

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

A. 510(k) Number:

k102673

B. Purpose for Submission:

New device

C. Measurand:

Rheumatoid Factors IgM and IgA

D. Type of Test:

Fluoroenzymeimmunoassay, Quantitative

E. Applicant:

Phadia AB

F. Proprietary and Established Names:

EliA™ RF IgM Immunoassay

EliA™ RF IgA Immunoassay

EliA™ RF Positive Control 100

EliA™ RF Positive Control 250

G. Regulatory Information:

1. Regulation section:

21 CFR§866.5775 – Rheumatoid Factor Immunological Test System

21 CFR§862.1660 – Quality Control Material (Assayed and Unassayed)

2. Classification:

Class II (assay)

Class I (control)

3. Product code:

DHR – System, Test, Rheumatoid Factor (RF)

JJY – Multi-Analyte Controls, All kinds (assays)

4. Panel:

Immunology (82)

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

EliA™ RF IgM is intended for the *in vitro* quantitative measurement of IgM class rheumatoid factor antibodies in human serum and plasma (Li-heparin, EDTA, citrate) to aid in the diagnosis of rheumatoid arthritis in conjunction with other laboratory and clinical findings. EliA™ RF IgM uses the EliA IgM method on the instruments Phadia 100 and Phadia 250.

EliA™ RF IgA is intended for the *in vitro* quantitative measurement of IgA class rheumatoid factor antibodies in human serum and plasma (Li-heparin, EDTA, citrate) to aid in the diagnosis of rheumatoid arthritis in conjunction with other laboratory and clinical findings. EliA™ RF IgA uses the EliA IgA method on the instruments Phadia 100 and Phadia 250.

EliA™ RF Positive Control 100 is intended for laboratory use in monitoring the

performance of *in vitro* measurement of rheumatoid factor (RF) with Phadia 100 using the EliA IgM or IgA method.

EliA™ RF Positive Control 250 is intended for laboratory use in monitoring the performance of *in vitro* measurement of rheumatoid factor (RF) with Phadia 250 using the EliA IgM or IgA method.

2. Indication(s) for use:
Same as Intended Use
3. Special conditions for use statement(s):
Prescription use only
4. Special instrument requirements:
For use on the Phadia 100 and Phadia 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™ RF IgM or IgA Test Specific Reagents consist of:

- 1) EliA™ RF IgM or IgA well, coated with aggregated rabbit IgG antigen;
- 2) EliA™ RF positive control, a multiparameter control containing IgA or IgM rheumatoid factor antibodies;
- 3) EliA™ IgG/IgM/IgA Negative Control, a multiparameter control containing normal human serum from healthy donors.

Also required for the test are:

- 1) *EliA™ Method-Specific Reagents:*
 - EliA™ method-specific sample diluent (PBS containing BSA, detergent and 0.095% sodium azide);
 - EliA™ IgM or IgA conjugate (β -galactosidase labeled mouse monoclonal anti-IgM or -IgA antibodies);
 - EliA™ IgM or IgA calibrators [human IgM or IgA in PBS at measured concentrations (0, 10, 35, 80, 500, 1000 μ g/L for the IgM, and 0, 0.3, 1.5, 5, 15, 80 μ g/L for IgA)];
 - EliA™ IgM or IgA Curve Control;
 - EliA™ IgM or IgA Calibrator Well.
- 2) *General Reagents:*
 - Development Solution, Stop Solution, and Washing Solution

J. Substantial Equivalence Information:

1. Predicate device name(s) and Predicate 510(k) number(s):
QUANTA Lite™ RF IgM ELISA, k971614
QUANTA Lite™ RF IgA ELISA, k983084
2. Comparison with predicate:

Similarities		
Item	New Device EliA™ RF IgM/IgA	Predicate Device QUANTA Lite™ RF IgM/IgA
Intended Use:	Measurement of IgM or IgA class rheumatoid factor antibodies to aid in the diagnosis of rheumatoid arthritis in conjunction with other laboratory and clinical findings.	Same
Controls	positive control and negative control	Same
Type of Assay	ELISA	Same
Antigen Used	Rabbit IgG	Same

Differences		
Item	New Device EliA™ RF IgM/IgA	Predicate Device QUANTA Lite™ RF IgM/IgA
Type of Test	Quantitative	Semi-quantitative
Sample Matrix	Serum and plasma (Li-heparin, EDTA, citrate)	Serum
Antigen Used	Aggregated rabbit IgG	Purified rabbit IgG
Assay type	Automated immunoassay	Manual ELISA
Instrumentation	Phadia 100 and 250 automated immunoassay analyzers	ELISA-Reader needed
Reaction Temperature	37°C controlled	Room temperature, 20-26°C
Detection Antibody (conjugate)	β-galactosidase labeled anti-IgM or -IgA (mouse monoclonal antibodies)	Horse-Radish Peroxidase labeled anti-human IgM or -IgA (goat)
Substrate	MUG	TMB
Signal	Fluorescence	Optical density
Calibration curve	Option to store curve for up to 28 days and run curve controls in each assay for calibration	5-point standard curve (Calibrator A-E)
Package	Modular reagents concept (test-method specific and general reagents)	All reagents in a single kit
Assay Cut-off	<u>EliA™ RF IgM:</u> Negative: <3.5 IU/mL Equivocal: 3.5 – 5.0 IU/mL Positive: >5.0 IU/mL <u>EliA™ RF IgA:</u> Negative: <14 IU/mL Equivocal: 14 – 20 IU/mL Positive: >20 IU/mL	<u>QUANTA Lite™ RF IgM:</u> Negative: ≤ 6 Units Positive: > 6 Units <u>QUANTA Lite™ RF IgA:</u> Negative: ≤ 6 Units Positive: > 6 Units

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

None referenced.

L. Test Principle:

The EliA™ wells are molded cups comparable to excised wells from a microtiter plate. They are made of polystyrene and are coated with the respective antigen. The wells are at the same time a holder of the coupled antigen for convenient automation and a reaction chamber with reaction/washing solution handling based on pipetting to add and aspiration to remove liquids. The EliA™ RF IgM and IgA wells are coated with aggregated rabbit IgG. If present in the patient's specimen, rheumatoid factor antibodies bind to the antigen. After washing away non-bound antibodies, enzyme-labeled mouse monoclonal antibodies against human IgM or IgA antibodies (EliA™ IgM Conjugate or EliA™ IgA conjugate, respectively) 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 fluorescence intensity is directly proportional to the concentration of specific IgM or IgA antibodies present in the specimen. Quantitation of RF IgM and IgA antibodies is determined based on standard curve of fluorescence intensity generated with the calibrators.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision of EliA™ RF IgM or EliA™ RF IgA assay was evaluated with analyses of six (6) samples across the claimed measuring range of the assay in six (6) replicates per run using three (3) instruments of each instrument family member for six (6) runs. The acceptance criteria for intra-assay and inter-assay precision were <10% CV and <8% CV, respectively. Results of the studies are shown in the tables below.

EliA™ RF IgM:

Sample	Mean Value (IU/mL)	Intra Assay		Inter Assay		Total	
		SD	%CV	SD	%CV	SD	%CV
<i>Instrument Phadia 100</i>							
1	3.8	0.26	6.8	0.24	6.4	0.35	9.3
2	6.4	0.44	6.8	0.27	4.2	0.52	8.0
3	157.7	8.04	5.1	5.52	3.5	9.75	6.2
4	2.4	0.18	7.7	0.07	2.7	0.20	8.2
5	3.2	0.22	6.9	0.16	5.0	0.27	8.6
6	38.2	1.95	5.1	1.55	4.1	2.49	6.5
<i>Instrument Phadia 250</i>							
1	2.9	0.13	4.5	0.11	3.7	0.17	5.8
2	6.2	0.23	3.7	0.18	3.0	0.30	4.8
3	152.8	4.06	2.7	2.02	1.3	4.54	3.0
4	2.4	0.10	4.4	0.09	4.0	0.14	5.9
5	3.0	0.15	4.9	0.08	2.6	0.17	5.5
6	36.4	1.14	3.1	0.74	2.0	1.36	3.8

EliA™ RF IgA

Sample	Mean Value (IU/mL)	Intra Assay		Inter Assay		Total	
		SD	%CV	SD	%CV	SD	%CV
<i>Instrument Phadia 100</i>							
1	11.3	0.75	6.6	0.51	4.5	0.90	8.0
2	18.8	0.97	5.1	0.59	3.2	1.13	6.0
3	51.6	3.56	6.9	1.60	3.1	3.90	7.6
4	2.7	0.22	8.3	0.09	3.3	0.24	8.9
5	3.6	0.22	6.2	0.16	4.3	0.27	7.6
6	170.6	12.54	7.4	7.55	4.4	14.64	8.6
<i>Instrument Phadia 250</i>							
1	13.2	0.55	4.2	0.41	3.2	0.69	5.2
2	19.3	0.68	3.5	1.33	6.9	1.49	7.7
3	58.5	1.86	3.2	2.19	3.7	2.87	4.9
4	2.8	0.15	5.4	0.11	4.0	0.19	6.7
5	4.3	0.25	5.9	0.11	2.6	0.27	6.4
6	189.5	10.11	5.3	6.16	3.3	11.84	6.3

b. *Linearity/assay reportable range:*

Six samples were serially diluted and analyzed with EliA™ RF IgM and EliA™ RF IgA kits with one set of system reagents each. Regression analyses of the observed results (y) and the expected results (x) for each sample are presented below:

EliA™ RF IgM:

Sample	Range (IU/mL)	Regression equation	Slope 95% CI	Intercept 95% CI
<i>Instrument Phadia 100</i>				
1	0.7 – 25.2	y=1.042x + 0.043	1.004 – 1.080	-0.238 – 0.323
2	0.7 – 15.0	y=0.941x + 0.166	0.910 – 0.972	0.018 – 0.313
3	1.2 – 25.3	y=0.968x + 0.024	0.944 – 0.991	-0.163 – 0.210
4	3.6 – 88.1	y=1.018x + 1.362	0.954 – 1.082	-0.419 – 3.143
5	3.6 – 85.5	y=1.024x + 0.517	0.971 – 1.078	-0.931 – 1.965
6	9.0 – 195.7	y=1.064x + 2.105	0.991 – 1.137	-2.406 – 6.616
<i>Instrument Phadia 250</i>				
1	1.7 – 24.2	y=1.047x + 0.151	1.036 – 1.058	0.059 – 0.242
2	0.9 – 14.9	y=1.087x – 0.010	1.073 – 1.101	-0.080 – 0.059
3	1.8 – 23.8	y=0.970x + 0.310	0.922 – 1.017	-0.137 – 0.757
4	1.4 – 69.2	y=1.042x + 0.625	1.006 – 1.077	-0.072 – 1.321
5	5.8 – 84.1	y=0.833x + 2.753	0.781 – 0.885	1.278 – 4.227
6	3.2 – 167.2	y=1.072x – 0.501	1.004 – 1.139	-3.687 – 2.685

The claimed measuring range for EliA™ RF IgM is 0.5 – 200 IU/mL.

EliA™ RF IgA:

Sample	Range (IU/mL)	Regression equation	Slope 95% CI	Intercept 95% CI
<i>Instrument Phadia 100</i>				
1	0.2 – 17.9	y=0.967x + 0.187	0.914 – 1.019	-0.078 – 0.452
2	0.2 – 15.7	y=1.012x + 0.101	0.980 – 1.043	-0.037 – 0.239
3	0.4 – 8.5	y=0.977x – 0.070	0.958 – 0.995	-0.122 – -0.018
4	14.8 – 192.3	y=1.020x + 3.795	0.968 – 1.073	0.169 – 7.421
5	8.3 – 224.6	y=0.913x + 3.649	0.872 – 0.954	0.697 – 6.602
6	4.0 – 113.6	y=1.060x + 0.716	1.019 – 1.100	-0.770 – 2.202
<i>Instrument Phadia 250</i>				
1	0.3 – 13.6	y=1.126x + 0.044	1.077 – 1.175	-0.139 – 0.228
2	0.3 – 7.6	y=1.110x + 0.049	1.059 – 1.161	-0.064 – 0.162
3	0.3 – 7.0	y=0.956x – 0.147	0.889 – 1.024	-0.314 – 0.021
4	3.1 – 69.2	y=1.157x – 0.495	1.080 – 1.233	-2.250 – 1.260
5	7.1 – 185.4	y=0.956x + 3.641	0.889 – 1.022	-0.316 – 7.598
6	9.7 – 272.3	y=0.939x + 2.468	0.918 – 0.960	0.624 – 4.313

The claimed measuring range for EliA™ RF IgA is 0.6 – 214 IU/mL.

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

The IgM and IgA 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. The EliA™ RF IgM and EliA™ RF IgA are calibrated against the WHO reference preparation W1066. Results are given in International Units (IU/mL).

EliA™ RF Positive Controls are prepared from selected pooled human sera. EliA™ RF Positive Control 100 is used with Phadia 100 and EliA™ RF Positive Control 250 is used with Phadia 250. The value for each lot of EliA™ RF Positive Control 100 is assigned with 4 consecutive control assays, each in 6 replicates. The ranges are calculated as mean ± 3SD. The value for each lot of EliA™ RF Positive Control 250 is assigned with 2 consecutive control assays, each in 6 replicates. The ranges are calculated as mean ± 3SD.

Stability: Except for the EliA™ RF IgM wells and EliA™ RF IgA wells, other components for EliA™ RF IgM and IgA kits have been previously cleared (k091845 for EliA IgM system and k062787 for EliA IgA system).

Stability of closed EliA™ RF IgM/IgA wells: Accelerated stability studies were performed for EliA™ RF IgM wells and EliA™ RF IgA wells. One lot of EliA™ RF IgM wells and one lot of IgA wells in plates were stored at 30°C (stressed) for 12 weeks. The same lots of EliA™ RF IgM wells and EliA™ RF IgA wells stored at 2-8°C were used as reference. All plates (with lid) were stored in closed sealed foil bags with desiccant bags. Three positive and two negative samples were tested in duplicate in one assay run with the

EliA™ RF IgM wells or EliA™ RF IgA wells stored at 30°C after 4, 8 or 12 weeks along with those reference wells stored at 2-8°C. The concentration (IU/mL) was calculated for each sample at each time point. The results from accelerated stability study support the shelf life of 36 months for the EliA™ RF IgM wells and EliA™ RF IgA wells.

Stability of open EliA™ RF IgM/IgA wells: The stability of open EliA™ RF IgM and EliA™ RF IgA wells were also evaluated. The results support the claim that EliA™ RF IgM wells and IgA wells are stable up to 9 months upon opening.

Stability for EliA™ RF Positive Controls: The EliA™ RF Positive Control is packaged in single use vials. An accelerated stability study was conducted to establish the shelf life of the EliA™ RF Positive Control. One lot of the EliA™ RF Positive Control was stored at 30°C (stressed) for 8 weeks. The same lot of positive control stored at 2-8°C was used as reference. The stressed positive control and the reference positive control were assayed in duplicate using EliA™ RF IgA and IgM wells and a full calibration curve. The results support the claim of 24 months stability for EliA™ RF Positive Control.

Stability for EliA™ IgM and EliA™ IgA calibration curve: Stability of calibration curves for EliA™ IgM and EliA™ IgA were evaluated. The results support the claim that the calibration curve can be stored up to 28 days and a new calibration curve is needed after any curve control failures and expiry of reagents.

d. Detection limit:

Limit of Blank (LoB): Analyte free EliA™ sample diluent was measured 100 times each on EliA™ RF IgM and IgA antigen wells. LoB was estimated as the 95th percentile of the distribution of the concentrations. LoB for EliA™ RF IgM and EliA™ RF IgA assays are 0.3 IU/mL and 0.4 IU/mL, respectively.

Limit of Detection (LoD): Five samples with antibody concentrations between LoB to 4xLoB were each measured 75 times using EliA™ RF IgA or RF IgM antigen wells. LoD was calculated as $LoD = LoB + 1.645 \sigma_{LoD}$. The claimed LoD for EliA™ IgM and EliA™ RF IgA are 0.5 IU/mL and 0.6 IU/mL, respectively.

e. Analytical specificity:

Endogenous interference: The study was done to investigate the effect on results of RF IgM and RF IgA in the presence of endogenous interfering substances using EliA™ RF IgM and EliA™ RF IgA. Two positive serum samples with concentration levels around the cut-off and one high positive serum sample with concentration level around calibrator 5 were spiked with bilirubin C, bilirubin F, hemoglobin and lipemic factor (LF =ClinOleic; 20%

emulsion of refined olive oil). The same samples spiked with substance specific vehicles were used as controls. All samples were tested in 3 replicates in two separate runs. No significant interference was noted for samples containing bilirubin F up to 191 mg/L, bilirubin C up to 216 mg/L, hemoglobin up to 49.4 mg/L and LF up to 1%.

Hook effect: A high positive sample that had a concentration up to 62 times above the upper limit of the measuring range of the EliA™ RF IgM assay was tested on EliA™ RF IgM wells and Cal-1000 was tested on EliA™ IgM calibrator wells. No hook effect was detected. A high positive sample that had a concentration up to 10 times above the upper limit of the measuring range of EliA™ RF IgA assay was tested on EliA™ RF IgA wells, and Cal-80 was used on EliA™ IgA calibrator wells. No hook effect was observed.

f. Assay cut-off:

Based on the results of the expected values/reference range study described below in Section M.5, the assay cutoffs (IU/mL) were set as follows:

	Negative	Equivocal	Positive
EliA™ RF IgM	<3.5 IU/mL	3.5 – 5.0 IU/mL	>5.0 IU/mL
EliA™ RF IgA	<14 IU/mL	14 – 20 IU/mL	>20 IU/mL

2. Comparison studies:

a. Method comparison with predicate device:

For RF IgM assays, 268 samples from the clinical study that were within the measuring ranges of both EliA™ RF IgM and QUANTA Lite™ RF IgM were tested. Percent agreements between EliA™ RF IgM and QUANTA Lite™ RF IgM are summarized in the following table.

		QUANTA Lite™ RF IgM		
		Positive > 6 Units	Negative ≤ 6 Units	Total
EliA™ RF IgM	Positive (>5.0 IU/mL)	72	7	79
	Equivocal (3.5 – 5.0 IU/mL)	4	5	9
	Negative (<3.5 IU/mL)	18	162	180
	Total	94	174	268
<u>Equivocal Results as Positive:</u>				
Positive Percent Agreement: 80.9% (95% CI: 71.4 – 88.2%)				
Negative Percent Agreement: 93.1% (95% CI: 88.3 – 96.4%)				
Total Agreement: 88.8% (95% CI: 84.4 – 92.3%)				

Equivocal Results as Negative:

Positive Percent Agreement: 76.6% (95% CI: 66.7 – 84.7%)
Negative Percent Agreement: 96.0% (95% CI: 91.9 – 98.4%)
Total Agreement: 89.2% (95% CI: 84.8 – 92.6%)

For RF IgA assays, 289 samples from the clinical study that were within the measuring ranges of both EliA™ RF IgA and QUANTA Lite™ RF IgA were tested. Negative percent agreement, positive percent agreement, and total agreement between EliA™ RF IgA and QUANTA Lite™ RF IgA are summarized in the following table.

		QUANTA Lite™ RF IgA		
		Positive > 6 Units	Negative ≤ 6 Units	Total
EliA™ RF IgA	Positive (>20 IU/mL)	60	3	63
	Equivocal (14 – 20 IU/mL)	1	12	13
	Negative (<14 IU/mL)	0	213	213
	Total	61	228	289

Equivocal Results as Positive:

Positive Percent Agreement: 100% (95% CI: 94.1 – 100%)
Negative Percent Agreement: 93.4% (95% CI: 89.4 – 96.3%)
Total Agreement: 94.8% (95% CI: 91.6 – 97.1%)

Equivocal Results as Negative:

Positive Percent Agreement: 98.4% (95% CI: 91.2 – 100%)
Negative Percent Agreement: 98.7% (95% CI: 96.2 – 99.7%)
Total Agreement: 98.6% (95% CI: 96.5 – 99.6%)

b. Matrix comparison:

Serum, Li-Heparin plasma, citrate plasma and EDTA plasma samples were collected from the same patient to demonstrate that the plasma results from EliA™ RF IgM assay or EliA™ RF IgA assay do not deviate from the corresponding serum result by $\pm 20\%$. The samples covering the measuring range were tested. Regression analyses of the plasma results (y) and the serum results (x) for each plasma sample type are presented below:

EliA™ RF IgM:

Matrix	N	Comparison	Slope 95% CI	Intercept 95% CI
Li-Heparin plasma	24	$y = 1.04x - 0.05$	1.01 – 1.06	-0.14 – 0.07
EDTA plasma	24	$y = 1.05x - 0.03$	1.03 – 1.06	-0.11 – 0.02
Citrate Plasma	24	$y = 1.08x - 0.20$	1.05 – 1.10	-0.25 – 0.01

EliA™ RF IgA:

Matrix	N	Comparison	Slope 95% CI	Intercept 95% CI
Li-Heparin plasma	29	$y = 1.00x + 0.11$	0.99 – 1.02	-0.06 – 0.30
EDTA plasma	29	$y = 1.02x + 0.05$	1.00 – 1.03	-0.28 – 0.19
Citrate Plasma	29	$y = 1.06x - 0.22$	1.04 – 1.11	-0.39 – -0.01

3. Clinical studies:

a. *Clinical Sensitivity/Clinical Specificity:*

A total of 300 serum samples were collected and tested to establish the clinical sensitivity and specificity of the EliA™ RF IgM and EliA™ RF IgA assays. They include 100 samples from patients who had been clinically defined as suffering from rheumatoid arthritis (RA) based on ACR criteria and 200 disease control samples consisting of 47 samples of systemic lupus erythematosus (SLE), 20 samples of systemic sclerosis, 10 samples of myositis, 20 samples of Sjögren's Syndrome, 10 samples of undifferentiated connective tissue disease (UCTD), 8 samples of seronegative spondyloarthritis, 17 samples of psoriatic arthritis, 20 samples of Morbus Crohn, 20 samples of colitis ulcerosa, 28 samples of non-inflammatory rheumatic diseases (osteoarthritis). All of the RA patients received medications. Clinical sensitivity and specificity were calculated based on the results from EliA™ RF IgM and EliA™ RF IgA assays and the clinical diagnosis. 20 Patients with Sjögren's Syndrome and 2 patients with SLE who were also diagnosed with Sjögren's Syndrome were excluded from calculation of specificity as they are known to have rheumatoid factor frequently. The results (n=278) were summarized in the following tables:

		Clinical Diagnosis of RA		
		Positive	Negative	Total
EliA™ RF IgM	Positive (>5.0 IU/mL)	58	15	73
	Negative ^[a] (≤5.0 IU/mL)	42	163	205
	Total	100	178	278
Sensitivity:		58.0% (58/100) (95% CI: 47.7 – 67.8%)		
Specificity:		91.6% (163/178) (95% CI: 86.5 – 95.2%)		

Note: ^[a]Negative includes those with equivocal results.

		Clinical Diagnosis of RA		
		Positive	Negative	Total
EliA™ RF IgA	Positive (>20 IU/mL)	49	13	62
	Negative ^[a] (≤20 IU/mL)	51	165	216
	Total	100	178	278
Sensitivity:		49.0% (49/100) (95% CI: 38.9 – 59.2%)		
Specificity:		92.7% (165/178) (95% CI: 87.8 – 96.1%)		

Note: ^[a]Negative includes those with equivocal results.

Additionally, 30 samples from patients diagnosed with unspecified viral infection, bacterial infection and Syphilis were tested. The clinical specificity of EliA™ RF IgM and EliA™ RF IgA in patients with other diseases was summarized in the following table.

Disease	N	EliA™ RF IgM		EliA™ RF IgA	
		Positive	Negative ^[a]	Positive	Negative ^[a]
SLE	47	6	41	4	43
Systemic Sclerosis	20	5	15	4	16
Myositis	10	0	10	0	10
Sjögren's Syndrome	20	13	7	12	8
UCTD	10	2	8	2	8
Seronegative Spondyloarthritis	8	0	8	0	8
Psoriatic Arthritis	20	2	18	2	18
Morbus Crohn	20	0	20	0	20
Colitis Ulcerosa	20	0	20	0	20
Non-inflammatory Rheumatic Disease (Osteoarthritis)	28	0	28	1	27
Bacterial and Viral Infection	20	7	13	5	15
Syphilis	10	0	10	0	10

Note: ^[a]Negative includes those with equivocal results.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

A total of 400 apparently healthy normal blood donor samples were collected from Caucasian individuals with different gender and age and tested to establish

reference range for EliA™ RF IgM and IgA assays in the normal population and to confirm the defined cut-off. The results are summarized in the tables below:

EliA™ RF IgM:

Sex	Total	Male					Female				
Age	20-69	20-29	30-39	40-49	50-59	60-69	20-29	30-39	40-49	50-59	60-69
N	400	40	40	40	40	40	40	40	40	40	40
Mean	1.7	0.9	1.2	1.7	1.6	2.3	1.6	1.3	1.4	2.1	3.2
SD	4.1	0.8	1.0	3.0	1.8	4.5	3.2	1.0	1.7	3.5	10.5
Median	0.9	0.7	0.8	0.8	0.9	0.8	1.1	1.1	1.0	1.0	0.9
95% Percentile	5.3	2.8	3.0	6.0	6.2	9.7	2.3	2.2	2.6	7.9	9.0
99% Percentile	18.2	3.3	4.4	14.0	7.3	19.4	14.2	4.8	8.1	16.8	45.3

For EliA™ RF IgM assay, the 95th percentile lies below the upper limit of the equivocal range as literature indicates that about 5% of the normal population may be found RF IgM positive. The results show that cut-off for the upper limit of the equivocal range for EliA™ RF IgM is 5.0 IU/mL.

EliA™ RF IgA:

Sex	Total	Male					Female				
Age	20-69	20-29	30-39	40-49	50-59	60-69	20-29	30-39	40-49	50-59	60-69
N	400	40	40	40	40	40	40	40	40	40	40
Mean	5.1	3.5	3.9	6.7	6.5	8.1	3.3	4.3	3.6	4.5	6.1
SD	6.0	1.6	3.2	12.2	5.0	10.0	1.3	2.5	1.4	5.0	5.1
Median	3.8	3.2	3.1	4.5	4.7	5.2	3.4	3.8	3.1	3.1	4.4
98% Percentile	18.6	7.4	12.2	29.3	22.4	48.1	6.2	12.2	7.3	16.0	19.8
99% Percentile	30.4	7.5	15.4	54.7	23.1	48.5	7.1	12.6	8.3	24.6	25.1

For EliA™ RF IgA, the 98th percentile lies below the upper limit of the equivocal range. The results show that cut-off for the upper limit of the equivocal range for EliA™ RF IgA is 20 IU/mL.

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.