	0.9988	0.9929	0.9915
Mean %recovery	101 %	103 %	105 %
Range of %recovery	91 – 117 %	92 – 114 %	93 – 120 %

Clinical studies:

Clinical studies were performed in cooperation with different sites. In total 1046 clinically characterized samples (65 from MCTD patients, 404 from SLE patients, 151 from myositis patients and 426 from control groups) were investigated for anti-nRNP/Sm antibodies (IgG). With the EUROIMMUN Anti-nRNP/Sm ELISA (IgG) a prevalence of 100.0% (95% C.I.: 94.5 – 100.0%) was found in MCTD (clinical sensitivity) and a prevalence of 23.3% (95% C.I.: 19.2 – 27.7%) in SLE with a specificity of 99.3% (95% C.I.: 98.0 – 99.9%). The myositis panel was not considered for calculation of sensitivity and specificity, because anti-nRNP/Sm antibodies may occur in this disease [Tomer 1993]. The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. *Clinical sensitivity:*

No.	Panel	n	Anti-nRNP/Sm ELISA (IgG)		
			positive	%	95% C.I.
1	Mixed connective tissue diseases	65	65	100.0%	94.5 – 100.0%
2	Systemic lupus erythematosus	404	94	23.3%	19.2 – 27.7%

b. *Clinical specificity:*

No.	Panel	n	Anti-nRNP/Sm ELISA (IgG)		
			negative	%	95% C.I.
3	Polymyositis/dermatomyositis	151	143	94.7%	89.8 – 97.7%
4	Rheumatoid arthritis	164	164	100.0%	97.8 – 100.0%
5	Systemic sclerosis	81	81	100.0%	95.5 – 100.0%
6	Sjögren's syndrome	88	86	97.7%	92.0 – 99.7%
7	Other autoimmune diseases*	63	62	98.4%	91.5 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	577	566	98.1%	96.6 – 99.9%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-nRNP/Sm antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	1
Negatives	199
Prevalence	0.5%
	Ratio
Lowest value	0.1
Highest value	1.3
Mean value	0.1
Std deviation	0.09

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.

Michael Locke — *Signature*

Dir. Regulatory Affairs — *Title*

12 June 2013 — *Date*

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-Sm autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-Sm ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5110 - Antinuclear antibody immunological test system
2. Classification:
Class II
3. Product code:
LKP
4. Panel:
Immunology

H. **Intended Use:**
1. Intended use(s):
The EUROIMMUN Anti-Sm ELISA (IgG) test kit is intended for the qualitative of IgG class autoantibodies against Sm in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of systemic lupus erythematosus, 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-Sm ELISA (IgG) consists of a microwell ELISA plate coated with Sm 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 Sm ELISA
2. Predicate 510(k) number(s):
K922831

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to Sm	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Antigen	Purified Sm antigen	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-Sm ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	5.7	3.7	2.0	1.2	0.8	0.4
Range of values:	5.4 – 5.8	3.5 – 3.9	1.9 – 2.0	1.2 – 1.3	0.7 – 0.9	0.4 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-Sm ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	5.8	3.9	1.7	1.1	0.8	0.4
Range of values:	5.3 – 7.4	3.5 – 4.6	1.5 – 2.2	1.0 – 1.2	0.6 – 1.0	0.3 – 0.5
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	2.5%	0%
% negative:	0%	0%	0%	0%	97.5%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-Sm ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	3.6	3.4	3.1	0.3	0.9	1.2
Range of values:	3.3 – 3.9	3.2 – 3.9	2.9 – 3.4	0.3 – 0.3	0.8 – 0.9	1.1 – 1.3
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-Sm ELISA (IgG) Ratio				
	Sample 7	Sample 8	Sample 9	Sample 10	Sample 11
n	9**	10**	10**	9**	10**
Mean value (x):	0.1	1.9	3.4	5.7	8.3
Range of values:	0.0 – 0.2	1.5 – 2.2	2.6 – 3.8	4.9 – 6.7	7.5 – 9.6
Expected result:	negative	positive	positive	positive	positive
% positive:	0%	100%	100%	100%	100%
% negative:	100%	0%	0%	0%	0%

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

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-Sm 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-Sm ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, nRNP/Sm, SS-A, SS-B, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-Sm ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-Sm concentrations (ratio 0.7 – 3.9) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 90 – 111 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 294 clinically characterized samples (128 SLE, 51 Sjögren's syndrome, 15 systemic sclerosis, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 60 men and 234 women. Age ranged from 14 to 85 years with an average age of 45 years. Anti-Sm antibodies are expected in SLE. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-Sm ELISA (IgG) and with the Inova Quanta Lite Sm ELISA as the predicate device. The results are shown in the table below. All of the 7 discrepant samples negative in the EUROIMMUN test were from controls. The 5 discrepant samples positive in the EUROIMMUN test were from SLE patients.

All samples n = 294		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-Sm ELISA (IgG)	positive	37	5
	negative	7	245

Negative agreement	245	/	250	=	98.0%	95% C.I.:	95.4%	- 99.3%
Positive agreement	37	/	44	=	84.1%	95% C.I.:	69.9%	- 93.4%
Overall agreement	282	/	294	=	95.9%	95% C.I.:	93.0%	- 97.9%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.99 and %recovery compared to serum was in the range of 89 to 118 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	16	16	16
Regression equation (y = plasma, x = serum)	y = 0.33 + 1.00 x	y = 0.19 + 0.97 x	y = 0.05 + 1.02
95% C.I. of intercept	-0.32 – 1.24	-0.92 – 1.95	-0.69 – 3.27
95% C.I. of slope	0.96 – 1.03	0.94 – 1.01	0.99 – 1.05
Coefficient of determination R^2	0.9953	0.9948	0.9931
Mean %recovery	102 %	99 %	103 %
Range of %recovery	94 – 115 %	90 – 111 %	89 – 118 %

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 1036 clinically characterized samples (414 from SLE patients and 622 from control groups) were investigated for anti-Sm antibodies (IgG). With the EUROIMMUN Anti-Sm ELISA (IgG) a prevalence of 11.4% (95% C.I.: 8.5 – 14.8%) was found in SLE with a specificity of 99.0% (95% C.I.: 97.9 – 99.6%). The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-Sm ELISA (IgG)		
			positive	%	95% C.I.
1	Systemic lupus erythematosus	414	47	11.4%	8.5 – 14.8%

b. Clinical specificity:

No.	Panel	n	Anti-Sm ELISA (IgG)		
			negative	%	95% C.I.
2	Rheumatoid arthritis	164	164	100.0%	97.8 – 100.0%
3	Systemic sclerosis	81	81	100.0%	95.5 – 100.0%
4	Sjögren's syndrome	88	88	100.0%	95.9 – 100.0%
5	Polymyositis/dermatomyositis	151	151	100.0%	97.6 – 100.0%
6	Mixed connective tissue diseases	45	39	86.7%	73.2 – 94.9%
7	Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	622	616	99.0%	97.9 – 99.6%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-Sm antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	0
Negatives	200
Prevalence	0.0%
	Ratio
Lowest value	0.1
Highest value	0.3
Mean value	0.1
Std deviation	0.02

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.

Michael Locke — Signature
Dir. Regulatory Affairs — Title
12 June 2013 — Date

ATTACHMENT 1

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-SS-A autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-SS-A ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5100 - Antinuclear antibody immunological test system
2. Classification:
Class II
3. Product code:
LLL
4. Panel:
Immunology

H. **Intended Use:**
1. Intended use(s):
The EUROIMMUN Anti-SS-A ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against SS-A in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of Sjögren's syndrome and systemic lupus erythematosus, 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-SS-A ELISA (IgG) consists of a microwell ELISA plate coated with SS-A 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 SS-A ELISA
2. Predicate 510(k) number(s):
K922830

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to SS-A	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Antigen	Purified SS-A antigen	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-SS-A ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	6.1	4.2	2.0	1.3	0.8	0.3
Range of values:	5.9 – 6.4	4.0 – 4.5	1.9 – 2.1	1.2 – 1.4	0.7 – 0.8	0.3 – 0.3
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-SS-A ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	6.0	4.0	1.8	1.2	0.8	0.3
Range of values:	5.0 – 6.4	3.7 – 4.5	1.6 – 1.9	1.0 – 1.4	0.7 – 0.9	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-SS-A ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	4.6	5.6	5.6	0.3	0.9	1.1
Range of values:	4.4 – 4.8	5.1 – 6.2	5.1 – 6.0	0.3 – 0.4	0.9 – 0.9	1.1 – 1.2
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-SS-A ELISA (IgG) Ratio				
	Sample 7	Sample 8	Sample 9	Sample 10	Sample 11
n	10**	11**	10**	9**	11**
Mean value (x):	0.1	1.6	2.7	4.6	7.8
Range of values:	0.1 – 0.2	1.3 – 1.8	2.3 – 3.1	4.3 – 5.2	7.4 – 8.3
Expected result:	negative	positive	positive	positive	positive
% positive:	0%	100%	100%	100%	100%
% negative:	100%	0%	0%	0%	0%

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

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-SS-A 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-SS-A ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, nRNP/Sm, Sm, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-SS-A ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-SS-A concentrations (15 – 124 RU/ml) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 93 – 107 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 305 clinically characterized samples (63 SLE, 77 Sjögren's syndrome, 23 systemic sclerosis, 1 SSc/SS, 15 fibromyalgia, 26 myositis, 35 RA, 30 borreliosis, 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 54 men and 251 women. Age ranged from 14 to 85 years with an average age of 48 years. Anti-SS-A antibodies are expected in either Sjögren's syndrome or SLE. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-SS-A ELISA (IgG) and with the Inova Quanta Lite SS-A ELISA as the predicate device. Of the 9 discrepant samples negative in the EUROIMMUN test, 2 were from patients with Sjögren's syndrome and one from a SLE patient, the other 6 were from controls. All 3 discrepant samples positive in the EUROIMMUN test were from SLE patients.

All samples n = 305		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-SS-A ELISA (IgG)	positive	116	3
	negative	9	177

Negative agreement	177	/	180	=	98.3%	95% C.I.:	95.2%	- 99.7%
Positive agreement	116	/	125	=	92.8%	95% C.I.:	86.8%	- 96.7%
Overall agreement	293	/	305	=	96.1%	95% C.I.:	93.2%	- 98.0%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.99 and %recovery compared to serum was in the range of 85 to 104 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	16	16	16
Regression equation (y = plasma, x = serum)	y = -1.59 + 0.99 x	y = -1.47 + 0.99 x	y = -0.54 + 0.98
95% C.I. of intercept	-4.49 – 3.01	-4.62 – 1.36	-4.65 – 3.32
95% C.I. of slope	0.95 – 1.02	0.95 – 1.02	0.94 – 1.04
Coefficient of determination R^2	0.9972	0.9929	0.9956
Mean %recovery	97 %	95 %	98 %
Range of %recovery	90 – 102 %	85 – 102 %	93 – 104 %

Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 1026 clinically characterized samples (88 from SS patients, 404 from SLE patients and 534 from control groups) were investigated for anti-SS-A antibodies (IgG). With the EUROIMMUN Anti-SS-A ELISA (IgG) a prevalence of 73.9% (95% C.I.: 63.4 – 82.7%) was found in Sjögren's syndrome (clinical sensitivity) and a prevalence of 40.6% (95% C.I.: 35.8 – 45.6%) was found in SLE with a specificity of 94.8% (95% C.I.: 92.5 – 96.5%). Systemic sclerosis and myositis panels were considered for calculation of specificity, however, it has been reported that anti-SS-A antibodies may occur in these diseases [Antonioli 2002, Ghirardello 2005]. The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. *Clinical sensitivity:*

No.	Panel	n	Anti-SS-A ELISA (IgG)		
			positive	%	95% C.I.
1	Sjögren's syndrome	88	65	73.9%	63.4 – 82.7%
2	Systemic lupus erythematosus	404	164	40.6%	35.8 – 45.6%

b. *Clinical specificity:*

No.	Panel	n	Anti-SS-A ELISA (IgG)		
			negative	%	95% C.I.
3	Systemic sclerosis	81	75	92.6%	84.6 – 97.2%
4	Polymyositis/dermatomyositis	151	138	91.4%	85.7 – 95.3%
5	Rheumatoid arthritis	164	159	97.0%	93.0 – 99.0%
6	Mixed connective tissue diseases	45	41	91.1%	78.8 – 97.5%
7	Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	534	506	94.8%	92.5 – 96.5%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-SS-A antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	2
Negatives	198
Prevalence	1.0%
	Ratio
Lowest value	0.0
Highest value	4.4
Mean value	0.1
Std deviation	0.33

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.

Michael Locke — Signature
Dir. Regulatory Affairs — Title
12 June 2013 — Date

ATTACHMENT 1

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-SS-B autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-SS-B ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5110 - Antinuclear antibody immunological test system
2. Classification:
Class II
3. Product code:
LLL
4. Panel:
Immunology

H. **Intended Use:**
1. Intended use(s):
The EUROIMMUN Anti-SS-B ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against SS-B in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of Sjögren's syndrome and systemic lupus erythematosus, 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-SS-B ELISA (IgG) consists of a microwell ELISA plate coated with SS-B 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 SS-B ELISA
2. Predicate 510(k) number(s):
K922832

1100 The American Road, Morris Plains, New Jersey 07950
Tel: 973.656 1000 1.800.913.2022 Fax: 973.656 1098 E-mail: info@euroimmun.us

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to SS-B	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Antigen	Purified SS-B antigen	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-SS-B ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	4.1	2.9	1.3	0.8	0.6	0.4
Range of values:	4.0 – 4.3	2.8 – 3.1	1.1 – 1.4	0.7 – 0.9	0.5 – 0.7	0.4 – 0.5
Expected result:	positive	positive	positive	negative	negative	negative
% positive:	100%	100%	100%	0%	0%	0%
% negative:	0%	0%	0%	100%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-SS-B ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	4.7	3.2	1.5	1.1	0.7	0.5
Range of values:	4.2 – 5.3	3.0 – 3.7	1.3 – 1.7	1.0 – 1.1	0 5.-.0.7	0.4 – 0.5
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-SS-B ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	3.9	3.9	3.8	0.3	0.9	1.2
Range of values:	3.6 – 4.2	3.4 – 4.4	3.3 – 4.1	0.3 – 0.3	0.9 – 0.9	1.1 – 1.3
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-SS-B ELISA (IgG) Ratio		
	Sample 7	Sample 8	Sample 9
n	11**	11**	11**
Mean value (x):	2.6	4.2	7.7
Range of values:	2.3 – 3.1	3.2 – 4.8	7.0 – 8.8
Expected result:	positive	positive	positive
% positive:	100%	100%	100%
% negative:	0%	0%	0%

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

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-SS-B 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-SS-B ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, nRNP/Sm, Sm, SS-A, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-SS-B ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-SS-B concentrations (18 – 123 RU/ml) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 92 – 116 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 275 clinically characterized samples (57 SLE, 64 Sjögren's syndrome, 23 systemic sclerosis, 1 SSc/SS, 4 SLE/SS, 15 fibromyalgia, 26 myositis, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 55 men and 220 women. Age ranged from 12 to 83 years with an average age of 48 years. Anti-SS-B antibodies are expected in either Sjögren's syndrome or SLE. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-SS-B ELISA (IgG) and with the Inova Quanta Lite SS-B ELISA as the predicate device. Of the 3 discrepant samples negative in the EUROIMMUN test, one was from a Sjögren's syndrome patient and the other 2 were from controls. The discrepant sample positive in the EUROIMMUN test was from a Sjögren's syndrome patient.

All samples n = 275		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-SS-B ELISA (IgG)	positive	82	1
	negative	3	189

Negative agreement	189	/	190	=	99.5%	95% C.I.:	97.1%	- 100.0%
Positive agreement	82	/	85	=	96.5%	95% C.I.:	90.0%	- 99.3%
Overall agreement	271	/	275	=	98.5%	95% C.I.:	96.3%	- 99.6%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.99 and %recovery compared toserum was in the range of 78 to 116 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	16	16	16
Regression equation (y = plasma, x = serum)	y = -1.56 + 1.05 x	y = -0.22 + 1.06 x	y = 0.55 + 1.01
95% C.I. of intercept	-5.46 – 0.19	-3.29 – 2.28	-1.56 – 5.62
95% C.I. of slope	1.04 – 1.09	1.01 – 1.09	0.97 – 1.05
Coefficient of determination R^2	0.9972	0.9968	0.9951
Mean %recovery	100 %	105 %	101 %
Range of %recovery	78 – 116 %	98 – 116 %	81 – 110 %

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 1026 clinically characterized samples (88 from SS patients, 404 from SLE patients and 534 from control groups) were investigated for anti-SS-B antibodies (IgG). With the EUROIMMUN Anti-SS-B ELISA (IgG) a prevalence of 39.8% (95% C.I.: 29.5 – 50.8%) was found in Sjögren's syndrome and a prevalence of 13.9% (95% C.I.: 10.6 – 17.6%) was found in SLE with a specificity of 98.1% (95% C.I.: 96.6 – 99.1%). The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-SS-B ELISA (IgG)		
			positive	%	95% C.I.
1	Sjögren's syndrome	88	35	39.8%	29.5 – 50.8%
2	Systemic lupus erythematosus	404	56	13.9%	10.6 – 17.6%

b. Clinical specificity:

No.	Panel	n	Anti-SS-B ELISA (IgG)		
			negative	%	95% C.I.
3	Rheumatoid arthritis	164	163	99.4%	96.6 – 100.0%
4	Systemic sclerosis	81	77	95.1%	87.8 – 98.6%
5	Polymyositis/dermatomyositis	151	149	98.7%	95.3 – 99.8%
6	Mixed connective tissue diseases	45	42	93.3%	81.7 – 98.6%
7	Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	534	524	98.1%	96.6 – 99.1%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-SS-B antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	0
Negatives	200
Prevalence	0.0%
	Ratio
Lowest value	0.0
Highest value	0.2
Mean value	0.0
Std deviation	0.02

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.

Michael Locke — Signature
Dir. Regulatory Affairs — Title
12 June 2013 — Date

ATTACHMENT 1

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-Scl-70 autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-Scl-70 ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5110 - Antinuclear antibody immunological test system
2. Classification:
Class II
3. Product code:
LLL
4. Panel:
Immunology

H. **Intended Use:**
1. Intended use(s):
The EUROIMMUN Anti-Scl-70 ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against Scl-70 in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of 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-Scl-70 ELISA (IgG) consists of a microwell ELISA plate coated with Scl-70 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 Scl-70 ELISA
2. Predicate 510(k) number(s):
K924898

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to Scl-70	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Antigen	Purified Scl-70 antigen	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-Scl-70 ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	6.4	4.2	2.1	1.4	0.8	0.4
Range of values:	5.8 – 6.7	3.8 – 4.5	2.0 – 2.3	1.3 – 1.5	0.7 – 0.9	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-Scl-70 ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	6.2	4.2	1.9	1.2	0.8	0.3
Range of values:	5.7 – 7.0	3.7 – 4.7	1.7 – 2.2	1.1 – 1.4	0.7 – 0.9	0.2 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-Scl-70 ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	4.5	4.7	3.6	0.3	0.9	1.1
Range of values:	4.0 – 5.0	4.1 – 5.4	3.3 – 3.8	0.3 – 0.3	0.8 – 0.9	1.0 – 1.2
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-Scl-70 ELISA (IgG) Ratio		
	Sample 7	Sample 8	Sample 9
n	11**	10**	11**
Mean value (x):	3.0	4.8	6.2
Range of values:	2.5 – 3.7	4.3 – 5.7	5.3 – 6.8
Expected result:	negative	positive	positive
% positive:	0%	100%	100%
% negative:	100%	0%	0%

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

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-Scl-70 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-Scl-70 ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, nRNP/Sm, Sm, SS-A, SS-B, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-Scl-70 ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-Scl-70 concentrations (17 – 100 RU/ml) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 86 – 109 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 309 clinically characterized samples (158 systemic sclerosis, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 62 men and 247 women. Age ranged from 14 to 88 years with an average age of 53 years. Anti-Scl-70 antibodies are expected in systemic sclerosis. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-Scl-70 ELISA (IgG) and with the Inova Quanta Lite Scl-70 ELISA as the predicate device.

All samples n = 309		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-Scl-70 ELISA (IgG)	positive	125	0
	negative	0	184

Negative agreement	184	/	184	=	100.0%	95% C.I.:	98.0%	- 100.0%
Positive agreement	125	/	125	=	100.0%	95% C.I.:	97.1%	- 100.0%
Overall agreement	309	/	309	=	100.0%	95% C.I.:	98.8%	- 100.0%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.98 and %recovery compared toserum was in the range of 86 to 113 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	16	16	16
Regression equation (y = plasma, x = serum)	y = -0.58 + 1.00 x	y = 0.17 + 1.02 x	y = -0.87 + 0.97
95% C.I. of intercept	-3.25 – 2.24	-1.99 – 1.64	-2.02 – 1.35
95% C.I. of slope	0.94 – 1.06	0.98 – 1.06	0.94 – 1.03
Coefficient of determination R^2	0.9895	0.9930	0.9953
Mean %recovery	98 %	101 %	96 %
Range of %recovery	86 – 107 %	92 – 113 %	87 – 103 %

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 909 clinically characterized samples (280 from systemic sclerosis patients and 629 from control groups) were investigated for anti-Scl-70 antibodies (IgG). With the EUROIMMUN Anti-Scl-70 ELISA (IgG) a prevalence of 23.2% (95% C.I.: 18.4 – 28.6%) was found in systemic sclerosis, a prevalence of 59.4% (95% C.I.: 48.9 – 69.3%) was found in diffuse systemic sclerosis and a prevalence of 5.3% (95% C.I.: 2.0 – 11.2%) was found in limited systemic sclerosis with a specificity of 99.8% (95% C.I.: 99.1 – 100.0%).The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-Scl-70 ELISA (IgG)		
			positive	%	95% C.I.
1	Systemic sclerosis	280	65	23.2%	18.4 – 28.6%
1a	Diffuse systemic sclerosis (from panel 1)	96	57	59.4%	48.9 – 69.3%
1b	Limited systemic sclerosis (from panel 1)	113	6	5.3%	2.0 – 11.2%

b. Clinical specificity:

No.	Panel	n	Anti-Scl-70 ELISA (IgG)		
			negative	%	95% C.I.
2	Systemic lupus erythematosus	213	213	100.0%	98.3 – 100.0%
3	Polymyositis/dermatomyositis	26	26	100.0%	86.8 – 100.0%
4	Rheumatoid arthritis	164	163	99.4%	96.6 – 100.0%
5	Sjögren's syndrome	88	88	100.0%	95.9 – 100.0%
6	Mixed connective tissue diseases	45	45	100.0%	92.1 – 100.0%
7	Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	629	628	99.8%	99.1 – 100.0%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-Scl-70 antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	0
Negatives	200
Prevalence	0.0%
	Ratio
Lowest value	0.0
Highest value	0.1
Mean value	0.0
Std deviation	0.01

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.

Michael Locke — Signature
Dir. Regulatory Affairs — Title
12 June 2013 — Date

ATTACHMENT 1

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-Centromeres autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-Centromeres ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5110 - 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-Centromeres ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against Centromeres in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of limited form of progressive systemic sclerosis (CREST syndrome), 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-Centromeres ELISA (IgG) consists of a microwell ELISA plate coated with Centromeres 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 Centromeres ELISA
2. Predicate 510(k) number(s):
K003959

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to Centromeres	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Antigen	1:201	Recombinant CENP-A and CENP-B
Sample dilution	1 calibrator 2 controls: 1 positive, 1 negative	1:101
Calibrators and controls	10x concentrate	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	0.5 M sulphuric acid	40x concentrate
Stop solution	Serum or plasma (EDTA, Li-heparin, Citrate)	0.344 M sulphuric acid
Sample types	Ratio	Serum
Reported results	Ratio 1.0	Units
Cut off level	Qualitative	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-Centromeres ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	4.5	2.9	1.5	1.2	0.6	0.4
Range of values:	4.4 – 4.6	2.7 – 2.9	1.5 – 1.6	1.1 – 1.2	0.6 – 0.6	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-Centromeres ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	4.7	3.0	1.5	1.2	0.7	0.4
Range of values:	4.1 – 5.0	2.8 – 3.3	1.4 – 1.6	1.1 – 1.3	0.6 – 0.7	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-Centromeres ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	4.1	4.9	3.9	0.3	0.9	1.1
Range of values:	3.8 – 4.5	4.6 – 5.3	3.7 – 4.2	0.3 – 0.3	0.8 – 0.9	1.1 – 1.2
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-Centromeres ELISA (IgG) Ratio			
	Sample 7	Sample 8	Sample 9	Sample 10
n	8**	10**	11**	10**
Mean value (x):	2.8	6.2	6.8	8.4
Range of values:	2.2 – 3.3	5.5 – 7.0	4.9 – 8.3	7.8 – 9.1
Expected result:	positive	positive	positive	positive
% positive:	100%	100%	100%	100%
% negative:	0%	0%	0%	0%

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

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-Centromeres 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-Centromeres ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, nRNP/Sm, Sm, SS-A, SS-B, Scl-70, Jo-1, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-Centromeres ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-Centromeres concentrations (12 – 106 RU/ml) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 91 – 111 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 297 clinically characterized samples (144 systemic sclerosis, 2 CREST, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 61 men and 230 women. Age ranged from 2 to 87 years with an average age of 50 years. Anti-centromeres antibodies are expected in systemic sclerosis. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-Centromeres ELISA (IgG) and with the Inova Quanta Lite Centromere ELISA as the predicate device. All of the 5 discrepant samples were from control groups.

All samples n = 297		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-Centromeres ELISA (IgG)	positive	73	0
	negative	5	219

Negative agreement	219	/	219	=	100.0%	95% C.I.:	98.3%	- 100.0%
Positive agreement	73	/	78	=	93.6%	95% C.I.:	85.7%	- 97.9%
Overall agreement	292	/	297	=	98.3%	95% C.I.:	96.1%	- 99.5%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.99 and %recovery compared toserum was in the range of 84 to 108 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	16	16	16
Regression equation (y = plasma, x = serum)	y = -1.54 + 1.02 x	y = 0.02 + 0.92 x	y = -0.99 + 0.98
95% C.I. of intercept	-3.85 – -0.06	-2.13 – 0.99	-2.48 – 0.69
95% C.I. of slope	0.98 – 1.08	0.89 – 0.96	0.94 – 1.01
Coefficient of determination R^2	0.9958	0.9973	0.9978
Mean %recovery	98 %	93 %	96 %
Range of %recovery	84 – 108 %	83 – 101 %	88 – 107 %

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 877 clinically characterized samples (280 from systemic sclerosis patients and 597 from control groups) were investigated for anti-centromeres antibodies (IgG). With the EUROIMMUN Anti-Centromeres ELISA (IgG) a prevalence of 19.0% (95% C.I.: 13.9 – 24.9%) was found in systemic sclerosis, a prevalence of 7.3% (95% C.I.: 3.0 – 14.4%) was found in diffuse systemic sclerosis and a prevalence of 74.3% (95% C.I.: 65.3 – 82.1%) was found in limited systemic sclerosis with a specificity of 99.0% (95% C.I.: 97.8 – 99.6%). The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-Centromeres ELISA (IgG)		
			positive	%	95% C.I.
1	Systemic sclerosis	280	105	37.5%	31.8 – 43.5%
1a	Diffuse systemic sclerosis (from panel 1)	96	7	7.3%	3.0 – 14.4%
1b	Limited systemic sclerosis (from panel 1)	113	84	74.3%	65.3 – 82.1%

b. Clinical specificity:

No.	Panel	n	Anti-Centromeres ELISA (IgG)		
			negative	%	95% C.I.
2	Systemic lupus erythematosus	181	180	99.4%	97.0 – 100.0%
3	Polymyositis/dermatomyositis	26	26	100.0%	86.8 – 100.0%
4	Rheumatoid arthritis	164	163	99.4%	96.6 – 100.0%
5	Sjögren's syndrome	88	85	96.6%	90.4 – 99.3%
6	Mixed connective tissue diseases	45	44	97.8%	88.2 – 99.9%
7	Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	597	591	99.0%	97.8 – 99.6%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-centromeres antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	1
Negatives	199
Prevalence	0.5%
	Ratio
Lowest value	0.0
Highest value	3.0
Mean value	0.1
Std deviation	0.21

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.

Michael Locke — Signature
Dir. Regulatory Affairs — Title
12 June 2013 — Date

ATTACHMENT 1

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

A. **510(k)Number:**
K123261

B. **Purpose for Submission:**
New device

C. **Measurand:**
Anti-Jo-1 autoantibodies

D. **Type of Test:**
Qualitative enzyme immunoassay

E. **Applicant:**
EUROIMMUN US INC.

F. **Proprietary and Established Names:**
EUROIMMUN Anti-Jo-1 ELISA (IgG)

G. **Regulatory Information:**
1. Regulation:
21 CFR 866.5110 - Antinuclear antibody immunological test system
2. Classification:
Class II
3. Product code:
LLL
4. Panel:
Immunology

H. **Intended Use:**
1. Intended use(s):
The EUROIMMUN Anti-Jo-1 ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against Jo-1 in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of polymyositis and dermatomyositis, 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-Jo-1 ELISA (IgG) consists of a microwell ELISA plate coated with Jo-1 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 Jo-1 ELISA
2. Predicate 510(k) number(s):
K926562

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to Jo-1	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Antigen	Purified Jo-1 antigen	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-Jo-1 ELISA ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	6.4	4.3	1.8	1.0	0.8	0.4
Range of values:	6.1 – 6.8	4.1 – 4.5	1.6 – 1.9	1.0 – 1.1	0.7 – 0.8	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-Jo-1 ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	6.0	4.2	2.2	1.1	0.8	0.4
Range of values:	5.6 – 6.6	3.7 – 4.6	2.0 – 2.3	1.0 – 1.2	0.7 – 0.8	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-Jo-1 ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	5.1	3.9	2.0	0.3	0.9	1.1
Range of values:	4.6 – 5.4	3.5 – 4.4	1.9 – 2.2	0.3 – 0.4	0.9 – 0.9	1.1 – 1.2
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-Jo-1 ELISA (IgG) Ratio			
	Sample 7	Sample 8	Sample 9	Sample 10
n	10**	11**	11**	11**
Mean value (x):	2.6	4.0	7.4	8.2
Range of values:	1.9 – 3.1	3.2 – 4.6	6.4 – 8.6	7.7 – 8.9
Expected result:	positive	positive	positive	positive
% positive:	100%	100%	100%	100%
% negative:	0%	0%	0%	0%

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

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-Jo-1 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-Jo-1 ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against rib.P-P, nRNP/Sm, Sm, SS-A, SS-B, Scl-70, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-Jo-1 ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-Jo-1 concentrations (15 – 106 RU/ml) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 91 – 122 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 297 clinically characterized samples (143 myositis, 3 PM/SSc, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 75 men and 221 women. Age ranged from 14 to 84 years with an average age of 52 years. Anti-Jo-1 antibodies are expected in myositis. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-Jo-1 ELISA (IgG) and with the Inova Quanta Lite Jo-1 ELISA as the predicate device. Both discrepant samples were from myositis patients.

All samples n = 297		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-Jo-1 ELISA (IgG)	positive	64	1
	negative	1	231

Negative agreement	231	/	232	=	99.6%	95% C.I.:	97.6%	- 100.0%
Positive agreement	64	/	65	=	98.5%	95% C.I.:	91.7%	- 100.0%
Overall agreement	295	/	297	=	99.3%	95% C.I.:	97.6%	- 99.9%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.98 and %recovery compared toserum was in the range of 85 to 117 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	15	15	15
Concentration range (serum)	ratio 0.3 – 9.2	ratio 0.3 – 9.2	ratio 0.3 – 9.2
Concentration range (plasma)	ratio 0.3 – 8.7	ratio 0.4 – 8.5	ratio 0.3 – 8.9
Regression equation (y = plasma, x = serum)	y = -0.09 + 0.99 x	y = 0.09 + 0.93 x	y = 0.73 + 0.99
95% C.I. of intercept	-3.77 – 1.83	-0.69 – 1.94	-0.49 – 2.66
95% C.I. of slope	0.93 – 1.10	0.89 – 0.99	0.96 – 1.01
Coefficient of determination R^2	0.9856	0.9956	0.9982
Mean %recovery	101 %	95 %	103 %
Range of %recovery	85 – 117 %	87 – 113 %	94 – 114 %

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 876 clinically characterized samples (177 from myositis patients and 699 from control groups) were investigated for anti-Jo-1 antibodies (IgG). With the EUROIMMUN Anti-Jo-1 ELISA (IgG) a prevalence of 18.6% (95% C.I.: 13.2 – 25.2%) was found in myositis with a specificity of 99.6% (95% C.I.: 98.8 – 99.9%). The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-Jo-1 ELISA (IgG)		
			positive	%	95% C.I.
1	Polymyositis/dermatomyositis	177	33	18.6%	13.2 – 25.2%

b. Clinical specificity:

No.	Panel	n	Anti-Jo-1 ELISA (IgG)		
			negative	%	95% C.I.
2	Systemic lupus erythematosus	213	211	99.1%	96.6 – 99.9%
3	Rheumatoid arthritis	164	163	99.4%	96.6 – 100.0%
4	Systemic sclerosis	81	81	100.0%	95.5 – 100.0%
5	Sjögren's syndrome	88	88	100.0%	95.9 – 100.0%
6	Mixed connective tissue diseases	45	45	100.0%	92.1 – 100.0%
7	Fibromyalgia	15	15	100.0%	78.2 – 100.0%
8	Other autoimmune diseases	63	63	100.0%	94.3 – 100.0%
9	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	699	696	99.6%	98.8 – 99.9%

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 anti-Jo-1 antibodies (IgG) were analyzed in a panel of 200 samples from apparently healthy blood donors (120 men and 80 women with an average age of 40 y; age range: 19 – 68 y). The results are shown in the table below.

n	200
Positives	0
Negatives	200
Prevalence	0.0%
	Ratio
Lowest value	0.0
Highest value	0.2
Mean value	0.1
Std deviation	0.03

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.

Michael Locke — *Signature*
Dir. Regulatory Affairs — *Title*
12 June 2013 — *Date*

ATTACHMENT 1

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

A. 510(k)Number:
K123261

B. Purpose for Submission:
New device

C. Measurand:
Anti-ribosomal P-proteins autoantibodies

D. Type of Test:
Qualitative enzyme immunoassay

E. Applicant:
EUROIMMUN US INC.

F. Proprietary and Established Names:
EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG)

G. Regulatory Information:

1. Regulation:
   21 CFR 866.5110 - Antinuclear antibody immunological test system
2. Classification:
   Class II
3. Product code:
   MQA
4. Panel:
   Immunology

H. Intended Use:

1. Intended use(s):
   The EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against ribosomal P-proteins in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of systemic lupus erythematosus, 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-ribosomal P-proteins ELISA (IgG) consists of a microwell ELISA plate coated with ribosomal P-proteins 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 Ribosomal P ELISA
2. Predicate 510(k) number(s):
   K981237

3. Comparison with predicate:

Similarities		
Item	**New Device**	**Predicate Device**
Intended use	Detection of IgG antibodies to ribosomal P-proteins	Same
Technology	ELISA	Same
Assay platform	96-well microtiter plates	Same
Calibration	Relative units	Same
Conjugate	Anti-human IgG labeled with horseradish peroxidase	Same
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**
Assay format	Qualitative	„Semi-quantitative" (using low positive control)
Antigen	Purified ribosomal P antigen	Synthetic ribosomal P antigen
Sample dilution	1:201	1:101
Calibrators and controls	1 calibrator 2 controls: 1 positive, 1 negative	3 controls: 1 high positive, 1 low positive (used for calculation of results), 1 negative
Wash buffer	10x concentrate	40x concentrate
Stop solution	0.5 M sulphuric acid	0.344 M sulphuric acid
Sample types	Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Reported results	Ratio	Units
Cut off level	Ratio 1.0	20 Units

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 calibrators 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 using sera with different concentrations. Intra-assay reproducibility is based on 20 determinations and inter-assay reproducibility on 40 determinations performed in 10 different runs on 5 days with 2 runs per day, each run performed according to the package insert. The following results were obtained:

Intra-assay reproducibility

n = 20	Anti-ribosomal P-proteins ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	5.5	3.6	1.9	1.0	0.6	0.4
Range of values:	5.1 – 6.0	3.2 – 4.1	1.8 – 2.1	1.0 – 1.1	0.6 – 0.7	0.3 – 0.5
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	0%	0%
% negative:	0%	0%	0%	0%	100%	100%

Inter-assay reproducibility

n = 10 x 4	Anti-ribosomal P-proteins ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Mean value (x):	5.7	3.8	1.9	1.1	0.7	0.4
Range of values:	5.3 – 6.1	3.5 – 4.1	1.7 – 2.2	1.0 – 1.3	0.6 – 1.0	0.3 – 0.4
Expected result:	positive	positive	positive	positive	negative	negative
% positive:	100%	100%	100%	100%	2.5%	0%
% negative:	0%	0%	0%	0%	97.5%	100%

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. The following results were obtained:

Lot to lot reproducibility

	Anti-ribosomal P-proteins ELISA (IgG) Ratio					
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
n	6*	6*	6*	6*	6*	6*
Mean value (x):	3.2	4.5	2.2	0.3	0.9	1.1
Range of values:	2.8 – 3.6	4.2 – 4.8	2.0 – 2.4	0.3 – 0.4	0.8 – 0.9	1.0 – 1.2
Expected result:	positive	positive	positive	negative	negative	positive
% positive:	100%	100%	100%	0%	0%	100%
% negative:	0%	0%	0%	100%	100%	0%

	Anti-ribosomal P-proteins ELISA (IgG) Ratio		
	Sample 7	Sample 8	Sample 9
n	11**	11**	11**
Mean value (x):	4.8	5.2	7.6
Range of values:	3.9 – 5.3	4.4 – 6.2	6.5 – 8.5
Expected result:	positive	positive	positive
% positive:	100%	100%	100%
% negative:	0%	0%	0%

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

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-ribosomal P-proteins 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-ribosomal P-proteins ELISA was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA.

e. *Limit of detection:*
Not applicable.

f. *Analytical specificity:*
Cross-reactivity: The quality of the antigen coated on the plates ensures a high specificity of the ELISA. Cross reactivity was investigated using a panel of 30 sera serologically positive for antibodies against nRNP/Sm, Sm, SS-A, SS-B, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi. All 30 sera were negative in the Anti-ribosomal P-proteins ELISA (IgG), so no cross reactivity is expected.
Interference: To investigate the influence from hemoglobin, triglycerides and bilirubin, 5 different sera at different anti-ribosomal P-proteins concentrations (13 – 104 RU/ml) were spiked with potential interfering substances and were incubated with the test system according to the package insert. Interferences from rheumatoid factor were investigated similarly by spiking with a RF positive serum. The recovery in relation to the unspiked sample without interferent was calculated. The individual recovery was within the range of 84 – 115 %. No significant interference was observed for concentrations of up to 1000 mg/dl for hemoglobin, 2000 mg/dl for triglyceride, 40 mg/dl for bilirubin and 500 IU/ml for rheumatoid factor.

g. *Assay cut-off:*
Ratio 1.0

2. Comparison studies:

a. *Method comparison with predicate device:*
A comparison study was performed using 243 clinically characterized samples (90 SLE, 1 SLE/SS, 1 CLE, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy), obtained from different sources from Europe and North America. The panel consisted of 49 men and 187 women. Age ranged from 14 to 83 years with an average age of 47 years. Anti-ribosomal P-proteins antibodies are expected in SLE. The other disease groups serve as control cohorts. The samples were tested with the EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG) and with the Inova Quanta Lite Ribosomal P ELISA as the predicate device. All of the 10 discrepant samples were from patients with SLE, SLE/SS, and CLE.

All samples n = 243		Predicate ELISA positive	Predicate ELISA negative
EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG)	positive	28	10
	negative	0	205

Negative agreement	205	/	215	=	95.3%	95% C.I.:	91.6%	- 97.7%
Positive agreement	28	/	28	=	100.0%	95% C.I.:	87.7%	- 100.0%
Overall agreement	233	/	243	=	95.9%	95% C.I.:	92.6%	- 98.0%

b. *Matrix comparison:*
The usability of plasma was investigated using sample pairs each of serum and corresponding plasma (EDTA, Li-heparin, Citrate). Passing-Bablok regression was calculated for the comparison of serum to plasma. The regression equation is near the ideal correlation (intercept 0; slope 1.0) indicating equivalence of concentrations between serum and the corresponding plasma matrices. Coefficients of determination were found to be above 0.99 and %recovery compared toserum was in the range of 79 to 107 % (serum = 100 %).

	EDTA plasma	Li-heparin plasma	Citrate plasma
n	16	16	16
Regression equation (y = plasma, x = serum)	y = -0.98 + 1.02 x	y = 0.18 + 0.98 x	y = -1.79 + 0.99
95% C.I. of intercept	-5.78 – 0.56	-2.42 – 3.26	-5.55 – 0.25
95% C.I. of slope	0.99 – 1.06	0.92 – 1.03	0.97 – 1.04
Coefficient of determination R^2	0.9966	0.9939	0.9959
Mean %recovery	97 %	98 %	95 %
Range of %recovery	79 – 107 %	80 – 107 %	85 – 107 %

3. Clinical studies:
Clinical studies were performed in cooperation with different sites. In total 876 clinically characterized samples (376 from SLE patients and 500 from control groups) were investigated for anti-ribosomal P-proteins antibodies (IgG). With the EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG) a prevalence of 5.3% (95% C.I.: 3.3 – 8.1%) was found in SLE with a specificity of 99.2% (95% C.I.: 98.0 – 99.8%). The results are shown in the table below. 95% C.I. are calculated by the exact method.

a. Clinical sensitivity:

No.	Panel	n	Anti-ribosomal P-proteins ELISA (IgG)		
			positive	%	95% C.I.
1	Systemic lupus erythematosus	376	20	5.3%	3.3 – 8.1%

b. Clinical specificity:

No.	Panel	n	Anti-ribosomal P-proteins ELISA (IgG)		
			negative	%	95% C.I.
2	Polymyositis/dermatomyositis	151	149	98.7%	95.3 – 99.8%
3	Rheumatoid arthritis	90	90	100.0%	96.0 – 100.0%
4	Systemic sclerosis	66	66	100.0%	94.6 – 100.0%
5	Sjögren's syndrome	55	54	98.2%	90.3 – 100.0%
6	Mixed connective tissue diseases	45	44	97.8%	88.2 – 99.9%
7	Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
8	Borreliosis	30	30	100.0%	88.4 – 100.0%
	Total	500	496	99.2%	98.0 – 99.8%

*from the following groups: AIH (n = 8), PBC (n = 9), Grave's disease (n = 12), Hashimoto (n = 11), celiac disease (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 anti-ribosomal P-proteins antibodies (IgG) were analyzed in a panel of 150 samples from apparently healthy blood donors (79 men and 71 women with an average age of 38 y; age range: 18 – 67 y). The results are shown in the table below.

n	150
Positives	0
Negatives	150
Prevalence	0.0%
	Ratio
Lowest value	0.0
Highest value	0.7
Mean value	0.1
Std deviation	0.08

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.

Michael Locke — Signature
Dir. Regulatory Affairs — Title
12 June 2013 — Date

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

June 12, 2013

THE BINDING SITE GROUP LTD
C/O MS. KATHRYN KOHL
MANAGING DIRECTOR
1100 THE AMERICAN ROAD
MORRIS PLAINS, NJ 07950

Re: K123261
Trade/Device Name: Euroimmun Anti-nRNP/Sm ELISA (IgG)
Euroimmun Anti-Sm ELISA (IgG)
Euroimmun Anti-SS-A ELISA (IgG)
Euroimmun Anti-SS-B ELISA (IgG)
Euroimmun Anti-Scl-70 ELISA (IgG)
Euroimmun Anti-Centromeres ELISA (IgG)
Euroimmun Anti-Jo-1 ELISA (IgG)
Euroimmun Anti-Ribosomal P-Proteins ELISA (IgG)
Regulation Number: 21 CFR 866.5110
Regulation Name: Antinuclear Antibody Immunological Test System
Regulatory Class: II
Product Code: LKO, LKP, LLL, LJM, MQA
Dated: May 16, 2013
Received: May 17, 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 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 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. 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

Enclosure

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-ribosomal P-proteins ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against ribosomal P-proteins in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of systemic lupus erythematosus, 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): K123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-nRNP/Sm ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-nRNP/Sm ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against nRNP/Sm in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of mixed connective tissue diseases and systemic lupus erythematosus, 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)

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

510(k): k123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-Sm ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-Sm ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against Sm in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of systemic lupus erythematosus, 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)

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Concurrence of CDRH; Office of In Vitro Diagnostics and Radiological Health (OIR)

Maria M. Chan -S

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Office of In Vitro Diagnostics and Radiological Health

510(k): k123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-SS-A ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-SS-A ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against SS-A in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of Sjögren's syndrome and systemic lupus erythematosus, 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)

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Concurrence of CDRH; Office of In Vitro Diagnostics and Radiological Health (OIR)

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Office of In Vitro Diagnostics and Radiological Health

510(k): k123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-SS-B ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-SS-B ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against SS-B in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of Sjögren's syndrome and systemic lupus erythematosus, 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)

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Concurrence of CDRH; Office of In Vitro Diagnostics and Radiological Health (OIR)

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

510(k): k123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-Scl-70 ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-Scl-70 ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against Scl-70 in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of 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)

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Concurrence of CDRH; Office of In Vitro Diagnostics and Radiological Health (OIR)

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

510(k): k123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-Centromeres ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-Centromeres ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against centromeres in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of limited form of progressive systemic sclerosis (CREST syndrome), 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)

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Maria M. Chan -S

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

510(k): k123261

Indications for Use

510(k) Number (if known): k123261

Device Name: Anti-Jo-1 ELISA (IgG)

Indications For Use:

The EUROIMMUN Anti-Jo-1 ELISA (IgG) test kit is intended for the qualitative determination of IgG class autoantibodies against Jo-1 in human serum and plasma (EDTA, Li-heparin, Citrate). It is used as an aid in the diagnosis of polymyositis and dermatomyositis, 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)

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Maria M. Chan -S

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

510(k): k123261