510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k123261

B. Purpose for Submission:

New Device

C. Measurand:

Anti-nRNP/Sm, anti-Sm, anti-SS-A, anti-SS-B, anti-Scl-70, anti-Centromeres, anti-Jo-1, anti-Ribosomal P-proteins IgG antibodies (bundled)

D. Type of Test:

Qualitative, ELISA

E. Applicant:

EUROIMMUN US Inc.

F. Proprietary and Established Names:

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)

G. Regulatory Information:

1. Regulation section:

   21 CFR§866.5110 – Antinuclear Antibody Immunological Test System

2. Classification:

   Class II

3. Product code:

Device	Product Code
Anti-nRNP/Sm ELISA (IgG)	LKO, Anti-RNP Antibody, Antigen, Control
Anti-Sm ELISA (IgG)	LKP, Anti-Sm Antibody, Antigen and Control
Anti-SS-A ELISA (IgG)	LLL, Extractable antinuclear antibody, antigen and control
Anti-SS-B ELISA (IgG)	
Anti-Scl-70 ELISA (IgG)	
Anti-Jo-1 ELISA (IgG)	
Anti-Centromeres ELISA (IgG)	LJM, Antinuclear antibody (Enzyme-labeled), antigen, control
Anti-Ribosomal P-Proteins ELISA (IgG)	MQA, Anti-ribosomal P antibodies

4. Panel:

   Immunology (82)

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.

   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.

   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.

   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.

   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.

   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.

   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.

   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 use statement(s):

   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 kit contains the following materials:

Device specific reagents: Microwell ELISA plate coated with antigen (nRNP-Sm, Sm, SS-A, SS-B, Scl-70, Jo-1, ribosomal P-proteins, centromeres, respectively)

Other reagents: 1 calibrator (20 RU/mL, IgG, human), positive and negative control (IgG, human), horseradish peroxidase (HRP)-labeled anti-human IgG conjugate, sample buffer concentrate, TMB chromogen/substrate solution and stop solution.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) number(s):

   INOVA Quanta Lite RNP ELISA (k922833)
   INOVA Quanta Lite Sm ELISA (k922831)
   INOVA Quanta Lite SS-A ELISA (k922830)
   INOVA Quanta Lite SS-B ELISA (k922832)
   INOVA Quanta Lite Scl-70 ELISA (k924898)
   INOVA Quanta Lite Jo-1 ELISA (k926562)
   INOVA Quanta Lite ribosomal P-proteins (k981237)
   INOVA Quanta Lite Centromeres ELISA (k003959)

2. Comparison with predicate:

Similarities			
Item		Device	Predicate
Intended Use	Anti-nRNP/Sm ELISA	Detection of IgG to nRNP/Sm	Same
	Anti-Sm ELISA	Detection of IgG to Sm	Same
	Anti-SS-A ELISA	Detection of IgG to SS-A	Same
	Anti-SS-B ELISA	Detection of IgG to SS-B	Same
	Anti-Scl-70 ELISA	Detection of IgG to Scl-70	Same
	Anti-Centromeres ELISA	Detection of IgG to centromeres	Same
	Anti-Jo-1 ELISA	Detection of IgG to Jo-1	Same
	Anti-Ribosomal P-Proteins ELISA	Detection of IgG to ribosomal P-Protein	Same

Similarities			
Item		Device	Predicate
Antigen	Anti-RNP/Sm ELISA	Purified U1-nRNP/Sm	Same
	Anti-Sm ELISA	Purified Sm	Same
	Anti-SS-A ELISA	Purified SS-A	Same
	Anti-SS-B ELISA	Purified SS-B	Same
	Anti-Scl-70 ELISA	Purified Scl-70	Same
	Anti-Jo-1 ELISA	Purified Jo-1	Same
Assay platform		96-well microtiter plates	Same
Substrate		TMB	Same
Method		ELISA	Same

Differences			
Item		Device	Predicate
Assay format		Qualitative	Semi-quantitative
Antigen	Anti-Centromeres ELISA	Recombinant centromeres protein B	Recombinant CENP-A and CENP-B
	Anti-Ribosomal P-Proteins ELISA	Purified ribosomal P antigen	Synthetic ribosomal P antigen
Conjugate		Rabbit anti-human IgG labeled with HRP	Goat anti-human IgG labeled with HRP
Samples		Serum or plasma (EDTA, Li-heparin, Citrate)	Serum
Sample dilution		1:201	1:101
Calibrator		1 Calibrator: 20 RU/mL	None The low positive control is used for single point calibration
Control		2 Controls: 1 positive and 1 negative	3 Controls: 1 high positive, 1 low positive, 1 negative
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 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 (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Intra- and inter-assay reproducibility: The reproducibility of each of eight tests was investigated for in the intra- and inter-assay using sera with values at different ratio. The intra-assay based on 20 determinations and the inter-assay based on 40 determinations performed in 5 days, 2 runs/day with 4 replicate/run. The precision data for all samples was analyzed to generate a summary of the qualitative reproducibility of the assay. The results are summarized below:

Anti-nRNP/Sm ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	5.1	100%	5.2	100%
2	3.3	100%	3.3	100%
3	1.9	100%	1.8	100%
4	1.2	100%	1.1	100%
5	0.8	0%	0.8	0%
6	0.4	0%	0.4	0%
Anti-Sm ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	5.7	100%	5.8	100%
2	3.7	100%	3.9	100%
3	2.0	100%	1.7	100%
4	1.2	100%	1.1	100%
5	0.8	0%	0.8	2.5%
6	0.4	0%	0.4	0%
Anti-SS-A ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	6.1	100%	6.0	100%
2	4.2	100%	4.0	100%
3	2.0	100%	1.8	100%
4	1.3	100%	1.2	100%
5	0.8	0%	0.8	0%
6	0.3	0%	0.3	0%

Anti-SS-B ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	4.1	100%	4.7	100%
2	2.9	100%	3.2	100%
3	1.3	100%	1.5	100%
4	0.8	0%	1.1	100%
5	0.6	0%	0.7	0%
6	0.4	0%	0.5	0%
Anti-Scl-70 ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	6.4	100%	6.2	100%
2	4.2	100%	4.2	100%
3	2.1	100%	1.9	100%
4	1.4	100%	1.2	100%
5	0.8	0%	0.8	0%
6	0.4	0%	0.3	0%
Anti-Centromeres ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	4.5	100%	4.7	100%
2	2.9	100%	3.0	100%
3	1.5	100%	1.5	100%
4	1.2	100%	1.2	100%
5	0.6	0%	0.7	0%
6	0.4	0%	0.4	0%
Anti-Jo-1 ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	6.4	100%	6.0	100%
2	4.3	100%	4.2	100%
3	1.8	100%	2.2	100%
4	1.0	100%	1.1	100%
5	0.8	0%	0.8	0%
6	0.4	0%	0.4	0%
Anti-ribosomal P-protein ELISA (IgG)				
Sample	Intra-assay (n=20)		Inter-assay (n=40)	
	Mean (Ratio)	% of positive	Mean (Ratio)	% of positive
1	5.5	100%	5.7	100%
2	3.6	100%	3.8	100%
3	1.9	100%	1.9	100%
4	1.0	100%	1.1	100%
5	0.6	0%	0.7	0%
6	0.4	0%	0.4	0%

Lot-to-Lot reproducibility: The lot to lot reproducibility was also investigated by using various lots with multiple samples at different ratio. The results are

summarized in the following tables.

Anti-nRNP/Sm ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=11 (11 lots x 1 run)	
	Mean ratio	% of Positive		Mean ratio	% of Positive
1	3.6	100%	7	0.2	0%
2	2.5	100%	8	3.4	100%
3	5.4	100%	9	5.2	100%
4	0.4	0%	10	6.6	100%
5	0.9	0%	11	8.5	100%
6	1.1	100%			
Anti-Sm ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=n (n lots x 1 run)	
	Mean ratio	% of Positive		Mean ratio (N)	% of Positive
1	3.6	100%	7	0.1 (9)	0 %
2	3.4	100%	8	1.9 (10)	100%
3	3.1	100%	9	3.4 (10)	100%
4	0.3	0%	10	5.7 (9)	100%
5	0.9	0%	11	8.3 (10)	100%
6	1.2	100%			
Anti-SS-A ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=n lots x 1 run	
	Mean Ratio	% of Positive		Mean Ratio (N)	% of Positive
1	4.6	100%	7	0.1 (10)	0 %
2	5.6	100%	8	1.6 (11)	100%
3	5.6	100%	9	2.7 (10)	100%
4	0.3	0%	10	4.6 (9)	100%
5	0.9	0%	11	7.8 (11)	100%
6	1.1	100%			
Anti-SS-B ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=11 (11 lots x 1 run)	
	Mean Ratio	% of Positive		Mean Ratio	% of Positive
1	3.9	100%	7	2.6	100%
2	3.9	100%	8	4.2	100%
3	3.8	100%	9	7.7	100%
4	0.3	0%			
5	0.9	0%			
6	1.2	100%			

Anti-Scl-70 ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=n (n lots x 1 run)	
	Mean Ratio	% of Positive		Mean Ratio (N)	% of Positive
1	4.5	100%	7	3.0 (11)	100%
2	4.7	100%	8	4.8 (10)	100%
3	3.6	100%	9	6.2 (11)	100%
4	0.3	0%			
5	0.9	0%			
6	1.1	100%			
Anti-Centromeres ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=n (n lots x 1 run)	
	Mean Ratio	% of Positive		Mean Ratio (N)	% of Positive
1	4.1	100%	7	2.8 (8)	100%
2	4.9	100%	8	6.2 (10)	100%
3	3.9	100%	9	6.8 (11)	100%
4	0.3	0%	10	8.4 (10)	100%
5	0.9	0%			
6	1.1	100%			
Anti-Jo-1 ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=n (n lots x 1 run)	
	Mean Ratio	% of Positive		Mean Ratio (N)	% of Positive
1	5.1	100%	7	2.6 (10)	100%
2	3.9	100%	8	4.0 (11)	100%
3	2.0	100%	9	7.4 (11)	100%
4	0.3	0%	10	8.2 (11)	100%
5	0.9	0%			
6	1.1	100%			
Anti-Ribosomal P-protein ELISA (IgG)					
Sample No.	N=6 (3 lots x 2 runs)		Sample No.	N=11 (11 lots x 1 run)	
	Mean Ratio	% of Positive		Mean Ratio	% of Positive
1	3.2	100%	7	4.8	100%
2	4.5	100%	8	5.2	100%
3	2.2	100%	9	7.6	100%
4	0.3	0%			
5	0.9	0%			
6	1.1	100%			

b. Linearity/assay reportable range:

Not applicable

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

Traceability: There is no reference standard for these analytes. The reactivity of each of eight devices was verified using the ANA reference panel of the CDC (Centers for

Disease Control and Prevention, Atlanta, USA). The ANA reference panel include native DNA, SS-B, RNP/SS-B/SS-A, RNP, Sm, U3-RNP, SS-A, Centromeres, Scl-70, Jo-1, PM-Scl, and ribosomal P-proteins. All eight devices showed the expected reactivity against the reference panel.

Calibrator and Controls: The cut-off calibrator and controls are derived from human serum and match pre-specified performance criteria. Each lot of cut-off calibrator and controls are traceable to a master lot.

Stability: Real time stability studies were conducted using three production lots of kit reagents. The results support a shelf life claim of 12 months for all components when stored at 2 – 8°C. The opened reagents are stable for 6 months when stored at 2 – 8°C. The reconstituted Wash Buffer is stable for up to 28 days.

d. Detection limit:

Not applicable

e. Analytical specificity:

Cross reactivity: To investigate the quality of the antigen coated on the plates to ensure a high specificity of the ELISA, cross reactivity was investigative using a panel of 30 sera containing antibodies serologically positive against the known antigens. The panel of antibodies used to test antigen coated for each device listed in the following table:

Device	Panel of antibodies used for Cross Reactivity Study
Anti-nRNP/Sm	Anti-Ribosomal P-protein, SS-A, SS-B, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi
Anti-Sm	Anti-Ribosomal P-protein, nRNP/Sm, SS-A, SS-B, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi
Anti-SS-A	Anti-Ribosomal P-protein, nRNP/Sm, Sm, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi
Anti-SS-B	Anti-Ribosomal P-protein, nRNP/Sm, Sm, SS-A, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi
Anti-Scl-70	Anti-Ribosomal P-protein, nRNP/Sm, Sm, SS-A, SS-B, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi
Anti-Centromeres	Anti-Ribosomal P-protein, nRNP/Sm, Sm, SS-A, SS-B, Scl-70, Jo-1, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi

Device	Panel of antibodies used for Cross Reactivity Study
Anti-Jo-1	Anti-Ribosomal P-protein, nRNP/Sm, Sm, SS-A, SS-B, Scl-70, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi
Anti-ribosomal P-proteins	Anti-nRNP/Sm, Sm, SS-A, SS-B, Scl-70, Jo-1, centromeres, Rubella virus, Measles virus, Herpes simplex virus type 1 and Borrelia burgdorferi

No cross reactivity is observed with the tested antibody panel for each device.

Endogenous interference: For each device, interference testing was performed by using 5 serum samples with various ratio of each analyte (negative, positive and near to cut-off). Samples were spiked with potential interfering substances, hemoglobin (250, 500, and 1000 mg/dL), triglycerides (500, 1000, 2000 mg/dL), bilirubin (10, 20, and 40 mg/dL) and rheumatoid factor (RF) (500 IU/mL). Recoveries of all spiked sample/interferent combinations compared to the measurements for unspiked samples were calculated. 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 RF,

f. Assay cut-off:

For each device, the assay cut-off is OD ratio of 1.0. Results $\geq$ 1.0 are positive, and results < 1.0 are negative.

2. Comparison studies:

a. Method comparison with predicate device:

Anti-nRNP/Sm ELISA (IgG): A total of 287 samples were tested with EUROIMMUN Anti-nRNP/Sm ELISA (IgG) and predicate device. The samples were from 52 mixed connective tissue disease (MCTD), 69 systemic lupus erythrematosus (SLE), 51 Sjögren's syndrome, 15 systemic sclerosis, 15 fibromyalgia, 35 rheumatoid arthritis (RA), 30 borreliosis, and 20 healthy individuals. Anti-nRNP/Sm antibodies are expected in either MCTD or SLE. The other disease groups serve as control cohorts. The results are shown in the table below. Of the 8 discrepant samples, one was from a MCTD patient and the other 7 were from controls.

		Inova Quanta Lite RNP ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-nRNP/Sm ELISA (IgG)	Positive	83	0	83
	Negative	8	196	204
	Total	91	196	287

Positive agreement: 91.2% (83/91) (95% CI: 83.4 – 96.1%)
Negative agreement: 100.0% (196/196) (95% CI: 98.1 – 100%)
Overall agreement: 97.2% (279/287) (95% CI: 94.6 – 98.8%)

Anti-Sm ELISA (IgG): A total of 294 clinical samples were tested with EUROIMMUN Anti-nRNP/Sm ELISA (IgG) and predicate device. The samples were from 128 SLE, 51 Sjögren's syndrome, 15 systemic sclerosis, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy individuals. The results are shown in the table below. Anti-Sm antibodies are expected in SLE. The other disease groups serve as control cohorts. 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.

		Inova Quanta Lite Sm ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-Sm ELISA (IgG)	Positive	37	5	42
	Negative	7	245	252
	Total	44	250	294

Positive agreement: 84.1% (37/44) (95% CI: 69.9 – 93.4%)
Negative agreement: 98.0% (245/250) (95% CI: 95.4 – 99.3%)
Overall agreement: 97.2% (279/287) (95% CI: 94.6 – 98.8%)

Anti-SS-A ELISA IgG:

A total of 305 samples were tested with EUROIMMUN Anti-SS-A ELISA (IgG) and predicate device. The samples were from 63 SLE, 77 Sjögren's syndrome, 23 systemic sclerosis, 1 systemic sclerosis/ Sjögren's syndrome, 15 fibromyalgia, 26 myositis, 35 RA, 30 borreliosis, 20 healthy individuals. Anti-SS-A antibodies are expected in either Sjögren's syndrome or SLE. The other disease groups serve as control cohorts. 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.

		Inova Quanta Lite SS-A ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-SS-A ELISA (IgG)	Positive	116	3	119
	Negative	9	177	186
	Total	125	180	305

Positive agreement: 92.8% (116/125) (95% CI: 86.8 – 96.7%)
Negative agreement: 98.3% (177/180) (95% CI: 95.2 – 99.7%)
Overall agreement: 96.1% (293/305) (95% CI: 93.2 – 98.0%)

Anti-SS-B IgG:

A total of 275 samples were tested with EUROIMMUN Anti-SS-B ELISA (IgG) and predicate device. The samples were from 57 SLE, 64 Sjögren's syndrome, 23 systemic sclerosis, 1 systemic sclerosis/Sjögren's syndrome, 4 SLE/ Sjögren's syndrome, 15 fibromyalgia, 26 myositis, 35 RA, 30 borreliosis and 20 healthy individuals. Anti-SS-B antibodies are expected in either Sjögren's syndrome or SLE. The other disease groups serve as control cohorts. Of 9 discrepant samples negative in the EUROIMMUN test, 2 were from Sjögren's syndrome patients and 1 were from

a SLE patient, the other 6 were from controls. All 3 discrepant samples positive in the ERUOIMMUN test were from SLE patients.

		Inova Quanta Lite SS-A ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-SS-A ELISA (IgG)	Positive	116	3	119
	Negative	9	177	186
	Total	125	180	305

Positive agreement: 84.1% (37/44) (95% CI: 69.9 – 93.4%)
Negative agreement: 98.0% (245/250) (95% CI: 95.4 – 99.3%)
Overall agreement: 97.2% (279/287) (95% CI: 94.6 – 98.8%)

Anti-Scl-70 IgG:

A total of 309 samples were tested with EUROIMMUN Anti-Scl-70 ELISA (IgG) and predicate device. The samples were from 158 systemic sclerosis, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy individuals. Anti-Scl-70 antibodies are expected in systemic sclerosis. The other disease groups serve as control cohorts.

		Inova Quanta Lite Scl-70 ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-Scl-70 ELISA (IgG)	Positive	125	0	125
	Negative	0	184	184
	Total	125	184	309

Positive agreement: 100.0% (125/125) (95% CI: 97.1 – 100%)
Negative agreement: 100.0% (184/184) (95% CI: 98.0 – 100%)
Overall agreement: 100.0% (309/309) (95% CI: 98.9 – 100%)

Anti-Centromeres ELISA IgG:

A total of 297 samples were tested with EUROIMMUN Anti-Centromeres ELISA (IgG) and predicate device. The samples were from 144 systemic sclerosis, 2 CREST, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy individuals. Anti-Centromeres antibodies are expected in systemic sclerosis. The other disease groups serve as control cohorts. All of the 5 discrepant samples were from control groups.

		Inova Quanta Lite Centromere ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-Centromeres ELISA (IgG)	Positive	73	0	73
	Negative	5	219	224
	Total	78	219	297

Positive agreement: 93.6% (73/78) (95% CI: 85.7 – 97.9%)
Negative agreement: 100.0% (219/219) (95% CI: 98.3 – 100%)
Overall agreement: 98.3% (292/297) (95% CI: 96.1 – 99.5%)

Anti-Jo-1 ELISA IgG:

A total of 297 samples were tested with EUROIMMUN Anti-Jo-1 ELISA (IgG) and predicate device. The samples were from 143 myositis, 3 Polymyositis/systemic sclerosis, 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy individuals. Anti-Jo-1 antibodies are expected in myositis. The other disease groups serve as control cohorts. Both discrepant samples were from myositis patients.

		Inova Quanta Lite Jo-1 ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-Jo-1 ELISA (IgG)	Positive	64	1	65
	Negative	1	231	232
	Total	65	232	297

Positive agreement: 98.5% (64/65) (95% CI: 91.7 – 100%)
Negative agreement: 99.6% (231/232) (95% CI: 97.6 – 100%)
Overall agreement: 99.3% (295/297) (95% CI: 97.6 – 99.9%)

Anti-ribosomal P-proteins ELISA (IgG):

A total of 243 samples were tested with EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG) and predicate device. The samples were from 90 SLE, 1 SLE/Sjögren's syndrome, 1 cutaneous lupus erythematosus (CLE), 51 Sjögren's syndrome, 15 fibromyalgia, 35 RA, 30 borreliosis and 20 healthy individuals. Anti-ribosomal P-proteins antibodies are expected in SLE. The other disease groups serve as control cohorts. All of the 10 discrepant samples were from patients with SLE, SLE/Sjögren's syndrome, and CLE.

		Inova Quanta Lite Ribosomal P ELISA		
		Positive	Negative	Total
EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG)	Positive	28	10	38
	Negative	0	205	205
	Total	28	215	243

Positive agreement: 100.0% (28/28) (95% CI: 87.7 – 100%)
Negative agreement: 95.3% (205/215) (95% CI: 91.6 – 97.7%)
Overall agreement: 95.9% (233/243) (95% CI: 92.6 – 98.0%)

b. Matrix comparison:

The matrix comparison was evaluated using sample pairs of serum and corresponding plasma (EDTA, Li-heparin, and Citrate) tested with each device. The results are summarized in the following table:

	Matrix compared to serum		
	EDTA	Li-Heparin	Citrate
Anti-nRNP/Sm ELISA			
N	15	15	15
Ratio range (serum)	0.3 – 10.4	0.3 – 10.4	0.3 – 10.4
Ratio range (plasma)	0.3 – 10.0	0.3 – 11.1	0.3 – 11.5
% recovery	91 – 117%	92 – 114%	93 – 120%
Anti-Sm ELISA			
N	16	16	16
Ratio range (serum)	0.2 – 9.9	0.2 – 9.9	0.2 – 9.9
Ratio range (plasma)	0.3 – 9.6	0.2 – 9.4	0.2 – 9.6
% recovery:	94 – 115%	90 – 111%	89 – 118%
Anti-SS-A ELISA			
N	22	22	22
Ratio range (serum)	0.2 – 9.8	0.2 – 9.8	0.2 – 9.8
Ratio range (plasma)	0.2 – 9.9	0.2 – 9.9	0.2 – 9.8
% recovery:	90 – 106%	85 – 117%	89 – 116%
Anti-SS-B ELISA			
N	16	15	15
Ratio range (serum)	0.3 – 9.4	0.3 – 9.4	0.3 – 9.4
Ratio range (plasma)	0.2 – 10.0	0.3 – 10.0	0.2 – 9.4
% recovery:	78 – 116%	98 – 116%	81 – 110%
Anti-Scl-70 ELISA			
N	18	18	18
Ratio range (serum)	0.3 – 9.7	0.3 – 9.7	0.3 – 9.7
Ratio range (plasma)	0.3 – 9.7	0.3 – 9.8	0.4 – 9.7
% recovery:	86 – 107%	92 – 113%	87 – 106%
Anti-Centromeres ELISA			
N	16	16	16
Ratio range (serum)	0.3 – 9.4	0.3 – 9.4	0.3 – 9.4
Ratio range (plasma)	0.3 – 9.2	0.3 – 8.4	0.3 – 9.2
% recovery:	84 – 108%	83 – 101%	88 – 107%
Anti-Jo-1 ELISA			
N	15	15	15
Ratio range (serum)	0.3 – 9.2	0.3 – 9.2	0.3 – 9.2
Ratio range (plasma)	0.3 – 8.7	0.4 – 8.5	0.3 – 8.9
% recovery:	85 – 117%	87 – 113%	94 – 114%
Anti-Ribosomal P-protein ELISA			
N	17	17	17
Ratio range (serum)	0.3 – 9.6	0.3 – 9.6	0.3 – 9.6
Ratio range (plasma)	0.3 – 9.4	0.3 – 9.7	0.3 – 9.5
% recovery:	79 – 107%	80 – 107%	85 – 107%

3. Clinical studies:

a. Clinical Sensitivity/Clinical Specificity:

Anti-nRNP/Sm IgG: A total of 1046 clinically characterized samples (65 MCTD, 404 SLE, and 577 from other control diseases) were evaluated for clinical sensitivity and specificity with EUROIMMUN anti-nRNP/Sm ELISA (IgG). The results are summarized in the following table.

Anti-nRNP/Sm ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
MCTD	65	65	100.0%	94.5 – 100.0%
SLE	404	94	23.3%	19.2 – 27.7%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
RA	164	164	100.0%	97.8 – 100.0%
Polymyositis/ Dermatomyositis	151	143	94.7%	89.8 – 97.7%
Systemic sclerosis	81	81	100.0%	95.5 – 100.0%
Sjögren's syndrome	88	86	97.7%	92.0 – 99.7%
Other autoimmune diseases*	63	62	98.4%	91.5 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	577	566	98.1%	96.6 – 99.0%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-Sm ELISA IgG: A total of 1038 clinically characterized samples (414 SLE, and 626 other control diseases) were evaluated for clinical sensitivity and specificity with EUROIMMUN anti-Sm ELISA (IgG). The results are summarized in the following table:

Anti-Sm ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
SLE	414	47	11.4%	8.5 – 14.8%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
RA	164	164	100.0%	97.8 – 100.0%
Systemic sclerosis	81	81	100.0%	95.5 – 100.0%
Sjögren's syndrome	88	88	100.0%	95.9 – 100.0%
Polymyositis/Dermatomyositis	151	151	100.0%	97.6 – 100.0%

MCTD	45	39	86.7%	73.2 – 94.9%
Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	622	616	99.0%	97.9 – 99.6%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-SS-A ELISA: A total of 1026 clinically characterized samples (88 from Sjögren's syndrome patients, 404 from SLE, and 534 from control diseases) were evaluated for clinical sensitivity and specificity with EUROIMMUN anti-SS-A ELISA (IgG). The results are summarized in the following table:

Anti-SS-A ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
Sjögren's syndrome	88	65	73.9%	63.4 – 82.7%
SLE	404	164	40.6%	35.8 – 45.6%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
Systemic sclerosis	81	75	92.6%	84.6 – 97.2%
Polymyositis/Dermatomyositis	151	138	91.4%	85.7 – 95.3%
RA	164	159	97.0%	93.0 – 99.0%
MCTD	45	41	91.1%	78.8 – 97.5%
Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	534	506	94.8%	92.5 – 96.5%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-SS-B IgG: A total of 1026 clinically characterized samples (88 from Sjögren's syndrome patients, 404 from SLE, and 534 from control diseases) were evaluated for clinical sensitivity and specificity with EUROIMMUN anti-SS-B ELISA (IgG). The results are summarized in the following table:

Anti-SS-B ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
Sjögren's syndrome	88	35	39.8%	29.5 – 50.8%
SLE	404	56	13.9%	10.6 – 17.6%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI

RA	164	163	99.4%	96.6 – 100.0%
Systemic sclerosis	81	77	95.1%	87.8 – 98.6%
Polymyositis/Dermatomyositis	151	149	98.7%	95.3 – 99.8%
MCTD	45	42	93.3%	81.7 – 98.6%
Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	534	524	98.1%	96.6 – 99.1%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-Scl-70 ELISA: A total of 909 clinically characterized samples (280 from systemic sclerosis patients and 629 from control groups) were evaluated for clinical sensitivity and specificity with EUROIMMUN anti-Scl-70 ELISA (IgG). The results are summarized in the following table:

Anti-Scl-70 ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
Systemic sclerosis	280	65	23.2%	18.4 – 28.6%
- Diffuse systemic sclerosis	96	57	59.4%	48.9 – 69.3%
- Limited systemic sclerosis	113	6	5.3%	2.0 – 11.2%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
SLE	213	213	100.0%	98.3 – 100.0%
Polymyositis/Dermatomyositis	26	26	100.0%	86.8 – 100.0%
RA	164	163	99.4%	96.6 – 100.0%
Sjögren's syndrome	88	88	100.0%	95.9 – 100.0%
MCTD	45	45	100.0%	92.1 – 100.0%
Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	629	628	99.8%	99.1 – 100.0%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-Centromeres ELISA: A total of 877 clinically characterized samples (280 from systemic sclerosis patients and 597 from control groups) were investigated for clinical sensitivity and specificity with EUROIMMUN Anti-Centromeres ELISA (IgG). The results are summarized in the following table:

Anti-Centromeres ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
Systemic sclerosis	280	105	37.5%	31.8 – 43.5%
- Diffuse systemic sclerosis	96	7	7.3%	3.0 – 14.4%
- Limited systemic sclerosis	113	84	74.3%	65.3 – 82.1%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
SLE	181	180	99.4%	97.0 – 100.0%
Polymyositis/Dermatomyositis	26	26	100.0%	86.8 – 100.0%
RA	164	163	99.4%	96.6 – 100.0%
Sjögren's syndrome	88	85	96.6%	90.4 – 99.3%
MCTD	45	44	97.8%	88.2 – 99.9%
Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	597	591	99.0%	97.8 – 99.6%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-Jo-1 IgG: A total of 876 clinically characterized samples (177 from myositis patients and 699 from control groups) were evaluated for clinical sensitivity and specificity with EUROIMMUN Anti-Jo-1 ELISA (IgG). The results are summarized in the following table:

Anti-Jo-1 ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
Polymyositis/ Dermatomyositis	177	33	18.6%	13.2 – 25.2%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
SLE	213	211	99.1%	96.6 – 99.9%
RA	164	163	99.4%	96.6 – 100.0%
Systemic sclerosis	81	81	100.0%	95.5 – 100.0%
Sjögren's syndrome	88	88	100.0%	95.9 – 100.0%
MCTD	45	45	100.0%	92.1 – 100.0%
Fibromyalgia	15	15	100.0%	78.2 – 100.0%
Other autoimmune diseases	63	63	100.0%	94.3 – 100.0%
Borreliosis	30	30	100.0%	88.4 – 100.0%
Total	699	696	99.6%	98.8 – 99.9%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

Anti-ribosomal P-proteins IgG*:* A total of 876 clinically characterized samples (376 from SLE patients and 500 from control groups) were evaluated for clinical sensitivity and specificity with EUROIMMUN Anti-ribosomal P-proteins ELISA (IgG). The results are summarized in the following table:

Anti-ribosomal P-proteins ELISA (IgG):

Clinial Sensitivity				
Panel	N	Positive	% Positive	95% CI
SLE	376	20	5.3%	3.3 – 8.1%
Clinical Specificity				
Panel	N	Negative	% Negative	95% CI
Polymyositis/Dermatomyositis	151	149	98.7%	95.3 – 99.8%
RA	90	90	100.0%	96.0 – 100.0%
Systemic sclerosis	66	66	100.0%	94.6 – 100.0%
Sjögren's syndrome	55	54	98.2%	90.3 – 100.0%
MCTD	45	44	97.8%	88.2 – 99.9%
Other autoimmune diseases*	63	63	100.0%	94.3 – 100.0%
Borreliosis[5]	30	30	100.0%	88.4 – 100.0%
Total	500	496	99.2%	98.0 – 99.8%

* Samples include: autoimmune hepatitis (n=8), primary biliary cirrhosis (n=9), Grave's disease (n=12), Hashimoto (n=11), celiac disease (n=11), Diabetes Type I (n=12)

b. 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, anti-Sm, anti-SS-A, anti-SS-B, anti-Scl-70, anti-Centromeres, anti-Jo-1 in healthy people were investigated with a total of 200 samples from apparently healthy blood donors (including 120 men and 80 women with an average age of 40 years old; age range from 19 to 68 years). For anti-ribosomal P-proteins, 150 healthy blood donor samples were tested. The samples included 79 mean and 71 women with an average age of 38 and age range from 18 to 67. The results are summarized in the following table:

	Anti-nRNP/Sm	Anti-Sm	Anti-SS-A	Anti-SS-B	Anti-Scl-70	Anti-Centro.	Anti-Jo-1	Anti- rib. P-proteins
n	200	200	200	200	200	200	200	150
Positives	1	0	2	0	0	1	0	0
Negatives	199	200	198	200	200	199	200	150
prevalence	0.5%	0.0%	1.0%	0.0%	0.0%	0.5%	0.0%	0.0%
Ratio Range	0.1-1.3	0.1-0.3	0.0-4.4	0.0-0.2	0.0-0.1	0.0-3.0	0.0- 0.2	0.0-0.7
Mean	0.1	0.1	0.1	0.0	0.0	0.1	0.1	0.1
Std	0.09	0.02	0.33	0.02	0.01	0.21	0.03	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.