510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K190710

B. Purpose for Submission:

Revision of assay, migration to new instrument

C. Measurand:

Human IgG autoantibodies to:

- U1RNP/RNP70 (A/C)
- SS-A/Ro (52, 60 kDa)
- SS-B/La
- Centromere B (CENP-B)
- Scl-70 (topoisomerase I)
- Jo-1 (histidyl tRNA synthetase)
- SmD3 peptide

D. Type of Test:

Automated qualitative multianalyte solid-phase immunoassay

E. Applicant:

Phadia US, Inc.

F. Proprietary and Established Names:

Phadia EliA Symphony^{S} Immunoassay

G. Regulatory Information:

1. Regulation section:

   21 CFR §866.5100– Antinuclear antibody immunological test system

2. Classification:

   Class II

3. Product code:

   LLL – Extractable Antinuclear Antibody, Antigen And Control

4. Panel:

   Immunology (82)

H. Intended Use:

1. Intended use:

   EliA Symphony^{S} is intended for the in vitro, qualitative measurement of antinuclear IgG antibodies in human serum and plasma (Li-heparin, EDTA). EliA Symphony^{S} is based on human recombinant U1RNP (RNP 70, A, C), SS-A/Ro (60 kDa, 52 kDa), SSB/La, Centromere B, Scl-70, Jo-1 proteins and a synthetic SmD3 peptide as antigen and is useful as an aid in the clinical diagnosis of patients with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), Sjögren's syndrome, scleroderma and polymyositis/dermatomyositis, in conjunction with other laboratory and clinical findings. EliA Symphony^{S} uses the EliA IgG method on the instrument Phadia 250.

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2. Indications for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   For use on the Phadia 250, Phadia 2500, or Phadia 5000 instruments

I. Device Description:

This IVD is a qualitative solid-phase fluoroimmunoassay, for the determination of autoantibodies against a panel of nine antigens: UIRNP/RNP70(A,C), SS-A/Ro (52,60), SS-

B/La, Centromere B (CENP), Scl-70, Jo-1, and SmD3^{P} peptide. All individual analytes have all been previously cleared in standalone formats.

General Description of the EliA Symphony^{S} Test System

Assay-specific reagents:

- EliA Symphony^{S} Wells are coated with nine human antigens (eight recombinant proteins, and one synthetic peptide) – 4 carriers (12 wells each), ready to use
- EliA ANA Positive Controls: Pooled human sera, containing IgG ANA against dsDNA, RNP, Sm, Ro, La, Scl-70, CENP, and Jo-1

EliA Method-specific reagents:

- EliA Sample Diluent: PBS containing BSA, detergent and 0.095% sodium azide – 6 bottles, 48 mL each, ready to use; or 6 bottles, 400 mL each, ready to use
- EliA IgG Conjugate 50 or 200: β-Galactosidase labeled anti-IgG (mouse monoclonal antibodies) in PBS containing BSA and 0.06% sodium azide – 6 wedge-shaped bottles, 5 mL each, ready to use; or 6 wedge-shaped bottles, 19 mL each, ready to use
- EliA IgG Calibrator Strips: Human IgG (0, 4, 10, 20, 100, 600 µg/L) in PBS containing BSA, detergent and 0.095% sodium azide – 5 strips, 6 single-use vials per strip, 0.3 mL each, ready to use
- EliA IgG Curve Control Strips: Human IgG (20 µg/L) in PBS containing BSA, detergent and 0.095% sodium azide – 5 strips, 6 single-use vials per strip, 0.3 mL each, ready to use
- EliA IgG Calibrator Well: Coated with mouse monoclonal antibodies – 4 carriers (12 wells each), ready to use.
- EliA IgG/IgM/IgA Negative Control 2500/5000: Human sera from healthy donors in PBS containing BSA, detergent and 0.095% sodium azide – 6 single-use vials, 0.3 mL each, ready to use

General Reagents:

- Development Solution, Stop Solution, and Washing Solution

Instrumentation

The EliA Symphony^{S} test is to be performed on the Phadia 250 or Phadia 2500/5000 instruments. The instruments are automated platforms for EliA test procedures from sample and reagent handling up to processing of results.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Phadia EliA Symphony Immunoassay

2. Predicate 510(k) number(s):

   K072149

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	EliA Symphony^S is intended for the in vitro, qualitative measurement of antinuclear IgG antibodies in human serum and plasma (Li-heparin, EDTA). EliA Symphony^S is based on human recombinant U1RNP (RNP 70, A, C), SS-A/Ro (60 kDa, 52 kDa), SSB/La, Centromere B, Scl-70, Jo-1 proteins and a synthetic SmD3 peptide as antigen and is useful as an aid in the clinical diagnosis of patients with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), Sjögren's syndrome, scleroderma and polymyositis/dermatomyositis, in conjunction with other laboratory and clinical findings. EliA Symphony^S uses the EliA IgG method on the instrument Phadia 250. EliA Symphony^S is intended for the in vitro, qualitative measurement of antinuclear IgG antibodies in human serum and plasma (Li-heparin, EDTA). EliA Symphony^S is based on human recombinant U1RNP (RNP 70, A, C), SS-A/Ro (60 kDa, 52 kDa), SSB/La, Centromere B, Scl-70, Jo-1 proteins and a synthetic SmD3 peptide as antigen and is useful as an aid in the clinical diagnosis of patients with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), Sjögren's syndrome, scleroderma and polymyositis/dermatomyositis, in conjunction with other laboratory and clinical findings. EliA Symphony^S uses the EliA IgG method on the instrument Phadia 2500/5000	EliA Symphony is intended for the in vitro, qualitative measurement of antinuclear IgG antibodies in human serum and plasma (heparin, EDTA and citrate). EliA Symphony is based on human recombinant U1RNP (RNP 70, A, C), SS-A/Ro (60 kDa, 52 kDa), SSB/La, Centromere B, Scl-70, Jo-1 proteins and native purified Sm proteins as antigen and is useful as an aid in the clinical diagnosis of patients with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), Sjögren's syndrome, scleroderma and polymyositis/dermatomyositis, in conjunction with other laboratory and clinical findings. EliA Symphony uses the EliA IgG method on the instrument ImmunoCAP 250.
Assay type	Solid-phase fluoroimmunoassay	Same
Assay output	Qualitative	Same
Incubation temperature	37°C	Same
Calibrators	6 point, total IgG	Same
Calibration Method	EliA 6-point total human IgG calibration	Same
Positive	EliA ANA Positive Control 250,	EliA ANA Positive Control 100,

Similarities		
Item	Device	Predicate
Control	2500/5000	250 (Same material, different package for Phadia instrument)
Negative Control	EliA IgG/IgM/IgA Negative Control 250, 2500/5000	EliA IgG/IgM/IgA Negative Control 100, 250 (Same material, different package for each Phadia instrument)
Conjugate (Detection antibody)	β-Galactosidase labeled monoclonal mouse anti-human IgG	Same
Detection substrate	0.01% 4-Methylumbelliferyl-β-D-galactoside (MUG)	Same
Sample Dilution	1:100	Same
Cutoff, Interpretation	Negative (−): <0.7 Equivocal (Eq): 0.7–1.0 Positive (+): >1.0	Same

Differences		
Item	Device	Predicate
Instrument platforms	Phadia 250 Phadia 2500 Phadia 5000	Phadia 100 Phadia 250
Matrices	Serum Plasma (Li-heparin, EDTA)	Serum Plasma (Li-heparin, EDTA, citrate)
Measurands	Autoantibodies to: • U1RNP/RNP70 (A/C) • SS-A/Ro (52, 60 kDa) • SS-B/La • Centromere B (CENP-B) • Scl-70 • Jo-1 • SmD3 peptide	Autoantibodies to: • U1RNP/RNP70 (A/C) • SS-A/Ro (52, 60 kDa) • SS-B/La • Centromere B (CENP-B) • Scl-70 • Jo-1 • native purified Sm antigens
Reagent Stability:	Closed-kit shelf- life: 18 mo. Open-kit: 9 mo. Onboard: 28d	Shelf-life: 24 mo. Expiration date: 18 mo.

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

Org	Standard ID	Version	Title
CLSI	EP05	A3	Evaluation of Precision Performance of Quantiative Measurement Methods
CLSI	EP7	ED3	Interference in Clinical Chemistry

Org	Standard ID	Version	Title
CLSI	EP17	A	Protocols for Determination of Limits of Detection and Limits of Quantification

L. Test Principle:

EliA tests are fluorescence immunoassays for the detection and measurement of human antibodies based on EliA solid-phase components, which contain specific antigens for the antibodies to be measured. EliA uses a modular reagent system. The test specific, method specific, and general reagents are packaged and purchased as separate units.

EliA Symphony^S: Polystyrene EliA wells are coated with a mixture of the target antigens: human U1RNP (RNP 70, A, C), SS-A/Ro (60 kDa, 52 kDa), SSB/La, Centromere B, Scl-70, Jo-1 proteins and a synthetic SmD3 peptide. Together, this grouping of autoantigenic targets are collectively referred to as extractable nuclear antigens (ENA). If present in the patient's specimen, autoantibodies to these proteins bind to the specific antigen. After washing away unbound antibodies, enzyme-labeled antibodies against human IgG antibodies (EliA IgG Conjugate) are added to form an antibody-conjugate complex. After incubation, non-bound conjugate is washed away and the bound complex is incubated with a fluorogenic development solution. After stopping the reaction, the fluorescence in the reaction mixture is measured. Fluorometric measurements are converted to an arbitrary unitless ratio, by scaling to EliA total IgG calibration. The higher the ratio, the more autoantigen-specific IgG is present in the specimen. Qualitative interpretation of this ratio value is summarized in the table below.

Qualitative interpretation of Symphony^S results	
Interpretation	[Ratio]
Negative (−)	< 0.7
Equivocal (Eq)	0.7–1.0
Positive (+)	> 1.0

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   Acceptance criteria for all parameters was met.

   a. Precision/Reproducibility:

   To evaluate reproducibility of the EliA Symphony^S assay on the **Phadia 250** instrument platform, six samples with a range of reactivities were tested. The samples were native samples or positive samples diluted with normal sera. Samples 2 through 6 were tested with three lots on three instruments × seven days × one run/day × four

replicates for a total of 252 possible datapoints per sample while Sample 1 (negative sample) was tested with one lot on three instruments × seven days × one run/day × four replicates for a total of 84 possible datapoints.

Reproducibility of EliA Symphony^{S} on Phadia 250 instrument:

Sample	Mean Ratio	Range of Ratios	Expected Result	Phadia 250 Results	
				Negative/Equivocal/Positive	% Correct
1	0.48	0.38–0.59	Negative	0/0/84	100
2	0.76	0.63–0.96	Equivocal	47/205/0	81.35
3	1.02	0.91–1.13	Positive	0/100/152	60.32
4	4.35	3.82–5.09	Positive	0/0/252	100
5	23.21	20.79–26.20	Positive	0/0/252	100
6	42.92	34.41–53.97	Positive	0/0/250	100

Lot-to-lot reproducibility on the Phadia 250 was calculated using Samples 2 through 6:

	Mean Ratio	Expected Result	Lot 1		Lot 2		Lot 3		Total	
			Neg/ Equiv/Pos	% Correct	Neg/ Equiv/Pos	% Correct	Neg/ Equiv/Pos	% Correct	Neg/ Equiv/Pos	% Correct
2	0.76	Equivocal	2/82/0	97.62	23/61/0	72.62	22/62/0	73.81	47/205/0	81.35
3	1.02	Positive	0/14/70	83.33	0/37/47	55.95	0/49/35	41.67	0/100/152	60.32
4	4.35	Positive	0/0/84	100	0/0/84	100	0/0/84	100	0/0/252	100
5	23.21	Positive	0/0/84	100	0/0/84	100	0/0/84	100	0/0/252	100
6	42.92	Positive	0/0/84	100	0/0/84	100	0/0/84	100	0/0/250	100

Instrument-to-instrument reproducibility on the Phadia 250 was calculated using Samples 2 through 6:

	Mean Ratio	Expected Result	Instrument 1		Instrument 2		Instrument 3		Total	
			Neg/ Equiv/Pos	% Correct	Neg/ Equiv/Pos	% Correct	Neg/ Equiv/Pos	% Correct	Neg/ Equiv/Pos	% Correct
2	0.76	Equivocal	1/83/0	98.81	7/77/0	91.66	39/45/0	53.57	47/205/0	81.35
3	1.02	Positive	0/24/60	71.43	0/21/63	75.00	0/55/29	34.53	0/100/152	60.32
4	4.35	Positive	0/0/84	100	0/0/84	100	0/0/84	100	0/0/252	100
5	23.21	Positive	0/0/84	100	0/0/84	100	0/0/84	100	0/0/252	100
6	42.92	Positive	0/0/84	100	0/0/84	100	0/0/84	100	0/0/250	100

Reproducibility on the **Phadia 2500/5000** instrument platform was tested using seven samples with a range of reactivities were tested with one lot on three instruments × seven days × one run/day × four replicates for a total of 84 possible datapoints per sample:

Reproducibility of EliA Symphony^{S} on Phadia 2500/5000 instrument:

Sample	Mean Ratio	Range of Ratios	Expected Result	Phadia 2500/5000Results	
				Negative/Equivocal/Positive	% Correct
1	0.63	0.38–0.59	Negative	67/17/0	79.76
2	0.76	0.61–0.87	Equivocal	12/72/0	85.7
3	0.92	0.76–1.04	Equivocal	0/77/7	91.7
4	0.98	0.90–1.07	Equivocal	0/55/29	65.5
5	4.15	3.72–4.63	Positive	0/0/84	100
6	28.07	25.53–33.11	Positive	0/0/84	100
7	47.11	41.02–54.55	Positive	0/0/84	100

Instrument-to-instrument reproducibility on the Phadia 2500/5000 was calculated:

			Instrument 1		**Instrument 2**		**Instrument 3**		**Total**	
	Mean Ratio	**Expected Result**	**Neg/ Equiv/Pos**	**% Correct**	**Neg/ Equiv/Pos**	**% Correct**	**Neg/ Equiv/Pos**	**% Correct**	**Neg/ Equiv/Pos**	**% Correct**
1	0.63	Negative	24/4/0	85.71	25/3/0	89.28	18/10/0	64.28	67/17/0	79.76
2	0.76	Equivocal	8/20/0	71.43	3/25/0	89.28	1/27/0	96.43	12/72/0	85.71
3	0.92	Equivocal	0/24/0	85.71	0/26/2	92.86	0/27/1	96.43	0/77/7	91.67
4	0.98	Equivocal	0/16/12	57.14	0/25/3	89.28	0/14/14	50.00	0/55/29	65.48
5	4.15	Positive	0/0/28	100	0/0/28	100	0/0/28	100	0/0/84	100
6	28.07	Positive	0/0/28	100	0/0/28	100	0/0/28	100	0/0/84	100
7	47.11	Positive	0/0/28	100	0/0/28	100	0/0/28	100	0/0/84	100

b. Linearity/assay reportable range:

Not applicable; the assay is qualitative.

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

Traceability:
The EliA IgG calibration method and traceablity were previously reviewed in K072149. There are no international standards for ANA antibodies. The positive and negative controls are prepared in house and arbitrary Ratio units are assigned during the development process.

Stability:

Closed-kit shelf-life stability at 2-8°C for EliA Symphony^{S} wells was determined as 18 months, based on accelerated and real-time stability studies. Opened-kit shelf-life claim is 9 months, based on real-time stability studies.

Onboard storage stability claim is 28 days, based on real-time stability studies using the storage capabilities of the Phadia 250 instrument.

For sample stability, the assay directions refer to CLSI H18-A4: Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline – Fourth Edition.

d. Detection limit:

Not applicable; the assay is qualitative.

e. Analytical specificity:

Endogenous Interference:
Three serum samples (a negative, an equivocal, and a positive sample) were spiked with the five endogenous interfering test substances at the concentrations in undiluted samples listed, or blank vehicle solvent. The negative and equivocal samples were native samples and the positive sample was generated by mixing a positive sample with normal sera. Samples were tested in triplicate over two runs on a Phadia 250 instrument. The ratio of blank/spiked sample ranged from 0.88–1.16 for EliA Symphony^{S}. None of the interferents changed the expected result. The substances tested and their tested concentrations are in the table below:

Interferent	Concentration
Bilirubin F	19.2 mg/dL
Bilirubin C	20.1 mg/dL
Hemoglobin	496 mg/dL
Lipemic factor (ClinOleic)	1%
Rheumatoid factor	500 IU/mL

Exogenous Interference:
Three serum samples (a negative, an equivocal, and a positive sample) were spiked with the six exogenous interfering test substances in undiluted samples listed, or blank vehicle solvent at the concentrations listed in the table below. The negative and equivocal samples were native samples and the positive sample was generated by mixing a positive sample with normal sera. Samples were tested in triplicate over two runs on a Phadia 250 instrument. The ratio of blank/spiked sample ranged from 0.83–1.13 for EliA Symphony^{S}. None of the interferents changed the expected result. The substances tested and their tested concentrations are in the table below:

Endogenous interference testing for EliA Symphony^{S} on Phadia 250	
Interferent	Concentration
Ibuprofen	0.219 mg/dL
Prednisone	0.09 µg/dL
Hydroxychloroquine	2.25 mg/dL
Azathioprine	2.58 µg/dL
Losartan	11.4 µg/dL
Infliximab[1]	0.264 mg/dL

Endogenous interference testing for EliA Symphony^S on Phadia 250	
Interferent	Concentration
[1] tested in two runs, independent of other exogenous interferents	

Reference Sera:
Reference panels of qualified sera for ANA from the Centers for Disease Control and Prevention (CDC) and the Association of Medical Laboratory Immunologists (AMLI) were tested with the EliA Symphony^S in duplicate 1:100 dilutions, using a single lot of EliA Symphony^S reagents. Among the 12 CDC panel samples, 100% returned the expected result. Among the 10 AMLI panel samples, two reference samples expected to be positive (i.e. RNP/Sm and Scl-70) returned negative results.

f. Assay cut-off:

To establish the assay cutoff, 70 samples from "apparently healthy" donors and 30 from SARD patients, known to be positive for the constituent single ANA autoantibody specificities represented in the EliA Symphony^S assay were tested, using a Phadia 250 instrument. All known ANA positive samples were found to be positive on the EliA Symphony^S assay, and the 95th percentile of the normal population lay below the equivocal range.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 633 serum samples were tested with the EliA Symphony^S and the predicate assay. Samples were selected to represent intended use SARD diseases and differential diagnosis controls, summarized in the table below.

Disease/Indication			
ANA-associated SARD samples		***Differential diagnosis controls***	
Systemic lupus erythematosus	97	Rheumatoid arthritis	85
Sjögren's syndrome	96	Hepatitis B virus	36
Systemic sclerosis	87	Hepatitis C virus	36
Polymyositis/dermatomyositis	78	HIV	27
Mixed connective tissue disease	46	Cancer	25
		Bacterial infection	20
n =	**404**	***n =***	**229**
Total n = 633			

All samples were run in singlicate on a Phadia 250 instrument. Qualitative agreement of positive and negative results were compared between the EliA Symphony^S test and

the predicate. Agreement measures were calculated, treating equivocal results as either positive or negative:

		Predicate			
		Positive	Equivocal	Negative	Total
EliA Symphony^S	Positive	279	4	2	285
	Equivocal	2	2	4	8
	Negative	5	19	316	340
	Total	286	25	322	633

Equivocal results considered positive (95% CI)			
PPA:	287/311	92.3%	(88.7 - 95.0%)
NPA:	316/322	98.1%	(96.0 - 99.3%)
Equivocal results considered negative (95% CI)			
PPA:	279/286	97.6%	(95.0 - 99.0%)
NPA:	341/347	98.3%	(96.3 - 99.4%)

To evaluate comparison of qualitative results for the EliA Symphony^S test between the two instrument platforms, 81 positive, 10 equivocal, and 19 negative samples were tested with the EliA Symphony^S in singlicate on both Phadia 250 and Phadia 2500/5000 instruments. Agreement measures were calculated, treating equivocal results as either positive or negative:

		Phadia 250			
		Positive	Equivocal	Negative	Totals
Phadia 2500/5000	Positive	80	3	0	83
	Equivocal	1	7	2	10
	Negative	0	0	17	17
	Totals	81	10	19	110

Equivocal results considered positive (95% CI)			
PPA:	93/91	98.8%	(93.3–100%)
NPA	17/19	89.7%	(72.6–97.8%)
Equivocal results considered negative (95% CI)			
PPA:	83/81	100%	(96.0–100%)
NPA:	27/29	89.5%	(66.9–98.7%)

b. Matrix comparison:

To evaluate the commutability of matrices intended for use with the EliA Symphony^S assay; 62 matched sets of serum, EDTA plasma, and lithium heparin plasma were tested on a Phadia 250 instrument. The cohort composed 29 negative, 10 equivocal, and 23 positive samples (as defined by serum results). The samples covered a range of ratios of the serum values (0.09–69.70).

Qualitative agreement for comparisons of serum samples to the plasma matrices are summarized below. No sample changed its evaluation from negative to positive or vice versa.

Matrix Comparison: Agreement for EliA Symphony^S between serum and EDTA plasma:

		Serum			
		Positive	Equivocal	Negative	Totals
EDTA plasma	Positive	22	0	0	22
	Equivocal	1	9	0	10
	Negative	0	1	29	30
	Totals	22	10	29	62

Equivocal results considered positive (95% CI)			
PPA:	32/33	97.0%	(84.7–99.5%)
NPA	29/29	100%	(88.3–100%)
Equivocal results considered negative (95% CI)			
PPA:	22/23	95.6%	(79.0–99.2%)
NPA:	39/39	100%	(91.0–100%)

Matrix Comparison: Agreement for EliA Symphony^S between serum and Li-Heparin plasma:

		Serum			
		Positive	Equivocal	Negative	Totals
Li-Heparin plasma	Positive	22	0	0	22
	Equivocal	1	8	0	10
	Negative	0	2	29	30
	Totals	23	10	29	62

Equivocal results considered positive (95% CI)			
PPA:	31/33	93.9%	(80.4–98.3%)
NPA	29/29	100%	(88.3–100%)
Equivocal results considered negative (95% CI)			
PPA:	22/24	91.7%	(74.2–97.7%)
NPA:	37/37	100%	(90.6–100%)

3. Clinical studies:

a-b. Clinical Sensitivity and Specificity:

A total of 444 clinical serum samples were tested with the EliA Symphony^{S} in singlicate on a Phadia 250 instrument. These samples included 194 samples from SARD diseases, and 250 from control disease categories that could be expected to be found in the differential diagnosis of the diseases in the Indications for Use.

Disease/Indication	**Total *n***	**N (%) Positive***
ANA-associated SARD samples	**194**	
Systemic lupus erythematosus	83	37 (44.6%)
SLE lupus nephritis	19	13 (68.4%)
Sjögren's syndrome	28	17 (60.7%)
Systemic sclerosis	32	16 (50.0%)
Mixed connective tissue disease	22	16 (72.7%)
Polymyositis/dermatomyositis	10	3 (30.0%)
Autoimmune disease controls	**190**	
Rheumatoid arthritis	40	0
Primary anti-phospholipid syndrome	28	4 (14.3%)
Graves' disease	28	1 (3.6%)
Hashimoto's thyroiditis	10	1 (10.0%)
Celiac disease	28	0
Crohn's disease	22	0
Ulcerative colitis	22	1 (4.5%)
Autoimmune hepatitis	6	3 (50.0%)
Primary biliary cholangitis	5	0
Granulomatosis with polyangiitis	1	0
Infectious disease controls	**60**	
bacterial	30	2 (6.7%)
viral	30	1 (3.3%)
Total:	**444**	

* Equivocal results evaluated as negative

Diagnostic performance, calculated as sensitivity and specificity values, is summarized in the table below. Two sets of clinical sensitivity and specificity measures were calculated, treating equivocal results as either positive or negative.

		Diagnoses		Totals
		SARD	Differential	
EliA Symphony^{S}	Positive	102	13	115
	Equivocal	5	1	6
	Negative	87	236	323
	Totals	194	250	444

Equivocal results considered positive (95% CI)			
Sensitivity:	107/194	55.2%	(47.9–62.3%)
Specificity	236/250	94.4%	(90.8–96.9%)
Equivocal results considered negative (95% CI)			
Sensitivity:	102/194	52.6%	(45.3–59.8%)
Specificity	237/250	94.8%	(91.3–97.2%)

4. Clinical cut-off**:**

   See Assay cutoff (M.1.f)

5. Expected values/Reference range:
   The frequency for ENA autoantibodies was investigated in a cohort of 558 apparently healthy subjects equally distributed across age and sex, using sera banked by the sponsor, as well as commercially obtained from the U.S. to enrich for racial and ethnic minority populations. Samples were tested with the EliA Symphony^{S} assay on a Phadia 250 instrument. Three samples (0.5%) were equivocal and seven samples (1.3%) were positive on Phadia 250. The results for the total cohort (*n*=558) are depicted in the table below:

Reference Ranges for EliA Symphony^{S}	
Median	0.1
Mean	0.3
95th Percentile	0.3
99th Percentile	1.1
Min	0.0
Max	25.9

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.