510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k082759

B. Purpose for Submission:
New assay

C. Measurand:
CENP, U1RNP, Sm, Ro, and La anti-nuclear antibodies

D. Type of Test:
Semi-quantitative fluoroenzyme immunoassay

E. Applicant:
Phadia US, Inc.

F. Proprietary and Established Names:
EliA™ CENP Well
EliA™ U1RNP Well
EliA™ Sm Well
EliA™ Ro Well
EliA™ La Well

G. Regulatory Information:
1. Regulation section:
   21 CFR§ 866.5100, Antinuclear Antibody Immunological Test System
2. Classification:
   Class II
3. Product code:
   LJM Antinuclear antibody (enzyme-labeled), antigen, controls
4. Panel:
   Immunology (82)

H. Intended Use:
1. Intended use(s):
   See Indications for Use below
2. Indication(s) for use:
   EliA CENP Well:
   EliA™ CENP is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to CENP in human serum and plasma (heparin, EDTA, citrate) as an aid in the clinical diagnosis of scleroderma (CREST Syndrome) in conjunction with other laboratory and clinical findings. EliA™ CENP uses the EliA IgG method on the instruments ImmunoCAP® 100 and ImmunoCAP® 250.

   EliA Sm Well:
   EliA™ Sm is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to Sm in human serum and plasma (heparin, EDTA, citrate) as an aid in the clinical diagnosis of systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA™ Sm uses the EliA IgG method on the instruments ImmunoCAP® 100 and ImmunoCAP® 250.

EliA La Well:

EliA™ La is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to La in human serum and plasma (heparin, EDTA, citrate) as an aid in the clinical diagnosis of Sjögren's syndrome and systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA™ La uses the EliA IgG method on the instruments ImmunoCAP® 100 and ImmunoCAP® 250.

EliA Ro Well:

EliA™ Ro is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to Ro in human serum and plasma (heparin, EDTA, citrate) as an aid in the clinical diagnosis of Sjögren's syndrome and systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA™ Ro uses the EliA IgG method on the instruments ImmunoCAP® 100 and ImmunoCAP® 250.

EliA U1RNP Well:

EliA™ U1RNP is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to U1RNP in human serum and plasma (heparin, EDTA, citrate) as an aid in the clinical diagnosis of mixed connective tissue disease (MCTD) and systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA™ U1RNP uses the EliA IgG method on the instruments ImmunoCAP® 100 and ImmunoCAP® 250.

3. Special conditions for use statement(s):
   The devices are for prescription use only.
4. Special instrument requirements:
   ImmunoCAP 100 and ImmunoCAP 250 (k061165)

I. Device Description:

The EliA reagents are available as modular packages, each purchased separately. The EliA wells are coated with human recombinant U1RNP (RNP 70, A, C), SS-A/Ro (60 kDa, 52 kDa), SS-B/La, Centromere B, Scl-70, Jo-1 and native purified Sm proteins. The EliA wells are packed in carriers which are stored in sealed aluminum foil bags containing a desiccant.

The EliA Method-Specific reagents for ImmunoCap 100 or ImmunoCap 250 consists of: six levels of ready-to-use EliA IgG calibrators (0, 4, 10, 20, 100, 600 μg/L); IgG calibrator well (coated with mouse monoclonal antibodies); ready-to-use positive and negative controls; ready-to-use IgG curve control (20 μg/L); IgG conjugate (ß-Galactosidase anti-IgG mouse monoclonal antibodies) in PBS and; ready-to-use sample diluent (PBS with BSA). The EliA general reagents consist of: ready-to-use development solution (0.1% 4-Methylumbelliferyl-ß-D-galactoside); ready-to-use stop solution (4% Sodium Carbonate); ready-to-use 96-MicroWell™ plates; and ImmunoCap washing solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Varelisa CENP Antibodies
Varelisa U1RNP Antibodies
Varelisa Sm Antibodies
Quanta Lite SS-A ELISA
Varelisa SS-B/La Antibodies

2. Predicate K number(s):
   K944171
   K993589
   K000312
   K922830
   K944168

3. Comparison with predicate:
   All five assays have the same similarities and differences from their predicates so only one assay illustrates them:

Similarities		
Item	Device	Predicate
Intended Use	EliA Ro is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to Ro in human serum and plasma (heparin, EDTA, citrate) as an aid in the clinical diagnosis of Sjögren's syndrome and systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA Ro uses the EliA IgG method on the instrument ImmunoCAP 100 and ImmunoCAP 250	QUANTA LiteTM SS-A is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative detection of SS-A (60kDa and 52kDa) antibodies in human serum. The presence of SS-A antibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of Systemic Lupus Erythematosus (SLE) and related connective tissue diseases, such as Sjogren's Syndrome.
Antigen	human recombinant SS-A/Ro (60 kDa, 52 kDa) proteins	Same
Test Format	ELISA – polystyrene microwells	Same

Differences		
Item	Device	Predicate
Instrumentation	ELISA-Reader needed	ImmunoCAP 100 and 250 are fully automated and integrated immunoassay analyzers

Differences		
Item	Device	Predicate
Detection Antibody	anti-human IgG horse-radish peroxidase (goat)	anti-human IgG ß-Galactosidase (mouse monoclonal antibodies)
Signal	Fluorescence	Optical Density
Calibration	Curve based on Total IgG Calibration	Curve based on analyte-specific IgG calibration

K. Standard/Guidance Document Referenced (if applicable):
   None referenced.

L. Test Principle:
   The EliA wells are coated with a specific antigen. If antibodies that recognize that specific antigen are present in the patient's specimen they will bind. After washing away non-bound antibodies, enzyme-labeled antibodies against human IgG antibodies EliA IgG conjugate is added to form an antibody-conjugate complex. After incubation, non-bound conjugate is washed away and the bound complex is incubated with a development solution. After stopping the reaction, the fluorescence in the reaction mixture is measured. The higher the response value, the more specific IgG is present in the specimen. To evaluate test results, the response for patient samples is compared directly to the response for calibrators. The EliA IgG calibration is a total IgG calibration. It is based on a set of six WHO-standardized IgG calibrators derived from human serum. The calibrators are required to perform an initial calibration curve, which can be stored in the ImmunoCAP instrument and may be used up to 28 days. Each assay outside of a calibration run includes curve controls that have to fall within defined ranges to verify that the stored calibration curve is still valid.

M. Performance Characteristics (if/when applicable):
   1. Analytical performance:
      a. *Precision/Reproducibility:*
         Imprecision of the assays on the ImmunoCap 100 instrument was assessed by testing five samples (seven for La) in duplicate over 18 runs (3 instruments x 6 runs each, n = 36 per sample). Imprecision of the assays on the ImmunoCap 250 instrument was assessed by testing five samples (seven for La) in duplicate over 21 runs (3 instruments x 7 runs each).

         EliA™ CENP Well:

ImmunoCap 100				ImmunoCap 250			
Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV	Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV
1	5.7	3.3	3.4	1	6.2	2.9	3.2
2	5.9	2.6	2.7	2	6.7	2.0	2.3
3	10.8	2.6	3.5	3	6.8	9.3	6.9
4	11.9	3.3	3.4	4	41.6	3.1	3.8
5	69.7	3.0	4.0	5	50.6	5.4	3.4

EliA™ U1RNP Well:

	ImmunoCap 100				ImmunoCap 250		
Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV	Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV
1	4.3	4.6	7.3	1	4.6	3.9	3.1
2	5.0	5.2	6.8	2	5.6	4.9	4.9
3	9.9	2.7	2.5	3	5.9	6.0	7.2
4	14.5	5.1	2.3	4	13.5	5.4	6.8
5	75.1	3.0	4.4	5	67.9	5.3	4.3

EliA™ Sm Well:

	ImmunoCap 100				ImmunoCap 250		
Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV	Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV
1	4.4	3.5	1.8	1	8.3	5.2	5.2
2	9.6	3.3	3.2	2	11.3	2.7	5.0
3	9.8	2.6	3.7	3	11.9	3.3	4.0
4	20.2	2.9	1.6	4	24.8	4.9	4.2
5	37.5	3.4	1.9	5	47.8	5.7	3.9

EliA™ Ro Well:

	ImmunoCap 100				ImmunoCap 250		
Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV	Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV
1	6.9	2.1	2.9	1	7.5	5.3	4.0
2	8.4	4.6	5.2	2	8.9	3.3	3.9
3	8.5	3.8	6.5	3	9.0	2.4	3.4
4	27.5	3.2	2.5	4	9.1	2.5	3.0
5	42.5	4.9	1.5	5	35.1	3.5	4.2

EliA™ La Well:

	ImmunoCap 100				ImmunoCap 250		
Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV	Sample	Mean (EliA U/mL)	Intra-run % CV	Inter-run % CV
1	5.6	3.3	6.3	1	5.2	6.7	4.9
2	6.3	3.8	6.4	2	5.6	3.2	3.1
3	8.5	4.0	3.7	3	6.2	3.4	2.0
4	9.2	3.1	2.2	4	8.7	4.2	2.7
5	10.0	5.3	2.8	5	9.2	2.8	3.3
6	19.4	4.7	4.4	6	11.1	6.4	4.7
7	59.8	5.1	2.8	7	61.0	6.2	6.4

b. *Linearity/assay reportable range:*
The recovery of each assay was tested by further diluting at least one sample near the positive value and at least one sample near the upper limit of the measuring range from the method-specific 1:100 dilution. The samples were tested in triplicate and recovery was determined by comparing the observed concentration to the expected concentration.

The measuring range is claimed from the detection limit to upper limit. The sponsor notes in the labeling that the upper limit of the reported results can vary due to a lot-specific conversion from μg/L to EliA U/mL. Results above the stated upper limit are reported as "above". They also state that due to differing binding characteristics of the antibodies in patient samples, not all sera can be diluted linearly within the measuring range.

Assay specific findings are described below:

EliA™ CENP Immunoassay:
Acceptable recovery was observed in four high samples (range 215.7 – 109.0 EliA U/mL) and in a low positive sample (13.0 EliA U/mL). The claimed measuring range of the EliA™ CENP Immunoassay is 0.4 – 240 EliA U/mL. Negative samples are <7 EliA U/mL, equivocal samples are 7 -10 EliA U/mL, and positive samples are >10 EliA U/mL.

EliA™ U1RNP Immunoassay:
Acceptable recovery was observed in three of four high samples (initial values 240 – 152.2 EliA U/mL). Acceptable recovery of a low positive sample (11.4 EliA U/mL) was found for the 1:2 and 1:3 dilution; the 1:5 dilution (expected value 2.3 EliA U/mL, observed value 1.8 EliA U/mL) and the 1:10 dilution (expected value 1.1 EliA U/mL, observed value 0.8 EliA U/mL) did not meet the acceptance criteria. These values are well below the equivocal range.

The claimed measuring range of the EliA™ U1RNP Immunoassay is 0.3 – 240 EliA U/mL. Negative samples are <5 EliA U/mL, equivocal samples are 5 - 10 EliA U/mL, and positive samples are >10 EliA U/mL.

EliA™ Sm Immunoassay:
Acceptable recovery was observed in two of four high samples (range 96.1 – 75.3 EliA U/mL). Samples that did not dilute linearly showed high recovery. Recovery of a sample in the equivocal zone (7.8 EliA U/mL) met acceptance criteria. The claimed measuring range of the EliA™ Sm Immunoassay is 0.1 – 120 EliA U/mL. Negative samples are <5 EliA U/mL, equivocal samples are 5 - 10 EliA U/mL, and positive samples are >10 EliA U/mL.

EliA™ Ro Immunoassay:
Acceptable recovery was observed in two of four high samples (range 281.8 –

109.3 EliA U/mL). Samples that did not dilute linearly showed high recovery. Recovery of a low positive sample (10.4 EliA U/mL) met acceptance criteria. The claimed measuring range of the EliA™ Ro Immunoassay is 0.3 – 240 EliA U/mL. Negative samples are <7 EliA U/mL, equivocal samples are 7 - 10 EliA U/mL, and positive samples are >10 EliA U/mL.

EliA™ La Immunoassay:
Acceptable recovery was observed in four high samples (range 307.4 – 279.7 EliA U/mL) and in a low positive sample (24.4 EliA U/mL). The claimed measuring range of the EliA™ La Immunoassay is 0.3 – 320 EliA U/mL. Negative samples are <3 EliA U/mL, equivocal samples are 3 - 8 EliA U/mL, and positive samples are >8 EliA U/mL.

Hook Effect:
The sponsor cites Peng and Craft [1] that no hook effects could be observed for concentrations up to 10 fold above the measuring ranges for these antigens.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
EliA IgG Calibrators and Curve Controls are derived from a purchased immunoglobulin preparation (GAMMANORM, Biovitrum AB, Stockholm, Sweden). The IgG calibrators are traceable (via an unbroken chain of calibrations) to the International Reference Preparation (IRP) 67/86 of Human Serum Immunoglobulins A, G and M from WHO. New batches of IgG Calibrators are compared to a secondary standard (standardized with the IRP) or the IRP directly and adjusted accordingly to meet the correct concentration. The instrument measures specific IgG concentrations in µg/L. By using a conversion factor given by the lot-specific code of the EliA ANA Wells, the results are automatically converted to EliA U/mL.

Assay Stability:
An accelerated shelf life study the shelf life showed that each assay is stable for 24 months. The results were confirmed with a real time stability study. A study supported the claim that the assays were stable for 9 months after initial opening.

Sample Stability:
The sponsor cites CLSI document H18-A3 in recommending the following storage conditions for samples:
- Separated serum/plasma should remain at room temperature for no longer than eight hours.
- If assays will not be completed within eight hours, serum/plasma should be refrigerated (2 to 8°C).
- If assays are not completed within 48 hours, or the separated

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[1] Peng SL, Craft JE (1996) Spliceosomal snRNPs autoantibodies. In: Peter JB, Shoenfeld Y (eds), Autoantibodies, pp 774-782, Elsevier, Amsterdam

serum/plasma will be stored beyond 48 hours, serum/plasma should be frozen at or below -20°C.

d. *Detection limit:*

The lower limit of the measuring range of each assay was determined by measuring dilutions (1:2, 1:4, and 1:8) of Calibrator 4.0 (4.0 μg/L) in the Calibrator Wells. The results in Response Units (RU) were compared with the result of the sample diluent on EliA dsDNA Wells. The discrimination ability (D) of the assay is the ability of the assay to discriminate a reading from background at a given concentration; the value should be >2.0.

EliA™ CENP Well, EliA™ U1RNP Well, EliA™ Ro Well,:

These new devices were able to discriminate samples containing 0.5 μg/L IgG (Cal 4.0 1:8) from the background. The corresponding detection limit was 0.25 EliA U/mL when using 0.5 as correction factor to convert μg/L to EliA U/mL.

EliA™ Sm Well:

The new device was able to discriminate samples containing 0.5 μg/L IgG (Cal 4.0 1:8) from the background. The corresponding detection limit was 0.125 EliA U/mL when using 0.25 as correction factor to convert μg/L to EliA U/mL.

EliA™ La Well:

The new device was able to discriminate samples containing 0.5 μg/L IgG (Cal 4.0 1:8) from the background. The corresponding detection limit was 0.33 EliA U/mL when using 0.66 as correction factor to convert μg/L to EliA U/mL.

e. *Analytical specificity:*

The specificity of the assays was evaluated by testing samples from the US Centers for Disease Control and Prevention (CDC) ANA serum panel and the Association of Medical Laboratory Immunologists (AMLI) consensus panel (2001). See below for the known specificity of each sample:

CDC ANA Human Reference Panel		
Sample	**Target**	**Diagnosis**
CDC 1	dsDNA, ssDNA, Histone, weak Sm	Not available
CDC 2	SS-B/La, weak SS-A/Ro	Not available
CDC 3	U1RNP, SS-B/La, SS-A/Ro, weak Sm	Not available
CDC 4	U1RNP	Not available
CDC 5	Histone, Sm	Not available
CDC 6	None	Not available
CDC 7	SS-A/Ro	Not available
CDC 8	CENP	Not available
CDC 9	Scl-70	Not available
CDC 10	Jo-1	Not available

AMLI Reference Panel 2001			
Sample	**Major Antibody**	**Other antibodies present**	**Diagnosis**
AMLI A	CENP	None	CREST
AMLI B	Scl-70	None	Scleroderma
AMLI D	U1RNP	SS-A/Ro (contaminant)	MCTD
AMLI E	SS-A/Ro	None	Sjögren's Syndrome
AMLI F	Jo-1	SS-A/Ro, RNP?	Polymyositis
AMLI G	SS-B/La	SS-A/Ro, U1RNP?	Sjögren's Syndrome
AMLI I	Sm	dsDNA, U1RNP, Scl-70?	SLE
AMLI J	dsDNA	SS-A/Ro, U1RNP?, Scl-70?	SLE
AMLI K	Negative	None	Healthy
AMLI L	Negative	None	Healthy

EliA™ CENP Well:
CDC 8 and AMLI A were positive in the EliA CENP Immunoassay and the predicate assay.

EliA™ U1RNP Well:
CDC3, CDC 4, CDC5, AMLI D, and AMLI I were positive in the EliA U1RNP Immunoassay and the predicate assay. CDC 5 is known to be a strongly immunoreactive serum and may cross-react with other snRNPs.

EliA™ Sm Well:
CDC 1, CDC3, CDC 5, AMLI I were positive in the EliA Sm Immunoassay and the predicate assay.

EliA™ Ro Well:
CDC 2, CDC 3, CDC 7, CDC 10, AMLI E, AMLI F, AMLI G, AMLI J were positive in the EliA Ro Immunoassay and the predicate assay. Anti-Jo-1 sera however are known to show anti-Ro52 activities quite often. EliA Ro can detect anti-Ro52 antibodies.

EliA™ La Well:
CDC 2, CDC 3, AMLI G were positive in the EliA La Immunoassay and the predicate assay.

Endogenous Interference:
For each assay, a low positive or equivocal sample and a high positive sample were diluted with sample diluent and spiked with different amounts of interfering substances or their respective blank solutions, and analyzed in triplicates. A calibration curve was run in duplicate.

The following final concentrations of additives in the samples were reached:
      Bilirubin C – 1,930 mg/dL
      Bilirubin F – 2,100 mg/dL
      Chyle – 95,000 Units/dL
      Hemoglobin – 47,000 mg/dL

Rheumatoid Factor IgM – 4,800 IU/mL

There was no demonstrated interference with any of the assays at these concentrations except for hemoglobin in EliA La. The sponsor demonstrated that hemoglobin did not interfere with the EliA La assay up to a concentration of 25,950 mg/dL in undiluted serum.

f. *Assay cut-off:*
See expected values below

2. Comparison studies:
   a. *Method comparison with predicate device:*
   Samples known to be positive or negative for respective ANA antibodies were analyzed together with a calibrator curve run in duplicates. Calibrators and Controls of the predicate device were also analyzed in duplicates. Test results were evaluated according to the description in the corresponding Directions for Use. For the calculation of Positive Percent Agreement, Negative Percent Agreement and Overall Agreement, equivocal results were excluded.

   EliA CENP Well:
   150 serum samples were collected from the serum bank at Phadia GmbH. In this study 50 samples from patients who had been clinically defined as suffering from CREST Syndrome were included. Other disease control samples included: 25 Rheumatoid Arthritis (RA) 50 infections 9 Vasculitis 10 Wegener's Granulomatosis 4 Panarteritis nodosa 2 Churg-Strauss-Syndrome.

		Varelisa CENP			
		Positive (>8 U/mL)	Equivocal (3-8 U/mL)	Negative (<3 U/mL)	Total
EliA CENP	Positive (>10 U/mL)	53	0	0	53
	Equivocal (7-10 U/mL)	0	0	0	0
	Negative (<7 U/mL)	1	20	76	97
	Total	54	20	76	150

Technical Agreement:

		Varelisa CENP		
		Positive (>8 U/mL)	Negative (<3 U/mL)	Total
EliA CENP	Positive (>10 U/mL)	53	0	53
	Negative (<7 U/mL)	1	76	77
	Total	54	76	130

Positive % agreement =   98.1% (53/54) (95%CI: 90.1 – 100.0)
Negative% agreement =   100.0% (76/76) (95%CI: 95.3 - 100.0)
Total agreement =   99.2% (129/130) (95%CI: 95.8 - 100.0)

EliA U1RNP Well:

191 serum samples were collected from the serum bank at Phadia GmbH. In this study samples from patients who had been clinically defined as suffering from mixed connective tissue disease (MCTD) (n = 50) and systemic lupus erythematosus (SLE). Other disease control samples included: 17 Rheumatoid Arthritis (RA), 19 monoclonal Gammopathy, 45 infections, and 14 Tumors

		Varelisa U1RNP			
		Positive (>10 U/mL)	Equivocal (5-8 U/mL)	Negative (<5 U/mL)	Total
EliA U1RNP	Positive (>10 U/ml)	44	0	0	44
	Equivocal (5-10 U/ml)	5	0	1	6
	Negative (<5 U/mL)	7	15	119	141
	Total	56	15	120	191

Technical Agreement:

		Varelisa U1RNP		
		Positive (>10 U/mL)	Negative (<5 U/mL)	Total
EliA U1RNP	Positive (>10 U/mL)	44	0	44
	Negative (<5 U/mL)	7	119	126
	Total	51	119	170

Positive % agreement = 86.3% (44/51) (95%CI: 73.7 – 94.3)
Negative% agreement = 100.0% (119/119) (95%CI: 96.9 - 100.0)
Total agreement = 95.9 % (163/170) (95%CI: 91.7 – 98.3)

EliA Sm Well:
293 serum samples were collected from the serum bank at Phadia GmbH. The study included samples from 193 patients who had been clinically defined as suffering from SLE m? (including 163 SLE, 2 SLE/Cerebritis, 1 SLE/CREST, 8 SLE/MCTD, 13 SLE/Nephritis, 2 SLE/Sjogren's Syndrome, 3 SLE/Thrombosis, 1 SLE/Vasculitis). Other disease control samples included: 50 infectious diseases, 25 Rheumatoid Arthritis, 10 Wegeners Granulomatosis, 9 Vasculitis, 4 Panarteritis nodosa, 2 Churg-Strauss-Syndrome.

		Varelisa Sm			
		Positive (>15 U/mL)	Equivocal (10-15 U/mL)	Negative (<10 U/mL)	Total
EliA Sm	Positive (>10 U/mL)	16	1	1	18
	Equivocal (5-10 U/mL)	1	0	2	3
	Negative (<5 U/mL)	7	12	253	272
	Total	24	13	256	293

Technical Agreement:

		Varelisa Sm		
		Positive (>15 U/mL)	Negative (<10 U/mL)	Total
EliA Sm	Positive (>10 U/mL)	16	1	17
	Negative (<5 U/mL)	7	253	260
	Total	23	254	277

Positive % agreement =   69.9% (16/23) (95% CI: 47.1 – 86.8)
Negative% agreement =   99.6% (253/254) (95% CI: 97.8 - 100.0)
Total agreement =   97.1% (269/277) (95% CI: 94.4 – 98.7)

EliA Ro Well:
299 serum samples were collected from the serum bank at Phadia GmbH. The study included samples from patients who had been clinically defined as suffering from Systemic Lupus Erythematosus (SLE) (n = 96) or Sjogren´s Syndrome (SS) (n = 46). Other disease control samples included: 42 Rheumatoid Arthritis (RA), 34 primary Sjogren's Syndrome (pSS), 33 Rheumafactor (RF), 20 Wegener Granulomatosis, 12 Vasculitis, 6 secondary Sjogren's Syndrome, 4 Churg Strauss Syndrome, 4 Polyarthritis Nodosa, and 2 others.

		INOVA SS-A			
		Positive (>40 U/mL)	Weak Positive (20-40 U/mL)	Negative (<20 U/mL)	Total
EliA Ro	Positive (>10 U/mL)	118	13	5	136
	Equivocal (5-10 U/mL)	0	0	2	2
	Negative (<5 U/mL)	0	3	158	161
	Total	118	16	165	299

Technical Agreement:

		INOVA SS-A		
		Positive (>40 U/mL)	Negative (<20 U/mL)	Total
EliA Ro	Positive (>10 U/mL)	118	5	123
	Negative (<5 U/mL)	0	158	158
	Total	118	163	281

Positive % agreement =   100.0% (118/118) (95%CI: 96.9 – 100.0)
Negative% agreement =   96.9% (158/163) (95%CI: 93.0 – 99.0)
Total agreement =   99.2% (276/281) (95%CI: 95.9 – 99.4)

EliA La Well:
170 serum samples were collected from the serum bank at Phadia GmbH. The study included samples from patients who had been clinically defined as suffering from Sjogren's Syndrome and/or Systemic Lupus Erythematosus (SLE). There were 28 SLE samples (including 3 SLE/Sjogren's Syndrome),

and 88 Sjogren's Syndrome samples (including 39 SS, 38 primary Sjogren's Syndrome, 6 secondary Sjogren's Syndrome, 3 SLE/SS). Other disease control samples included: 7 infectious diseases, 25 Rheumatoid Arthritis, 10 Wegeners Granulomatosis, 9 Vasculitis, 4 Panarteritis nodosa, 2 Churg-Strauss-Syndrome.

		Varelisa La			
		Positive (>8 U/mL)	Equivocal (3 - 8 U/mL)	Negative (<3 U/mL)	Total
EliA La	Positive (>10 U/mL)	48	1	1	50
	Equivocal (7-10 U/mL)	5	1	0	6
	Negative (<7 U/mL)	1	0	113	114
	Total	54	2	114	170

Technical Agreement:

		Varelisa La		
		Positive (>8 U/ml)	Negative (<3 U/ml)	Total
EliA La	Positive (>10 U/ml)	48	1	49
	Negative (<5 U/ml)	1	113	114
	Total	49	114	163

Positive % agreement =   98.0% (48/49) (95%CI: 89.1 – 99.9)
Negative% agreement = 99.1% (113/114) (95%CI: 95.2 - 100.0)
Total agreement =   98.8% (161/163) (95%CI: 95.6 – 99.9)

b. *Matrix comparison:*
The suitability of different sample matrices for each assay was determined by collecting serum, EDTA, heparin and citrate plasma samples from fifty different donors. Sample values spanned the range of the assays. Negative samples did not switch to positive in any serum/plasma combination in any assay. Linear regression of the equivocal and positive samples for each serum/plasma combination in each assay demonstrated that the matrices were equivalent.

3. Clinical studies:
   a. *Clinical Sensitivity:*
   Not applicable.

   b. *Clinical specificity:*
   Not applicable.

   c. Other clinical supportive data (when a. and b. are not applicable):
   None provided.

4. Clinical cut-off:
   Not applicable.

5. Expected values/Reference range:
The sponsor tested 400 apparently healthy Blood Donor samples from Caucasian individuals equally distributed by sex and age to evaluate expected values in the normal population and to confirm the previously defined cut-offs. The sponsor's acceptance criteria for validating the cut-offs was that the 95th percentile should lie below the lower limit of the equivocal range and the 99th percentile should lie below the upper limit of the equivocal range.

Test	Equivocal Range (ELiA U/mL)	Mean (ELiA U/mL)	95th Percentile (EliA U/mL)	99th Percentile (EliA U/mL)
EliA CENP	7 - 10	0.5	1.0	1.3
EliA U1RNP	5 - 10	1.6	2.8	8.2
EliA Sm	5 - 10	0.3	0.5	1.1
EliA Ro	7 - 10	0.5	0.8	2.3
EliA La	3 - 8	0.4	0.9	2.4

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.