

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

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

k131821

**B. Purpose for Submission:**

New device

**C. Measurand:**

IgA antibodies to cardiolipin

**D. Type of Test:**

Fluoroenzymeimmunoassay assay, Semi-quantitative

**E. Applicant:**

Phadia US Inc.

**F. Proprietary and Established Names:**

EliA™ Cardiolipin IgA Immunoassay  
EliA™ APS Positive Control 100  
EliA™ APS Positive Control 250  
EliA™ IgG/IgM/IgA Negative Control 100  
EliA™ IgG/IgM/IgA Negative Control 250

**G. Regulatory Information:**

1. Regulation section:

21 CFR §866.5660, Multiple autoantibodies immunological test system  
21 CFR §862.1660, Quality Control Material (assayed and unassayed)

2. Classification:

Class II (Assays)  
Class I (Controls)

3. Product code:

MID, System, Test, Anti-cardiolipin Immunological  
JJY, Multi-Analyte Controls, All Kinds (assayed)

4. Panel:

Immunology (82) (Assays)  
Chemistry (75) (Controls)

**H. Intended Use:**

1. Intended use(s):

EliA™ Cardioliipin IgA is intended for the *in vitro* semi-quantitative measurement of IgA antibodies directed to cardioliipin in human serum and plasma (heparin, EDTA, citrate) to aid in the diagnosis of antiphospholipid syndrome (APS) as well as thrombotic disorders related to systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings. EliA™ Cardioliipin IgA uses the EliA™ IgA method on the instruments Phadia® 100 and Phadia® 250.

EliA™ APS Positive Control 100/250 is intended for laboratory use in monitoring the performance of *in vitro* measurement of antibodies to cardioliipin and β2-glycoprotein I with Phadia® 100 and Phadia® 250 using the EliA IgG, IgM or IgA method.

EliA™ IgG/IgM/IgA Negative Control 100/250 is intended for laboratory use in monitoring the performance of *in vitro* measurement of autoantibodies with Phadia® 100 and Phadia® 250 using the EliA IgG, IgM or IgA method.

2. Indication(s) 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 instruments Phadia® 100 and Phadia® 250 (formerly known as ImmunoCAP 100 and 250) (k061165).

**I. Device Description:**

EliA™ uses a modular reagent system. The test specific, method specific and general reagents are packaged and purchased as separate units. The reagents on Phadia® 100 and Phadia® 250 are identical; they are only filled in different containers.

EliA™ Cardioliipin Test-Specific Reagents consist of:

- 1) EliA™ Cardioliipin IgA wells coated with bovine cardioliipin (isolated from heart tissue) and bovine β2-glycoprotein I (isolated from serum) as co-factor
- 2) EliA™ APS Positive Control, containing human monoclonal IgG/IgM/IgA antibodies specific to cardioliipin

- 3) EliA™ IgG/IgM/IgA Negative Control containing normal human serum from healthy donors.

Also required for the test are *EliA™ Method-Specific Reagents*:

EliA™ IgA Calibrators (human IgA in PBS at measured concentrations (0, 0.3, 1.5, 5, 15, 80 µg/L), EliA™ IgA Curve Control (human IgA in PBS), EliA™ Sample Diluent (PBS containing BSA, detergent, and 0.095% sodium azide), EliA™ IgA Conjugate (β-galactosidase labeled mouse monoclonal anti- human IgA), and EliA™ IgA Calibrator Well.

**J. Substantial Equivalence Information:**

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

Quanta Lite ACA IgA III (k953366)

2. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>New Device</b> EliA™ Cardiolipin IgA Immunoassay	<b>Predicate</b> Quanta Lite ACA IgA III
Intended Use/Indications for Use	Measurement of IgA antibodies directed to cardiolipin aids in the diagnosis of antiphospholipid syndrome (APS) as well as thrombotic disorders related to systemic lupus erythematosus (SLE) in conjunction with other laboratory and clinical findings.	Measurement of IgA antibodies directed to cardiolipin aids in assessing the risk of thrombosis in individuals with SLE or lupus-like disorders in conjunction with other laboratory and clinical findings.
Type of Test	Semi-quantitative	Same
Coating Antigens	Purified bovine cardiolipin and bovine β2-Glycoprotein I (GPI) as co-factor	Same
Solid Phase	Polystyrene microwells	Same

<b>Differences</b>		
<b>Item</b>	<b>New Device</b> EliA™ Cardiolipin IgA Immunoassay	<b>Predicate</b> Quanta Lite ACA IgA III
Assay Type	Automated immunoassay	Manual ELISA
Sample Matrix	Serum and plasma (heparin, EDTA, citrate)	Serum
Sample Dilution	1:10 (manual or instrument dilution)	1:101 (manual dilution only)
Reaction Temperature	37°C (controlled)	Room temperature (20-25°C)
Detection Antibody (Conjugate)	Mouse anti-human IgA β-Galactosidase	Goat anti-human IgA horseradish peroxidase
Substrate/Chromogen	4-Methylumbelliferyl-βD-Galactoside	Tetramethylbenzidine (TMB)

<b>Differences</b>		
<b>Item</b>	<b>New Device EliA™ Cardioliipin IgA Immunoassay</b>	<b>Predicate Quanta Lite ACA IgA III</b>
Stop Solution	Sodium Carbonate (4%)	Sulfuric Acid (0.344 M)
Signal	Fluorescence	Optical density
Instrumentation	Phadia 100 and 250 are fully automated immunoassay analyzers	Microwell plate reader (450 nm)
Calibration	Total IgA calibration	Analyte-specific IgA calibration
Calibrators	Set of 6 lyophilized IgA calibrators: 0, 0.3, 1.5, 5, 15, 80 µg/L	Set of 5 pre-diluted IgA calibrators: 9.4, 18.8, 37.5, 75, 150 APL-U/mL
Calibration Curve	Option to store the calibration curve for up to 28 days and run curve controls in each assay for calibration	A new calibration curve must be run with each assay
Internal Controls	Positive and Negative Control sera provided in a separate package	Positive and Negative Control included in the assay kit
Reportable Range	0.3 – 181 APL-U/mL	Not specified
Limit of detection	0.27 APL-U/mL	Not specified
Results Interpretation	Negative: <14 APL-U/mL Equivocal: 14 – 20 APL-U/mL Positive: >20 APL-U/mL	Negative: <12 APL Units Indeterminate: 12 – 20 APL Units Low to medium positive: 20-80 APL Units High positive: >80 APL Units

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

CSLI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

**L. Test Principle:**

The EliA™ Cardioliipin IgA Wells are coated with bovine cardioliipin. If present in the patient's specimen, antibodies bind to their specific antigen. After washing away non-bound antibodies, enzyme-labeled antibodies against human IgA antibodies (EliA IgA 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 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.

The total IgA calibration is based on a set of six WHO-standardized IgA Calibrators derived from human serum. The IgA Calibrators are used to establish the initial calibration curve, which may be used for up to 28 days on additional assays and can be stored by the instrument. Each additional assay includes calibrator (curve) controls that have to recover in defined ranges to

ensure that the stored calibration curve is still valid. The Fluorescence-Immunoassay test system includes test, method specific reagents and general reagents that are packaged as separate units.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Eight serum samples selected from different parts of the claimed assay ranges were tested on Phadia® 100 and Phadia® 250 instruments to establish intra- and inter-run precision. Lot-to-lot repeatability was assessed with six samples on the Phadia 250. Each sample was run in 4 replicates on 3 instruments over 7 days. One batch was used to determine the precision of the assays on Phadia® 100 (equal to 84 replicate determinations per sample). Three batches were used to determine the precision of the assays on Phadia® 250 (equal to 252 replicate determinations per sample). Results are summarized below:

<b>EliA™ Cardiolipin IgA on Phadia 100 (n = 84)</b>						
Mean value APL-U/mL	Intra-Run		Inter-Run		Total Imprecision	
	SD	CV%	SD	CV%	SD	%CV
6.1	0.5	8.2	0.5	8.3	0.7	11.6
13.5	0.6	4.3	0.3	2.0	0.6	4.8
15.4	0.5	3.4	0.7	4.2	0.8	5.4
19.9	0.7	3.6	1.1	5.5	1.3	6.6
21.6	0.7	3.1	0.9	4.4	1.2	5.3
22.6	0.7	3.2	1.1	4.9	1.3	5.8
35.9	1.0	2.9	1.3	3.6	1.7	4.6
160.2	5.6	3.5	4.7	2.9	7.3	4.5

<b>EliA™ Cardiolipin IgA on Phadia® 250 (n = 252)</b>						
Mean value APL-U/mL	Intra-Run		Inter-Run		Total Imprecision	
	SD	CV%	SD	CV%	SD	%CV
5.0	0.6	11.1	0.1	1.6	0.6	11.3
13.6	0.3	2.0	0.3	2.4	0.4	3.1
15.9	0.4	2.2	0.5	2.9	0.5	3.6
19.0	1.1	5.6	0.3	1.3	1.1	5.8
20.0	1.2	6.1	0.3	1.3	1.2	6.2
21.9	0.8	3.7	0.4	1.8	0.9	4.1
35.9	1.5	4.1	0.5	1.5	1.6	4.3
162.4	8	4.9	5.5	3.4	9.7	6.0

The SD and %CV for lot-to-lot reproducibility on the Phadia® 250 ranged from 0.4 to 6.1 and 2.3% to 8.3%, respectively.

b. *Linearity/assay reportable range:*

Eight patient serum samples were serially diluted using EliA™ Sample Diluent. Each dilution was tested in three replicates in one run with one batch of EliA™ Cardiolipin IgA and one set of system reagents on the Phadia® 100 or Phadia® 250 instrument. The observed values were graphed against the calculated values and a linear regression was performed. Results are summarized below:

<b>EliA™ Cardiolipin IgA on Phadia® 100</b>					
Sample	Dilution range (APL-U/mL)	Slope (95% CI)	Y-Intercept (95% CI)	R <sup>2</sup>	%CV Range
1	0.4 - 4.6	1.02 (0.95 to 1.09)	0.08 (-0.08 to 0.24)	0.997	2.5 - 8.2
2	0.3 - 4.2	1.00 (0.93 to 1.06)	0.01 (-0.13 to 0.15)	0.997	1.1 - 16.7
3	1.3 - 75.4	1.02 (1.00 to 1.04)	0.33 (-0.19 to 0.84)	0.999	1.5 - 7.5
4	2.3 - 85.7	1.06 (1.04 to 1.09)	0.85 (-0.03 to 1.73)	0.999	1.5 - 6.0
5	2.3- 95.9	0.99 (0.98 to 1.00)	-0.34 (-0.75 to 0.08)	1.000	1.6 - 8.7
6	2.7- 90.9	0.96 (0.92 to 1.00)	1.08 (-0.43 to 2.60)	0.998	2.6 - 8.3
7	65.9 - 190.1	1.01 (0.96 to 1.06)	14.33 (8.52 to 20.14)	0.996	1.1 - 5.2
8	65.6 - 191.5	1.04 (0.97 to 1.12)	14.39 (5.01 to 23.77)	0.991	0.5 - 12.6

<b>EliA™ Cardiolipin IgA on Phadia® 250</b>					
Sample	Dilution range (APL-U/mL)	Slope (95% CI)	Y-Intercept (95% CI)	R <sup>2</sup>	%CV Range
1	0.3 - 3.2	1.04 (0.98-1.11)	0.07 (-0.03 to 0.17)	0.997	0.5 - 4.6
2	0.4 - 3.8	1.02 (0.96 to 1.08)	0.11 (-0.02 to 0.25)	0.997	0.8 - 4.0
3	1.5 - 55.1	1.04 (1.00 to 1.09)	0.69 (-0.30 to 1.69)	0.997	0.4 - 1.7
4	6.5 - 62.2	0.98 (0.90 to 1.05)	2.62 (0.35 to 4.89)	0.996	1.2 - 4.3
5	2.0 - 109.3	0.97 (0.96 to 0.97)	0.40 (0.02 to 0.78)	1.000	0.2 - 3.6
6	10.5 - 103.8	1.03 (0.94 to 1.12)	3.27 (-1.23 to 7.78)	0.994	0.3 - 1.5
7	64.2 - 204.3	0.93 (0.84 to 1.02)	21.01 (9.43 to 32.59)	0.984	1.3 - 12.7
8	66.1 - 215.6	0.84 (0.75 to 0.93)	31.63 (19.50 to 43.75)	0.980	1.4- 14.4

The claimed reportable range (detection limit, upper limit) for EliA™ Cardiolipin IgA is from 0.3 to  $\geq 181$  APL-U/mL. Depending on the lot specific EliA™ well factor, the upper limit of the measuring range may vary from 181 APL-U/mL to 271.2 APL-U/mL for different solid phase batches. Results above the upper limit of the measuring range are reported as “above”. No recommendations are made for dilution of samples outside the measuring range in the package insert. For very low signals, where the Response Units (RU) of the sample are less than the RU of Calibrator 0, the Error message “Low RU” will appear on the printout to indicate possible instrument failure.

High dose hook effect: A hook effect was not observed when analyzing a high positive serum sample with an estimated concentration 15 times above the upper limit of the measuring range.

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

i) *Traceability:*

Calibrators: There is no international standard for IgA antibodies directed to cardiolipin. The instrument measures specific IgA concentration in  $\mu\text{g/L}$  which is automatically converted to APL-U/mL by using a conversion factor given by the lot-specific bar code printed on the EliA™ Cardiolipin IgA Well.

The IgA calibrators are traceable (via unbroken chain of calibrations) to the International Reference Preparation (IRP) 67/86 of Human Serum Immunoglobulins A, G and M from the World Health Organization (WHO). Calibrators are compared to a secondary standard (standardized with the IRP) or the IRP directly and adjusted accordingly to meet the correct concentration.

Controls: The EliA™ Positive APS Control was prepared from human monoclonal antibodies and contains IgG, IgM and IgA antibodies to cardiolipin and  $\beta 2$ -Glycoprotein I. This Control was cleared under k091845. The EliA™ IgG/IgM/IgA Negative Control was prepared from normal human serum. This Control was cleared under k072393. The IgA target ranges for the EliA™ Controls for the two platforms are summarized below:

<b>Instrument</b>	<b>EliA™ Positive APS Control</b>
Phadia 100	33.2 – 86.2 APL-U/mL
Phadia 250	33.4 – 86.5 APL-U/mL
<b>EliA™ IgG/IgM/IgA Negative Control</b>	
Phadia 100	$\leq 11.2$ APL-U/mL
Phadia 250	$\leq 11.2$ APL-U/mL

The EliA IgA system reagents were cleared under k063775.

ii) *Kit Stability:*

Closed and open stability - An accelerated stability study initially determined the shelf-life of

the EliA™ Cardioliipin IgA Well was 24 months. A real-time stability study t supported the 24 months stability claim. All studies were performed on three batches of EliA™ Cardioliipin IgA Well. Other required components (previously reviewed) of the assay method have a shelf life of 18 to 24 months. The sponsor notes that it is important to store the wells in dry conditions at 2-8°C.

On-board stability - The on-board stability of the EliA™ Cardioliipin IgA Wells packed in carriers were tested for 2, 4 and 6 weeks at 10 °C and 80% humidity in duplicates in one run using 3 positive and 2 negative samples only on the Phadia 250 instrument since for Phadia 100 instrument the reagents are stored outside the instrument and are only loaded as needed for an assay. A separate stability study was performed under maximum misusage conditions in which EliA Cardioliipin IgA Wells were stored at 32°C ± 20% and 80% ± 20% humidity to support the room temperature on-board stability claim. As reference, IgA Wells packed in carriers were sealed in desiccant-containing foil bag and stored at 2-8°C in parallel. The on-board stability for the EliA™ Cardioliipin IgA Wells was determined to be 28 days at 2-8°C or 24 hours at room temperature.

iii) *Sample Storage:*

The sponsor recommends following the guidelines in CLSI H18-A3 for sample storage. 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 serum/plasma will be stored beyond 48 hours, serum/plasma should be frozen at or below -20°C. Freezing and thawing should be avoided.

d. *Detection limit:*

The analytical sensitivity was determined in accordance with CLSI EP17-A. The limit of blank (LoB) and limit of detection (LoD) studies were estimated parametrically by measuring the concentration of one negative and five low antibody samples in 12 replicates in each of six runs on six different days on both Phadia 100 and Phadia 250 instruments. Determinations on the Phadia 250 were divided between three instruments with two runs performed on each instrument. Determinations on the Phadia 100 were performed on one instrument. The results are summarized in the table below:

<b>EliA™ Cardioliipin IgA</b>	<b>LoB</b>	<b>LoD</b>
Phadia 100	0.18 APL-U/mL	0.27 APL-U/mL
Phadia 250	0.15 APL-U/mL	0.20 APL-U/mL

The LoB and LoD were set to 0.18 APL-U/mL and 0.27 APL-U/mL, respectively, for both Phadia instruments.

e. *Analytical specificity:*

i) *Endogenous Interference:*

Interferences were assessed by testing five serum samples: one negative (<14 APL-

U/mL), two within the equivocal range (18 and 20 APL-U/mL), a low positive (34 APL-U/mL) and a high positive (>120 APL-U/mL). Each sample was spiked with the interfering substances or substance-specific blanks and analyzed using one lot of EliA™ Cardioliipin IgA Well and one lot of system reagents in two runs, each in three replicates (n=6). The data demonstrated that EliA Cardioliipin IgA was not adversely affected by high levels of the following substances tested up to the concentrations listed in the table below:

Potential Interfering Compound	Concentration
Bilirubin F	20.6 mg/dL
Bilirubin C	21.1 mg/dL
Hemoglobin	519 mg/dL
Lipemic factor (ClinOleic)	1 g/dL (1%)
Rheumatoid factor	500 IU/mL

The use of sera containing lipemic, hemolyzed or microbial contaminations is not recommended as stated in the package insert.

*f. Assay cut-off:*

Based on the results of the expected values/reference range study described below in Section M.5, the 99<sup>th</sup> percentile lies below the upper limit of the equivocal range for EliA™ Cardioliipin IgA. The assay cutoffs were set as follows:

<14 APL-U/mL	Negative
14 – 20 APL-U/mL	Equivocal
>20 APL-U/mL	Positive

In case of equivocal results, it is recommended to retest the patient after 4-6 weeks. Good laboratory practice requires that each laboratory establishes its own range of expected values.

2. Comparison studies:

*a. Method comparison with predicate device:*

A total of 381 serum samples from patients with Antiphospholipid Syndrome (APS, n= 212), Systemic Lupus Erythematosus (SLE, n = 66), viral infections (n = 30), connective tissue diseases (n = 15), rheumatoid arthritis (RA, n = 15), non-viral infections (n = 20), syphilis (n = 20) or asymptomatic (n = 3) were assayed once on both Quanta Lite ACA IgA III and EliA™ Cardioliipin IgA. Of the APS samples, 10 were classified as Primary APS (PAPS) and 30 as Secondary APS (SAPS); the remaining APS samples (172) were not classified. Seven samples (1 PAPS, 2 SAPS and 4 non-classified APS) with values outside the measuring range were excluded. The results are summarized below:

		<b>Quanta Lite ACA IgA III (APL Units)</b>			
		Positive: >20	Indeterminate: 12-20	Negative: <12	Total
<b>EliA™ Cardiolipin IgA (APL- U/mL)</b>	Positive: >20	56	2	6	64
	Equivocal : 14-20	3	9	11	23
	Negative: <14	4	4	279	287
	Total	63	15	296	374

Agreements were calculated by grouping each assay's equivocal results with its test negative results, and then agreement was calculated again by grouping each assay's equivocal results with the test positive results:

Equivocal Quanta Lite results considered as negative		<b>Quanta Lite ACA IgA III (APL Units)</b>		
		Positive: >20	Negative: <20	Total
<b>EliA™ Cardiolipin IgA (APL-U/mL)</b>	Positive: >20	56	8*	64
	Negative: <20	7**	303	310
	Total	63	311	374

\* 3 SAPS, 4 non-classified APS, 1 SLE

\*\* 2 SAPS, 5 non-classified APS

Positive percent agreement: 88.9% (56/63) 95% CI: 78.4 – 95.4%

Negative percent agreement: 97.4% (303/311) 95% CI: 95.0 – 98.9%

Total percent agreement: 96.0% (359/374) 95% CI : 93.5 – 97.7%

Equivocal Quanta Lite results considered as positive		<b>Quanta Lite ACA IgA III (APL Units)</b>		
		Positive: >12	Negative: <12	Total
<b>EliA™ Cardiolipin IgA (APL-U/mL)</b>	Positive: >14	70	17*	87
	Negative: <14	8**	279	287
	Total	78	296	374

\* 14 APS (1 PAPS, 3 SAPS, 11 non-classified APS), 2 SLE, and 1 RA

\*\* 8 APS (1 SAPS, 1 SAPS, 6 non-classified APS)

Positive percent agreement: 89.7% (70/78) 95% CI: 80.8 – 95.5%

Negative percent agreement: 94.3% (279/296) 95% CI: 91.0 – 96.6%

Total percent agreement: 93.3% (369/374) 95% CI: 90.3 – 95.6%

*b. Matrix comparison:*

A study was performed to demonstrate that heparin plasma, citrate plasma and EDTA plasma matrices yield comparable values as serum in the EliA™ Cardiolipin IgA assay. A total of 62 matrix-matched samples spread across the assay range were assayed on Phadia 100.

Passing & Bablok regression analysis was performed using the values of the serum samples as the comparator and the results are summarized below:

	<b>Range tested (APL-U/mL)</b>	<b>Slope (95% CI)</b>	<b>Intercept (95% CI)</b>	<b>R<sup>2</sup></b>
Serum vs. Citrate plasma	1.2 – 160.6	0.99 (0.97 – 1.01)	-0.12 (-0.41 – 0.10)	0.99
Serum vs. EDTA plasma	1.4 – 160.7	0.99 (0.97 – 1.00)	0.15 (0.05 – 0.35)	1.00
Serum vs. Heparin plasma	1.3 – 169.7	1.01 (0.98 – 1.03)	-0.14 (-0.37 – 0.07)	1.00

c. *Instrument comparison:*

A study was performed to demonstrate that the performance of EliA™ Cardiolipin IgA was equivalent on the Instrument Phadia 100 and Phadia 250. A total of 36 samples (32 positive and 4 negative) spanning the assay range were analyzed on 3 different instruments in 6 runs (2 runs on each instrument) in single replicate. Regression analysis yielded a slope of 1.04 (95%CI 1.01 to 1.07) and a y-intercept of -1.54 (95%CI: -2.39 to -0.153).

3. Clinical studies:

a. *Clinical sensitivity and specificity:*

The performance of EliA™ Cardiolipin IgA Immunoassay was compared to a clinical diagnosis of APS and SLE. The validation set consisted of clinically characterized sera from APS and non-APS diseased controls for a total of 381 patient samples. The results of the EliA™ Cardiolipin IgA Immunoassay for each disease category are shown below:

<b>APS Patient Sub-Group</b>	<b>N</b>	<b>No (%) Positive</b>
Primary APS (PAPS)	10	6 (60%)
Secondary APS (SAPS)	30	20 (66.7%)
APS not classified as PAPS or SAPS	172	35 (29.3%)
<b>Total APS</b>	<b>212</b>	<b>61 (28.8%)</b>

<b>Non-APS Patient Sub-Group</b>	<b>N</b>	<b>No (%) Positive</b>
SLE	66	8 (12%)
Connective Tissue Diseases	15	0 (0%)
Syphilis	20	0 (0%)
Viral infections	30*	0 (0%)
Non-viral infections	20**	0 (0%)
Rheumatoid arthritis	15	0 (0%)
Asymptomatic	3	1 (33%)
<b>Total</b>	<b>169</b>	<b>9 (5.3%)</b>

\* 14 Epstein-Barr Virus (EBV), 1 Hepatitis C Virus (HCV), 8 Human Immunodeficiency Virus (HIV), 7 Parvo Virus

\*\* 19 Borrelia, 1 Helicobacter pylori

The following table summarizes the clinical sensitivities for the APS groups:

<b>Disease</b>	<b>Clinical Sensitivity (95% CI)</b>
Primary APS (PAPS)	60% (26.2 - 87.8 %)
Secondary APS (SAPS)	66.7% (47.2 - 82.7 %)
APS not classified as PAPS or SAPS	20.3% (14.6 - 27.1 %)
<b>Total APS</b>	<b>28.8% (22.8- 35.4 %)</b>

b. Other clinical supportive data (when a. is not applicable):

Not applicable

4. Clinical cut-off:

Same as assay cut-off

5. Expected values/Reference range:

A total of 400 apparently healthy blood donor samples from a Caucasian population equally distributed by gender and age were measured on the Phadia 250 instrument. The results are summarized below:

	<b>APL-U/mL</b>
Mean	3.6
Median	2.8
Range	0.3 – 48.9
95th percentile	7.1
99th percentile	17.1

The proportion of sera from apparently healthy, asymptomatic individuals found positive by the EliA™ Cardiolipin IgA is 1%, increasing with age, and men tend to show higher values. One percent (1%) of the samples fell in the equivocal range. Expected values may vary depending on the population tested.

**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.