510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K253367

B Applicant

Phadia AB

C Proprietary and Established Names

EliA CTD 13 Screen

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LLL	Class II	21 CFR 866.5100 – Antinuclear Antibody Immunological Test System	IM - Immunology

II Submission/Device Overview:

A Purpose for Submission:

New assay

B Measurand:

Human IgG autoantibodies to U1RNP-A, U1RNP-C, RNP-70, SS-A/Ro 52, SS-A/Ro 60, SS-B/La, Centromere B, Scl-70, Jo-1, RNA Pol III, Rib-P, Sm, and dsDNA

C Type of Test:

Automated qualitative solid phase fluoroenzymeimmunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below

B Indication(s) for Use:

EliA CTD 13 Screen is intended for the in vitro qualitative detection of antinuclear IgG antibodies in human serum as an aid in the diagnosis of systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM) and mixed connective tissue disease (MCTD), in conjunction with other laboratory and clinical findings. EliA CTD 13 Screen detects antibodies against RNP70, U1RNP-A, U1RNP-C, SS-A/Ro60, SS-A/Ro52, SS-B/La, Centromere B, Scl-70, Jo-1, RNA Pol III, Rib-P, Sm and dsDNA. EliA CTD 13 Screen uses the EliA IgG method.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

D Special Instrument Requirements:

For use on the Phadia 250 instrument

IV Device/System Characteristics:

A Device Description:

The EliA CTD 13 Screen test system is a fully integrated and automated system which comprises of assay-specific reagents, EliA method-specific reagents, and general reagents.

Assay-specific reagents:

- EliA CTD 13 Screen Well, coated with native purified dsDNA, synthetic SmD_3 peptide and human recombinant Rib-P, SS-A/Ro (60 kDa, 52 kDa), SS-B/La, Scl-70, Centromere B, RNA Polymerase III, Jo-1, U1RNP-A, U1RNP-C, and RNP70, proteins – 4 carriers (16 Wells each), sufficient for 64 determinations, ready for use
- EliA ANA Positive Control 250: Human blood preparation and monoclonal antibodies containing IgG antibodies against dsDNA, RNP, Sm, Ro, La, Scl-70, CENP, and Jo-1, in PBS containing BSA, detergent and sodium azide (0.095% (w/v)) – 6 single-use vials, 0.3 mL each, sufficient for two determinations per vial, ready for use
- EliA IgG/IgM/IgA Negative Control 250: Human blood preparation in PBS containing BSA, detergent and sodium azide (0.095% (w/v)) – 6 single-use vials, 0.3 mL each, ready for use.

EliA Method-specific reagents:

- EliA Sample Diluent: PBS containing BSA, detergent and sodium azide (0.095% (w/v)) – 6 bottles, 48 mL each, ready for use
- EliA IgG Conjugate 50 or 200: β-Galactosidase anti-IgG (mouse monoclonal antibodies) in PBS containing BSA and sodium azide (0.06% (w/v)) – 6 wedge-shaped bottles, 5 mL

each (Conjugate 50), ready to use; 6 wedge-shaped bottles, 19 mL each (Conjugate 200), ready for use.

- EliA IgG Calibrator Strips: Human IgG (0, 4, 10, 20, 100, 600 µg/L); in PBS containing BSA, detergent and sodium azide (0.095% (w/v)) – 5 strips, 6 single-use vials per strip, 0.3 mL each, ready for use.
- EliA IgG Curve Control Strips: Human IgG (20 µg/L); in PBS containing BSA, detergent and sodium azide (0.095% (w/v)) – 5 strips, 6 single-use vials per strip, 0.3 mL each, ready for use.
- EliA IgG Calibrator Well: Coated with mouse monoclonal antibodies – 4 carriers (12 wells each), ready for use.

General Reagents:

- Development Solution: 0.01% 4-Methylumbelliferyl-β-D-galactoside, <0.0010% preservative – 6 bottles (11 mL or 17 mL each), ready for use.
- Stop Solution: 4% Sodium Carbonate – 6 bottles (65 mL or 119 mL each), ready for use.
- Dilution Plates: MicroWell™ plates with 96 wells, 0.5 mL each – 100 plates/package, ready for use.
- Washing Solution:
    - Washing Solution Additive: detergent, preservative <0.13% – 6 x 17.2 mL or 2 x 86mL.
    - Washing Solution Concentrate: phosphate buffer, preservative <0.0015% – 6 x 80 mL or 2 x 400 mL.

B Principle of Operation:

The EliA CTD 13 Screen Wells are coated with native purified dsDNA, synthetic SmD_3 peptide and human recombinant Rib-P, SS-A/Ro 60, SS-A/Ro 52, SS-B/La, Scl-70, Centromere B, RNA Polymerase III, Jo-1 and U1RNP-A, U1RNP-C, and RNP70 proteins. If present in the patient's specimen, antibodies to the antigens bind to their specific antigen.

After washing away non-bound 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 Development Solution. After stopping the reaction, the fluorescence in the reaction mixture is measured. The assay directly measures the amount of antibody of interest bound to the antigen coating the EliA Well, therefore the higher the value of fluorescent signal detected by the instrument, the higher the amount of antibody bound and detected in the sample tested. To evaluate test results, the response for patient samples is compared directly to the response for calibrators.

V Substantial Equivalence Information:

A Predicate Device Name(s):

EliA Symphony^S, EliA dsDNA, EliA Rib-P, and EliA RNA Pol III

B Predicate 510(k) Number(s):

K190710, K072939, K202540, and K202541

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251440 (Candidate)	K190710 (Predicate)
Device Trade Name	EliA CTD 13 Screen	EliA Symphony^{S}
General Device Characteristic Similarities		
Sample Matrix	Serum	Serum and Plasma
Detection	Qualitative	Same
Technology	Enzyme Linked Immunosorbent Assay (ELISA)	Same
Result Reporting	Ratio	Same
Cut-off	1.0	Same
Interpretation	Negative: < 0.7 Ratio Equivocal: 0.7-1.0 Ratio Positive: > 1.0 Ratio	Same
General Device Characteristic Differences		
Intended Use/ Indications For Use	EliA CTD 13 Screen is intended for the in vitro qualitative detection of antinuclear IgG antibodies in human serum as an aid in the diagnosis of systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM) and mixed connective tissue disease (MCTD), in conjunction with other laboratory and clinical findings. EliA CTD 13 Screen detects antibodies against RNP70, U1RNP-A, U1RNP-C, SS-A/Ro60, SS-A/Ro52, SS-B/La, Centromere B, Scl-70, Jo-1, RNA Pol III, Rib-P, Sm and dsDNA. EliA CTD 13 Screen uses the EliA IgG method.	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), SS-B/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.
Antigens	Native purified dsDNA, synthetic SmD3 peptide and human recombinant Rib-P, SS-A/Ro 60 SSA-A/Ro 52, SS-B/La, Scl-70, Centromere B, RNA Polymerase III, Jo-1 and U1RNP-A, U1RNP-C, and RNP70 proteins	Human recombinant U1RNP (RNP70, A, C), SS-A/Ro (60 kDa, 52 kDa), SS-B/La, Centromere B, Scl-70 and Jo-1 proteins, synthetic SmD_3 peptide

Device & Predicate Device(s):	**K251440 (Candidate)**	**K072939 (Predicate)**
Device Trade Name	EliA CTD 13 Screen	EliA dsDNA
General Device Characteristic Similarities		
Technology	Enzyme Linked Immunosorbent Assay (ELISA)	Same
General Device Characteristic Differences		
Sample Matrix	Serum	Serum and Plasma
Intended Use/ Indications For Use	EliA CTD 13 Screen is intended for the in vitro qualitative detection of antinuclear IgG antibodies in human serum as an aid in the diagnosis of systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM) and mixed connective tissue disease (MCTD), in conjunction with other laboratory and clinical findings. EliA CTD 13 Screen detects antibodies against RNP70, U1RNP-A, U1RNP-C, SS-A/Ro60, SS-A/Ro52, SS-B/La, Centromere B, Scl-70, Jo-1, RNA Pol III, Rib-P, Sm and dsDNA. EliA CTD 13 Screen uses the EliA IgG method.	EliA dsDNA is intended for the in vitro quantitative measurement of IgG antibodies directed to dsDNA in human serum and plasma (Li-heparin, EDTA) as an aid in the clinical diagnosis of systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA dsDNA uses the EliA IgG method.
Detection	Qualitative	Quantitative
Result Reporting	Ratio	IU/mL
Antigens	Native purified dsDNA, synthetic SmD3 peptide and human recombinant Rib-P, SS-A/Ro 60 SSA-A/Ro 52, SS-B/La, Scl-70, Centromere B, RNA Polymerase III, Jo-1 and U1RNP-A, U1RNP-C, and RNP70 proteins	dsDNA
Cut-off	1.0	15 IU/mL
Interpretation	Negative: < 0.7 Ratio Equivocal: 0.7-1.0 Ratio Positive: > 1.0 Ratio	Negative: < 10 IU/mL Equivocal: 10-15 IU/mL Positive: > 15 IU/mL

Device & Predicate Device(s):	K251440 (Candidate)	K202540 (Predicate)
Device Trade Name	EliA CTD 13 Screen	EliA Rib-P
General Device Characteristic Similarities		
Sample Matrix	Serum	Same
Technology	Enzyme Linked Immunosorbent Assay (ELISA)	Same
General Device Characteristic Differences		
Intended Use/ Indications For Use	EliA CTD 13 Screen is intended for the in vitro qualitative detection of antinuclear IgG antibodies in human serum as an aid in the diagnosis of systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM) and mixed connective tissue disease (MCTD), in conjunction with other laboratory and clinical findings. EliA CTD 13 Screen detects antibodies against RNP70, U1RNP-A, U1RNP-C, SS-A/Ro60, SS-A/Ro52, SS-B/La, Centromere B, Scl-70, Jo-1, RNA Pol III, Rib-P, Sm and dsDNA. EliA CTD 13 Screen uses the EliA IgG method.	EliA Rib-P is intended for the in vitro semi-quantitative measurement of IgG antibodies directed to Rib-P in human serum as an aid in the diagnosis of systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA Rib-P uses the EliA IgG method.
Detection	Qualitative	Semi-quantitative
Result Reporting	Ratio	EliA U/mL (arbitrary)
Cut-off	1.0	10 U/mL
Antigens	Native purified dsDNA, synthetic SmD3 peptide and human recombinant Rib-P, SS-A/Ro 60 SSA-A/Ro 52, SS-B/La, Scl-70, Centromere B, RNA Polymerase III, Jo-1 and U1RNP-A, U1RNP-C, and RNP70 proteins	Rib-P
Interpretation	Negative: < 0.7 Ratio Equivocal: 0.7-1.0 Ratio Positive: > 1.0 Ratio	Negative: < 7 EliA U/mL Equivocal: 7-10 EliA U/mL Positive: > 10 EliA U/mL

Device & Predicate Device(s):	K251440 (Candidate)	K202541 (Predicate)
Device Trade Name	EliA CTD 13 Screen	EliA RNA Pol III
General Device Characteristic Similarities		
Sample Matrix	Serum	Same
Technology	Enzyme Linked Immunosorbent Assay (ELISA)	Same
General Device Characteristic Differences		
Intended Use/Indications For Use	EliA CTD 13 Screen is intended for the in vitro qualitative detection of antinuclear IgG antibodies in human serum as an aid in the diagnosis of systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM) and mixed connective tissue disease (MCTD), in conjunction with other laboratory and clinical findings. EliA CTD 13 Screen detects antibodies against RNP70, U1RNP-A, U1RNP-C, SS-A/Ro60, SS-A/Ro52, SS-B/La, Centromere B, Scl-70, Jo-1, RNA Pol III, Rib-P, Sm and dsDNA. EliA CTD 13 Screen uses the EliA IgG method.	EliA RNA Pol III is intended for the in vitro semi-quantitative measurement of antinuclear IgG antibodies directed to RNA polymerase III (RNA Pol III) in human serum as an aid in the diagnosis of systemic sclerosis (diffuse form) in conjunction with other laboratory and clinical findings. EliA RNA Pol III uses the EliA IgG method.
Detection	Qualitative	Semi-quantitative
Result Reporting	Ratio	EliA U/mL (arbitrary)
Cut-off	1.0	10 U/mL
Antigens	Native purified dsDNA, synthetic SmD3 peptide and human recombinant Rib-P, SS-A/Ro 60 SSA-A/Ro 52, SS-B/La, Scl-70, Centromere B, RNA Polymerase III, Jo-1 and U1RNP-A, U1RNP-C, and RNP70 proteins	
Interpretation	Negative: < 0.7 Ratio Equivocal: 0.7-1.0 Ratio Positive: > 1.0 Ratio	Negative: < 7 EliA U/mL Equivocal: 7-10 EliA U/mL Positive: > 10 EliA U/mL

VI Standards/Guidance Documents Referenced:

The following Clinical and Laboratory Standards Institute (CLSI) guidelines were used:

- CLSI EP07, Interference Testing in Clinical Chemistry, 3rd Edition,

- CLSI EP12-Ed3, Evaluation of Qualitative, Binary Output Examination Performance, 3rd Edition,
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, 2nd Edition
- CLSI EP28-A3c, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, 3rd Edition
- CLSI EP34, Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking, 1st Edition
- CLSI EP37, Supplemental Tables for Interference Testing in Clinical Chemistry, 1st Edition
- CLSI GP44-A4, Procedures for the handling and processing of blood specimens for common laboratory tests, 4th Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision and reproducibility of EliA CTD 13 Screen were evaluated in accordance with the CLSI guideline EP12-Ed3.

Single-site precision

To evaluate the within-laboratory precision of the EliA CTD Screen, 10 samples were prepared by diluting positive native serum samples with negative serum samples. The prepared samples, containing various concentrations of autoantibodies, were assayed in duplicate, twice a day, for 20 or 21 days, using one reagent lot, one instrument, and one operator, for a total of 80 or 84 measurements per sample.

Sample	Mean Ratio (interpretation)	Range of Ratio	N# of Positive/Equivocal/ Negative	% of Positive/Equivocal/ Negative
1	0.3 (negative)	0.2 – 0.3	0/0/84	0/0/100
2	0.3 (negative)	0.3 – 0.4	0/0/84	0/0/100
3	0.5 (negative)	0.4 – 0.6	0/0/80	0/0/100
4	0.8 (equivocal)	0.7 – 0.9	0/78*/5	0/94/6
5	1.0 (positive)	0.8 – 1.2	48/36/0	57/43/0
6	1.2 (positive)	1.0 – 1.4	84/0/0	100/0/0
7	4.5 (positive)	3.8 – 5.8	84/0/0	100/0/0
8	5.3 (positive)	4.4 – 6.0	84/0/0	100/0/0
9	23 (positive)	19 – 28.1	81**/0/0	100/0/0
10	26 (positive)	22 – >31	84*/0/0	100/0/0

* Result for one replicate was not reported due to instrument error

** Results for three replicates were not reported due to instrument error in 3 separate runs (1 rep/run)

Site-to-site reproducibility

The reproducibility of the EliA CTD Screen was evaluated by assaying 10 samples prepared by diluting positive native serum samples with negative serum samples. The prepared samples, containing various concentrations of autoantibodies, were assayed in quintuplicate, once a day, for five days, using one reagent lot at each site, on three instruments for a total of 75 measurements per sample. The instrument and operator variables were nested within the multiple site component. The resulting data are summarized in the following table:

Sample	Mean Ratio (Result Interpretation)	Range of Ratio	N of Positive/ Equivocal/ Negative	% of Positive/ Equivocal/ Negative	Instrument 1		Instrument 2		Instrument 3	
					Positive/ Equivocal/ Negative	%Positive/ Equivocal/ Negative	Positive/ Equivocal/ Negative	%Positive/ Equivocal/ Negative	Positive/ Equivocal/ Negative	%Positive/ Equivocal/ Negative
1	0.6 (negative)	0.5 - 0.6	0/0/75	0/0/100	0/0/25	0/0/100	0/0/25	0/0/100	0/0/25	0/0/100
2	0.6 (negative)	0.6 - 0.7	0/1/74	0/1/99	0/0/25	0/0/100	0/0/25	0/0/100	0/1/24	0/4/96
3	0.7 (equivocal)	0.6 - 0.8	0/34/41	0/45/55	0/18/7	0/72/28	0/7/18	0/28/72	0/9/16	0/36/64
4	0.8 (equivocal)	0.7 - 0.9	0/74/1	0/99/1	0/25/0	0/100/0	0/24/1	0/96/4	0/25/0	0/100/0
5	0.9 (equivocal)	0.8 - 1.0	0/75/0	0/100/0	0/25/0	0/100/0	0/25/0	0/100/0	0/25/0	0/100/0
6	1.1 (positive)	0.9 - 1.4	70/5/0	93/7/0	22/3/0	88/12/0	25/0/0	100/0/0	23/2/0	92/8/0
7	3.6 (positive)	3.3 - 3.9	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0
8	4.8 (positive)	4.2 - 5.3	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0
9	23 (positive)	20 - 25	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0
10	30 (positive)	25 - >31	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0

Between-lot imprecision

Between-lot imprecision of EliA CTD 13 Screen was evaluated by assaying 10 samples prepared by diluting positive native serum samples with negative serum samples. The prepared samples were tested in quintuplicate once a day for five days with 3 reagent lots on one instrument, for a total of 75 replicates per sample.

Sample	Mean Ratio (Result Interpretation	Range of Ratio	N of Positive/ Equivocal/ Negative	% of Positive/ Equivocal/ Negative	Lot 1		Lot 2		Lot 3	
					Positive/ Equivocal/ Negative	%Positive/ Equivocal/ Negative	Positive/ Equivocal/ Negative	%Positive/ Equivocal/ Negative	Positive/ Equivocal/ Negative	%Positive/ Equivocal/ Negative
1	0.6 (negative)	0.6 - 0.7	0/4/71	0/5/95	0/1/24	0/4/96	0/3/22	0/12/88	0/0/25	0/0/100
2	0.6 (negative)	0.5 - 0.6	0/0/75	0/0/100	0/0/25	0/0/100	0/0/25	0/0/100	0/0/25	0/0/100
3	0.7 (equivocal)	0.6 - 0.8	0/30/45	0/40/60	0/9/16	0/36/64	0/9/16	0/36/64	0/12/13	0/48/52
4	0.8 (equivocal)	0.6 - 0.9	0/65/10	0/87/13	0/25/0	0/100/0	0/25/0	0/100/0	0/15/10	0/60/40
5	0.9 (equivocal)	0.8 - 1.0	0/75/0	0/100/0	0/25/0	0/100/0	0/25/0	0/100/0	0/25/0	0/100/0
6	1.2 (positive)	0.9 - 1.4	68/7/0	91/9/0	25/0/0	100/0/0	25/0/0	100/0/0	18/7/0	72/28/0
7	3.7 (positive)	3.3 - 4.1	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0
8	4.8 (positive)	4.0 - 5.6	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0
9	23 (positive)	20 - 28	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0
10	30 (positive)	25 - >31	75/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0	25/0/0	100/0/0

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

Endogenous and exogenous interference
Four serum samples (including a negative, equivocal and positive sample) were prediluted in EliA Sample Diluent and spiked with different interfering substances or blank solution. Six replicates were measured for all test samples and control samples. The aliquots (test and control) of each sample were assayed in the same run. A calibration and curve controls were included in each run. None of the interferents changed the expected result at the indicated testing concentrations as shown in the table below.

Endogenous Substances	
Potential interfering substance	**Concentration**
Albumin	6000 mg/dL
Bilirubin, unconjugated	40 mg/dL
Bilirubin, conjugated	40 mg/dL
Hemoglobin	1000 mg/dL
Rheumatoid factor IgM	500 IU/mL

Exogenous Substances	
Potential interfering substance	**Concentration**
Triglycerides	2000 mg/dL
Alendronate	0.0034 mg/dL
Amlodipine	0.0075 mg/dL
Amoxicillin	12.9 mg/dL
Atorvastatin	0.075 mg/dL
Azathioprine	0.26 mg/dL
Belimumab	94.0 mg/dL
Cyclophosphamide	54.9 mg/dL
Diltiazem	0.09 mg/dL
Enalapril	0.0819 mg/dL
Erythromycin	13.8 mg/dL
Hydroxychloroquine	0.36 mg/dL
Ibuprofen	21.9 mg/dL
Infliximab	90 mg/dL
Losartan	0.09 mg/dL
Methotrexate	205.0 mg/dL
Mycophenolic acid	33.0 mg/dL
Omeprazole	0.84 mg/dL

Exogenous Substances	
Potential interfering substance	**Concentration**
Prednisone	0.01 mg/dL
Ranitidine	1.05 mg/dL
Rituximab	114.3 mg/dL
Simvastatin	0.168 mg/dL

Reference Sera:

Selected Antinuclear Antibodies(ANA) IUIS Reference Standards samples, previously known as the CDC (Center for Disease Controls and Prevention) ANA Reference Panel, were tested in singlicate using one reagent lot of the EliA CTD 13 Screen to illustrate the analytical specificity of the assay. The results are outlined below.

Sample	Description/Assigned Specificity	EliA CTD Screen Result
CDC ANA #1	Homogeneous Rim Pattern in FANA test due to antibodies to dsDNA	Positive
CDC ANA #2	Speckled pattern in FANA test due to antibodies to SS-B/La	Positive
CDC ANA #3	Speckled pattern in FANA due to antibodies to U1-RNP, SS-B/La and SS-A/Ro	Positive
CDC ANA #4	High levels of antibodies to U1-RNP	Positive
CDC ANA #5	High levels of antibodies to Sm	Positive
CDC ANA #6	Nucleolar pattern in FANA test (due antibodies to U3-RNP)	Negative
CDC ANA #7	High levels of antibodies to SS-A/Ro	Positive
CDC ANA #8	Centromere pattern in FANA test	Positive
CDC ANA #9	High levels of antibodies to Scl-70	Positive
CDC ANA #10	High levels of antibodies to Jo-1	Positive
CDC ANA #11	High levels of antibodies to PM/Scl	Negative
CDC ANA #12	High levels of antibodies to Ribosomal P	Positive

FANA= Fluorescent Antinuclear Antibody

4. Detection Limit and Assay Reportable Range:

   Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Traceability

   This EliA test uses EliA IgG Calibrators. EliA IgG Calibrators are traceable to an internal reference material which is based on the WHO International Standard Immunoglobulins A, G and M, Human Serum (NIBSC code: 67/086).

   Reagent stability:

   Shelf-life: The stability of the EliA CTD 13 Screen wells was evaluated with a real-time study on the Phadia 250 instrument. Three lots of EliA CTD 13 Screen wells were stored

under recommended conditions at 2 – 8°C and tested at different timepoints using 10 positive, nine (9) negative, and two (2) equivocal samples. The results support a shelf-life of 9 months at 2 – 8°C for EliA CTD 13 Screen.

Transport stability: Transport stability was evaluated on the Phadia 250 instrument with real-time stability study. EliA CTD 13 Screen wells were incubated under two different transport stress conditions (24 hours at -20°C and 5 days at 35°C) and tested using 10 positive, nine (9) negative, and two (2) equivocal samples after stress. The results support a claim that transport conditions like heat (35°C) and cold (-20°C) or storage for up to 5 days at up to 35°C are possible without any impact on the shelf-life up to 12 weeks.

On-board (storage chamber) stability: The on-board stability of EliA CTD 13 Screen Well carriers was evaluated at 80% humidity and at 11°C for 15, 29 and 43 days in the Phadia 250 carrier storage tray using eight (8) positive serum samples, two (2) equivocal serum samples, two (2) negative serum samples and a positive control. The on-board stability in the storage chamber of the Phadia 250 instrument was determined to be 28 days under operating conditions at 2– 8°C.

On-board (loading tray) stability: The on-board stability of EliA CTD 13 Screen Well carriers was evaluated on the loading tray of the Phadia 250 instrument at 32°C and 80% relative humidity (RH). The wells were stored on a loading tray in a climate chamber for 12 hours, 24 hours, 25 hours and 72 hours and tested with eight (8) positive serum samples, two (2) equivocal serum samples, nine (9) negative serum samples and positive control. The on-board stability of EliA CTD 13 Screen Well on the loading tray of the Phadia 250 instrument was determined to be 24 hours.

In-use stability: For evaluation of Stability after first opening, foil bags containing the EliA CTD 13 Screen wells in carriers (stored under standard conditions, at 2 – 8 °C) were opened. The process of opening and sealing of the foil bags was repeated multiple times over the study duration exposing the wells to 11°C and 80% RH. Ten (10) positive serum samples (including one high- and one low-positive), two (2) equivocal serum samples and three (3) negative serum samples were tested. The in-use stability after first opening of EliA CTD 13 Screen Well was determined to be 12 weeks at 2 – 8°C.

Sample Stability: The sample stability was evaluated to support the stability of samples, when stored frozen for 27 months from blood draw using 10 serum samples (across the reportable range of EliA CTD 13 Screen) were included in this study. Four (4) positive serum samples, four (4) equivocal serum samples and two (2) negative serum samples were tested at 7 weeks, 5 months, 8 months, 14 months, 16 months, 24 months, 24.5 months and 27 months timepoints. All tested serum samples fulfilled the study specifications, when stored frozen up to 27 months and supported the sample stability claim of 24.5 months.

6. Assay Cut-Off:

To define the cut-off, a study was performed using a cohort consisting of 70 apparently healthy blood donors, four (4) serum samples from MCTD patients, eight (8) serum samples from IIM patients, seven (7) serum samples from systemic sclerosis patients, six (6) serum

samples from SLE patients and five (5) serum samples from Sjögren's syndrome patients. The samples were measured on a Phadia 250 instrument.

The cut-off was set as follows for EliA CTD 13 Screen:

	Negative	Equivocal	Positive
Result [Ratio]	<0.7	0.7 – 1.0	>1.0

In case of equivocal results, the manufacturer recommends retesting the patient after 8–12 weeks.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A total of 1082 serum samples were tested with EliA CTD 13 Screen and compared to the combination of the predicate devices EliA SymphonyS, EliA dsDNA, EliA Rib-P and EliA RNA Pol III assays. The tests were run in single determination and evaluated according to the Directions for Use of both assays. The results are summarized in the tables below:

n=1082		Combination of Predicate Devices			
		Positive	Equivocal	Negative	Total
EliA CTD 13 Screen	Positive <0.7	572	35	24	631
	Equivocal 0.7 – 1.0	3	4	55	62
	Negative >1.0	7	14	386	389
	Total	582	53	447	1082

Equivocal results considered negative	Agreement (%)	95% CI
Positive Percent Agreement	98.3	96.9–99.2
Negative Percent Agreement	88.2	85.0–90.9
Total Percent Agreement	93.6	92.0–95.0

Equivocal results considered positive	Agreement (%)	95% CI
Positive Percent Agreement	96.7	95.0–97.9
Negative Percent Agreement	82.3	78.5–85.8
Total Percent Agreement	90.8	88.9–92.4

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

Clinical Sensitivity and Specificity:

A cohort of 1027 clinically defined serum samples were used to determine sensitivity and specificity of the assay. Samples with a diagnosis of polymyositis (PM), dermatomyositis (DM),

mixed connective tissue disease (MCTD), Raynaud's phenomenon, Sjögren's syndrome (SS), systemic lupus erythematous (SLE) (including lupus nephritis) and systemic sclerosis (SSc) (including limited systemic sclerosis (lSSc) represented the diagnostic group (target disease group, n=575). Samples with various autoimmune and infectious disease diagnosis represent the disease control group (n=452).

The distribution of the cohort and the EliA CTD 13 Screen positivity rate for each clinical subgroup is summarized in the following table.

Disease	N	N# of Positive[a]	% of Positive[a]	95% CI
Target Disease				
Systemic Lupus Erythematous (SLE)	200	200	100	98.2 – 100.0
Lupus Nephritis	11	11	100	71.5 – 100.0
Polymyositis (PM)	45	31	68.9	53.4 – 81.8
Dermatomyositis (DM)	51	24	47.1	32.9 – 61.5
Mixed Connective Tissue Disease (MCTD)	53	29	54.7	40.4 – 68.4
Sjogren's Syndrome (SS)	97	97	100	96.3 – 100.0
Systemic Sclerosis (SSc)	57	50	87.7	76.3 – 94.9
Limited Systemic Sclerosis (lSSc)	22	21	95.5	77.2 – 99.9
Raynaud's Phenomenon	39	36	92.3	79.1 – 98.4
Disease Controls				
Antiphospholipid Syndrome (pAPS+sAPS)[b]	47	27	57.4	42.2 – 71.7
Autoimmune Hepatitis (AIH)	20	18	90	68.3 – 98.8
Bacterial Infection	35	5	14.3	4.8 – 30.3
Celiac Disease	28	4	14.3	4.0 – 32.7
Crohn's Disease	21	0	0	0.0 – 16.1
Graves' Disease	27	0	0	0.0 – 12.8
HIV	24	0	0	0.0 – 14.2
Hashimoto's Thyroiditis	10	0	0	0.0 – 30.8
Hepatitis C	19	0	0	0.0 – 17.6
Leukemia	20	0	0	0.0 – 16.8
Lymphoma	20	0	0	0.0 – 16.8
Polymyalgia Rheumatica	25	0	0	0.0 – 13.7
Primary Biliary Cholangitis (PBC)	20	2	10	1.2 – 31.7
Primary Sclerosing Cholangitis (PSC)	24	0	0	0.0 – 14.2
Rheumatoid Arthritis (RA)	40	25	62.5	45.8 – 77.3
Ulcerative Colitis	22	1	4.5	0.1 – 22.8
Vasculitis	32	3	9.4	2.0 – 25.0
Other Viral Infections (EBV, HBV etc.)	18	0	0	0.0 – 18.5

[a] Equivocal results were considered as negative in this evaluation.
[b] Primary Antiphospholipid Syndrome (pAPS) = 27; Antiphospholipid Syndrome associated with SLE (sAPS) = 20.

Clinical sensitivity and specificity of EliA CTD 13 Screen are summarized in the tables below.

n= 1027		Clinical Diagnosis		
		Target Diseases	Disease Controls	Total
EliA CTD 13 Screen	Positive <0.7	499	84	583
	Equivocal 0.7 – 1.0	21	40	61
	Negative >1.0	55	328	383
	Total	575	452	1027

Equivocal results are considered negative		
Sensitivity	86.8%	95% CI: 83.7 - 89.4
Specificity	81.2%	95% CI: 77.3 – 84.7

Equivocal results are considered positive		
Sensitivity	90.4%	87.7 - 92.7
Specificity	72.6%	68.2 - 76.6

D Expected Values/Reference Range:

The frequency distribution for antinuclear antibodies was investigated in 330 apparently healthy subjects equally distributed by age and gender, using blood bank sera reflecting the ethnical distribution of the United States. The results of the cohort are depicted in the table below:

EliA CTD 13 Screen	Ratio
Median	0.1
Mean	0.3
Minimum	0.0
Maximum	26.1
95^{th} percentile	0.5
97^{th} percentile	0.8

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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