

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION

DECISION SUMMARY

A. 510(k) Number:

k103834

B. Purpose for Submission:

New Device

C. Measurand:

IgG and IgA antibodies to Cardiolipin (CL)

IgG and IgA antibodies to Beta-2-Glycoprotein I (β 2GPI)

D. Type of Test:

Semi-quantitative multiplex flow, bead-based immunoassay

E. Applicant:

Bio-Rad Laboratories, Inc.

F. Proprietary and Established Names:

BioPlex® 2200 APLS IgG kit

BioPlex® 2200 APLS IgA kit

BioPlex® 2200 APLS IgG and IgA Calibrator sets

BioPlex® 2200 APLS IgG and IgA Control sets

G. Regulatory Information:

1. Regulation section:

21 CFR §866.5660 – Multiple autoantibodies immunological test system

21 CFR §862.1150 – Calibrator

21 CFR § 862.1660 – Quality Control Material (assayed and unassayed)

2. Classification:

Class II (Assays, Calibrator)

Class I (Controls)

3. Product code:

MID, System Test, Anti-Cardiolipin Immunological

MSV, Antibodies, β 2- Glycoprotein I (β 2-GPI)

JIX, Calibrator, Mult-Analyte Mixture

JJX, Single (specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Immunology (82) (Assays)

Chemistry (75) (Controls)

H. Intended Use:

1. Intended use(s):

The BioPlex® 2200 APLS IgG and IgA kits are multiplex flow immunoassays intended for the semi-quantitative detection of IgG and IgA antibodies to Cardiolipin (CL) and Beta-2 Glycoprotein I (β2GPI) in human serum and plasma (lithium heparin, sodium heparin, and sodium citrate). In conjunction with other clinical findings, the test systems are used as an aid in the diagnosis of primary Antiphospholipid Syndrome (APS) and those secondary to systemic lupus erythematosus (SLE) or SLE-like disorders.

The BioPlex® 2200 APLS IgG and IgA kits are intended for use with the Bio-Rad BioPlex® 2200 System

The BioPlex® 2200 APLS IgG and IgA Calibrator Sets are intended for the calibration of the corresponding BioPlex® 2200 APLS IgG and IgA Reagent Packs.

The BioPlex® 2200 APLS IgG and IgA Control Sets are intended for use as an assayed quality control to monitor the overall performance of the BioPlex® 2200 instrument and the corresponding BioPlex® 2200 APLS IgG and IgA Reagent Packs in the clinical laboratory. The performance of the BioPlex® 2200 APLS IgG and IgA Control Sets has not been established with any other anti-Cardiolipin and anti- Beta-2 Glycoprotein I IgG or IgA APS assays.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For Prescription Use only

4. Special instrument requirements:

BioRad BioPlex® 2200 Instrument and Software Version 4.0

I. Device Description:

BioPlex® 2200 Anti-Phospholipid Syndrome (APLS) IgG and IgA kits include the following components:

- One (1) 100 mL vial of Bead Set containing two different populations of dyed beads coated with Cardiolipin (CL) and Beta-2-Glycoprotein I (β2GPI), an Internal Standard Bead (ISB), a Serum Verification Bead (SVB) and a Reagent Blank Bead (RBB) in a MOPS (3-[N-Morpholino] propanesulfonic acid) buffer supplemented with glycerol and protein stabilizers (bovine); ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.
- One (1) 5 mL-vial of Conjugate containing phycoerythrin conjugated murine monoclonal anti-human IgG or IgA antibody and phycoerythrin conjugated murine monoclonal anti-human FXIII antibody in MOPS buffer supplemented with protein stabilizer (bovine), and ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives,

- One (1) 10-mL vial of Sample Diluent containing buffer with protein stabilizers (bovine and murine), and ProClin 300 (0.3%), sodium benzoate (0.1%) and sodium azide (< 0.1%) as preservatives.

BioPlex® 2200 APLS IgG and IgA Calibrator sets contains seven (IgG) or three (IgA) vials of human antibodies to CL or β2GPI in a human serum matrix made from defibrinated plasma with ProClin 300 (≤ 0.3%) and sodium azide (< 0.1%) as preservatives.

BioPlex® 2200 APLS IgG and IgA Control sets contains four 1.5-mL vials of Positive controls of human antibodies to CL or β2GPI and two vials of Negative Controls in a human serum matrix made from defibrinated plasma; and, in a human serum matrix made from defibrinated plasma with ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.

Additional materials required but not supplied include BioPlex® 2200 Sheath Fluid containing Phosphate Buffered Saline (PBS) with ProClin® 300 (0.03%) and sodium azide (<0.1%) as preservatives; and BioPlex® 2200 Wash Solution containing Phosphate Buffered Saline (PBS) and Tween 20 with ProClin® 300 (<0.03%) and sodium azide (<0.1%) as preservatives.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) number(s)
 REAADS anti-Cardiolipin IgG/IgM Semi-Quantitative Test Kit (2 assays), k022992
 REAADS IgA anti-Cardiolipin Semi-Quantitative Test Kit, k022990
 REAADS IgG anti-Beta 2 Glycoprotein I Semi-quantitative Test Kit, k013080
 REAADS IgA anti-Beta 2 Glycoprotein I Semi-Quantitative Test Kit, k013079
2. Comparison with predicate:

Similarities			
Item	Device: BioPlex® 2200 APLS IgG and IgA Kits	Predicate: REAADS Anti-CL IgG and IgA Kits	Predicate: REAADS Anti-β2GPI IgG and IgA Kits
Intended Use	Semi-quantitative detection of IgG and IgA antibodies to Cardiolipin (CL) and Beta-2 Glycoprotein I (β2GPI) in human serum and plasma as an aid in the diagnosis of primary Antiphospholipid Syndrome (APS) and those secondary to systemic lupus	Semi-quantitative determination of anti-cardiolipin IgG, IgM, and IgA antibodies in human serum or plasma in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (anti-phospholipid syndrome)	Semi-quantitative determination of anti-β2 Glycoprotein I (β2GPI) IgG, IgM, and IgA antibodies in human serum or citrated plasma in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (anti-phospholipid

Similarities			
Item	Device: BioPlex® 2200 APLS IgG and IgA Kits	Predicate: REAADS Anti-CL IgG and IgA Kits	Predicate: REAADS Anti-β2GPI IgG and IgA Kits
	erythematosus (SLE) or SLE-like disorders.		syndrome)
Sample Type	Serum and plasma (lithium heparin, sodium heparin, and sodium citrate)	Serum or plasma	Serum or citrated plasma
Capture Antigen	Cardiolipin	Same	N/A
	β2GPI	N/A	Same
Assay Type	Semi-Quantitative detection	Same	Same
Analyte Detected	Human IgG or IgA antibodies to Cardiolipin	Same	Not applicable
	Human IgG or IgA antibodies to β2GPI	Not applicable	Same
Controls	One Negative and one Positive Controls	Same	Same

Differences			
Item	Device: BioPlex® 2200 APLS IgG and IgA Kits	Predicate: REAADS Anti-CL IgG and IgA Kits	Predicate: REAADS Anti-β2GPI IgG and IgA Kits
Assay Technology	Automated multiplex flow immunoassay	Manual, microtitre plate format, Enzyme-linked Immunosorbent assay (ELISA)	Manual, microtitre plate format, Enzyme-linked Immunosorbent assay (ELISA)
Conjugate Antibody	Phycoerythrin conjugated murine monoclonal anti-human IgG or IgA.	Goat anti-human IgG or IgA HRP-conjugated antibody solution	Goat anti-human IgG or IgA HRP-conjugated antibody solution
Substrate	None	Tetramethylbenzidine (TMB) and hydrogen peroxide (H ₂ O ₂)	Tetramethylbenzidine (TMB) and hydrogen peroxide (H ₂ O ₂)
Specimen Type	Serum and plasma (citrated and heparin)	Serum and plasma (citrated only)	Serum and plasma (citrated only)
Signal Detection	Fluorescence	Color, read at 450nm	Color, read at 450nm

Differences			
Item	Device: BioPlex® 2200 APLS IgG and IgA Kits	Predicate: REAAADS Anti-CL IgG and IgA Kits	Predicate: REAAADS Anti-β2GPI IgG and IgA Kits
Solid Phase	Antigen-coated paramagnetic microbead reagent.	Antigen-coated solid phase microtitre wells	Antigen-coated solid phase microtitre wells
Calibrator(s)	4 levels of Calibrator for IgG 2 levels of calibrator for IgA	3 levels of Calibrator for IgG and IgA	3 levels of Calibrator for IgG and IgA
Assay Range	Anti-CL: IgG: 1.6 – 112 GPL U/mL IgA: 0.5 – 28 APL U/mL	Anti-CL: IgG: 0 – 100 GPL U/mL IgA: 0 – 80 APL U/mL	Not applicable
	Anti-β2GPI: IgG: 1.4 – 112 U/mL IgA: 0.6 – 28 U/mL	Not applicable	Anti-β2GPI: IgG: 0 – 200 U//mL IgA: 0 – 200 U/mL
Calibrators and Controls	Sold separately	Kit components	Kit components
Quantitation	Results are determined from a standard calibration curve utilizing a point-to-point calculation.	Results are derived from a linear regression analysis	Results are derived from a linear regression analysis
Instrumentation	Bio-Rad BioPlex® 2200 System	Spectrophotometer	Spectrophotometer

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

CEN 13640:2002, Stability Testing of In Vitro Diagnostic Reagents

EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition.

EP06-A2, Evaluation of Linearity of Quantitative Measurement, Approved Guideline, Second Edition.

EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition

EP12-A2, User Protocol for Evaluation of Qualitative test Performance, Approved Guideline, Second Edition.

EP14-A2, Evaluation of Matrix Effects, Approved Guideline, Second Edition.

EP15-A2, User Verification of Performance for Precision and Trueness, Approved Guideline, Second Edition.

EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantification, Approved Guideline.

L. Test Principle:

The BioPlex® 2200 APLS IgG and IgA kits use multiplex flow immunoassay, a methodology similar to traditional EIA; however, this method permits simultaneous detection and identification of many antibodies in a single tube. In the BioPlex APLS assays, two different populations of dyed beads are coated with antigens. One bead population is coated with β 2-glycoprotein I and a second population is coated with both cardiolipin and β 2-glycoprotein I. Three additional populations of fluorescent beads function as assay controls. The system combines an aliquot of patient sample, sample diluent, and bead reagent into a reaction vessel and incubates the mixture at 37°C. After a wash cycle to remove unbound antibody, the secondary conjugate containing either phycoerythrin conjugated murine monoclonal anti-human IgG or anti-human IgA and phycoerythrin conjugated murine monoclonal anti-human FXIII antibody (a control) is added and the mixture is incubated at 37°C. Excess conjugate is removed in another wash cycle and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of antibody captured by the antigen is determined by the fluorescence of the attached phycoerythrin. Raw data are calculated in relative fluorescence intensity (RFI).

Three additional dyed beads, Internal Standard Bead (ISB), Serum Verification Bead (SVB), and a Reagent Blank Bead (RBB) are present in each reaction mixture to verify detector response, the addition of serum to the reaction vessel, and the absence of significant non-specific binding in serum, respectively.

The anti-phospholipid assays are calibrated using a set of calibrators supplied separately by Bio-Rad Laboratories. Results are calculated for both of the antibodies and are compared against their own respective cut-off. For anti- β 2-glycoprotein I, the results are provided in units/mL (U/mL). The anti-cardiolipin results are similar except that the units are GPL-U/mL and APL-U/mL for the IgG and IgA assays, respectively. The negative/positive assay cutoff for four analytes of the two BioPlex® 2200 APLS kits is 20 units.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision testing of the BioPlex® 2200 APLS IgG and IgA kits on the BioPlex® 2200 instrument was performed in accordance with CLSI EP5-A2. Two serum and heparinized plasma panels consisting of samples spanning the measuring range were assayed in replicate twice daily over 20 days (n=80) except for the mid negative samples were run over 10 days (n=40). One positive and one negative control were included. The data were analyzed for within-run, between-run, between-day, and total precision and the standard deviation and percent coefficient of variation are summarized below:

BioPlex® 2200 APLS IgG – Anti- Cardiolipin: Serum Samples

Precision Sample	N	Mean GPL-U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Mid Negative	40	8.9	0.4	4.2%	0.4	5.0%	0.0	0.0%	0.2	2.7%
Mid Negative	40	9.0	0.3	2.8%	0.3	3.3%	0.1	1.2%	0.1	1.3%
Mid Negative	40	9.9	0.4	4.3%	0.5	5.1%	0.3	2.8%	0.0	0.0%
Negative Near Cut-off	80	17.7	0.5	3.0%	0.7	4.0%	0.5	2.6%	0.2	0.9%
Near Cut-off	80	18.7	1.0	5.4%	1.2	6.2%	0.0	0.0%	0.6	3.0%
Near Cut-off	80	20.9	0.7	3.3%	0.8	3.8%	0.2	0.9%	0.4	1.7%
Low Positive	80	29.1	1.0	3.3%	1.2	4.1%	0.4	1.4%	0.6	2.0%
Low Positive	80	30.2	0.6	2.0%	0.8	2.8%	0.5	1.5%	0.3	1.1%
Low Positive	80	32.5	0.8	2.3%	1.1	3.4%	0.7	2.2%	0.4	1.2%
High Positive	80	77.9	3.1	3.9%	5.0	6.5%	2.3	3.0%	3.3	4.2%
High Positive	80	81.4	3.7	4.5%	5.3	6.5%	3.8	4.6%	0.0	0.0%
Pos Control	40	57.0	1.8	3.2%	2.6	4.5%	1.8	3.1%	0.4	0.7%

BioPlex® 2200 APLS IgG – Anti-Cardiolipin: Heparin Samples

Precision Sample	N	Mean GPL-U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Mid Negative	40	8.6	0.5	5.3%	0.5	5.4%	0.1	1.0%	0.0	0.0%
Mid Negative	40	9.5	0.3	3.4%	0.4	3.8%	0.2	1.7%	0.0	0.0%
Mid Negative	40	9.7	0.3	3.0%	0.4	4.3%	0.2	2.4%	0.2	1.9%
Mid Negative	80	10.6	0.3	2.8%	0.3	2.8%	0.0	0.0%	0.1	0.5%
Negative Near Cut-off	80	15.4	0.9	5.7%	1.3	8.5%	1.0	6.3%	0.0	0.0%

Precision Sample	N	Mean GPL-U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Near Cut-off	80	19.3	0.8	3.9%	1.1	5.7%	0.2	1.1%	0.8	4.0%
Near Cut-off	80	20.1	0.9	4.3%	1.1	5.6%	0.7	3.6%	0.0	0.0%
Low Positive	80	26.1	1.1	4.1%	1.4	5.5%	0.9	3.6%	0.2	0.6%
Low Positive	80	28.5	1.1	3.7%	1.6	5.6%	1.2	4.1%	0.1	0.4%
High Positive	80	88.0	2.5	2.8%	3.2	3.7%	0.7	0.7%	2.0	2.3%
High Positive	80	91.2	2.9	3.1%	3.5	3.9%	1.0	1.1%	1.8	1.9%

BioPlex® 2200 APLS IgG – Anti- β 2GPI: Serum Samples

Precision Sample	N	Mean U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Mid Negative	40	12.6	0.4	2.9%	0.5	4.0%	0.2	1.9%	0.3	2.0%
Mid Negative	40	12.8	0.4	3.0%	0.4	3.4%	0.2	1.6%	0.1	0.7%
Mid Negative	40	15.2	0.4	2.9%	0.6	4.0%	0.4	2.8%	0.0	0.0%
Negative Near Cut-off	80	15.5	0.5	3.3%	0.7	4.2%	0.4	2.7%	0.0	0.0%
Near Cut-Off	80	20.5	0.5	2.6%	0.7	3.3%	0.2	1.1%	0.3	1.6%
Near Cut-off	80	22.6	0.6	2.4%	0.7	3.1%	0.3	1.2%	0.4	1.6%
Low Positive	80	23.1	1.1	4.9%	1.2	5.4%	0.0	0.0%	0.5	2.3%
Low Positive	80	27.9	0.9	3.1%	1.0	3.7%	0.0	0.0%	0.6	2.1%
Low Positive	80	35.2	0.8	2.3%	1.8	5.1%	0.5	1.3%	1.5	4.4%
High Positive	80	108.2	4.1	3.7%	6.5	6.0%	2.8	2.6%	4.3	4.0%
High Positive	80	111.9	3.8	3.4%	5.9	5.2%	4.5	4.0%	0.0	0.0%

Precision Sample	N	Mean U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Pos. Control	80	54.6	2.0	3.7%	3.0	5.5%	2.3	4.2%	0.0	0.0%

BioPlex® 2200 APLS IgG – Anti-β2GPI: Heparin-Plasma Samples

Precision Sample	N	Mean U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Mid Negative	40	11.9	0.6	4.6%	0.6	4.7%	0.1	0.5%	0.1	0.8%
Mid Negative	40	13.1	0.4	2.9%	0.4	3.0%	0.1	0.9%	0.0	0.0%
Mid Negative	40	14.6	0.4	2.6%	0.6	3.8%	0.4	2.8%	0.0	0.0%
Negative Near Cut-off	80	18.0	0.7	3.6%	0.8	4.7%	0.5	2.9%	0.0	0.0%
Near Cut-off	80	18.7	0.8	4.2%	0.9	4.5%	0.2	1.1%	0.3	1.4%
Near Cut-off	80	20.9	1.0	4.6%	1.5	7.0%	1.1	5.3%	0.0	0.0%
Low Positive	80	28.8	1.1	3.7%	1.4	4.9%	0.5	1.6%	0.8	2.8%
Low Positive	80	29.0	0.8	2.8%	1.2	4.0%	0.8	2.6%	0.4	1.3%
Low Positive	80	32.5	1.5	4.6%	1.9	5.7%	0.9	2.8%	0.6	1.8%
High Positive	80	71.1	2.0	2.8%	2.5	3.6%	1.1	1.5%	1.1	1.6%
High Positive	80	84.6	2.8	3.3%	4.1	4.8%	2.4	2.9%	1.7	2.1%

BioPlex® 2200 APLS IgA – Anti-Cardiolipin: Serum Samples

Precision Sample	N	Mean APL-U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Negative Near Cut-off	80	15.3	1.18	7.7%	1.42	9.3%	0.00	0.0%	0.79	5.1%
Negative Near Cut-off	80	15.6	0.39	2.5%	0.67	4.3%	0.31	2.0%	0.44	2.8%

Precision Sample	N	Mean APL-U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Near Cut-off	80	18.3	0.85	4.6%	1.12	6.1%	0.45	2.5%	0.57	3.1%
Near Cut-off	80	18.7	0.62	3.3%	1.02	5.4%	0.76	4.1%	0.27	1.5%
Low Positive	80	22.7	1.01	4.5%	1.49	6.6%	0.85	3.7%	0.69	3.0%
Low Positive	80	23.6	1.00	4.3%	1.25	5.3%	0.36	1.5%	0.64	2.7%
Mid Negative	40	7.9	0.26	3.3%	0.44	5.6%	0.35	4.5%	0.00	0.0%
Mid Negative	40	8.4	0.36	4.3%	0.55	6.5%	0.42	4.9%	0.00	0.0%

BioPlex® 2200 APLS IgA – Anti-Cardiolipin: Heparin-Plasma Samples

Precision Sample	N	Mean APL-U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Low Negative	80	15.8	0.88	5.6%	1.27	8.0%	0.88	5.6%	0.23	1.5%
Low Negative	80	16.4	0.59	3.6%	0.86	5.2%	0.29	1.8%	0.55	3.3%
Near Cut-off	80	18.6	1.30	7.0%	1.41	7.6%	0.26	1.4%	0.50	2.7%
Near Cut-off	80	19.4	1.33	6.9%	1.53	7.9%	0.00	0.0%	0.76	3.9%
Low Positive	80	22.7	0.99	4.4%	1.45	6.4%	1.03	4.6%	0.27	1.2%
Low Positive	80	23.1	1.76	7.6%	1.85	8.0%	0.15	0.6%	0.57	2.5%
Mid Negative	40	8	0.36	4.5%	0.47	5.9%	0.30	3.8%	0.00	0.0%
Mid Negative	40	7.5	0.44	5.9%	0.44	5.9%	0.00	0.0%	0.00	0.0%

BioPlex® 2200 APLS IgA – Anti-β2GPI: Serum Samples

Precision Sample	N	Mean U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
Negative Near Cut-off	80	14.5	0.98	6.8%	1.26	8.7%	0.00	0.0%	0.78	5.4%
Negative Near Cut-off	80	14.8	0.40	2.7%	0.59	4.0%	0.24	1.6%	0.37	2.5%
Near Cut-off	80	17.6	0.81	4.6%	1.01	5.7%	0.39	2.2%	0.47	2.7%
Near Cut-off	80	18.1	0.54	3.0%	0.95	5.2%	0.71	3.9%	0.32	1.8%
Low Positive	80	21.8	0.92	4.2%	1.33	6.1%	0.64	2.9%	0.72	3.3%
Low Positive	80	22.6	0.84	3.7%	1.18	5.2%	0.49	2.2%	0.67	2.9%
Mid Negative	40	8.4	0.30	3.6%	0.41	4.8%	0.28	3.3%	0.00	0.0%
Mid Negative	40	8.8	0.40	4.6%	0.55	6.3%	0.35	4.0%	0.14	1.6%

BioPlex® 2200 APLS IgA – Anti- β 2GPI: Heparin-Plasma Samples

Precision Sample	N	Mean U/mL	Within Run		Total		Between Run		Between Day	
			SD	CV	SD	CV	SD	CV	SD	CV
High Negative	80	15.3	0.73	4.8%	1.05	6.8%	0.74	4.8%	0.12	0.8%
High Negative	80	15.7	0.58	3.7%	0.77	4.9%	0.25	1.6%	0.44	2.8%
Near Cut-off	80	17.8	1.07	6.0%	1.19	6.7%	0.21	1.2%	0.48	2.7%
Near Cut-off	80	18.6	1.15	6.2%	1.31	7.1%	0.00	0.0%	0.63	3.4%
Low Positive	80	21.5	0.74	3.5%	1.25	5.8%	1.01	4.7%	0.00	0.0%
Low Positive	80	22.5	1.44	6.4%	1.57	7.0%	0.54	2.4%	0.34	1.5%
Mid Negative	40	8.1	0.34	4.2%	0.43	5.3%	0.26	3.2%	0.00	0.0%
Mid Negative	40	8.4	0.48	5.7%	0.48	5.7%	0.00	0.0%	0.00	0.0%

An additional internal lot-to-lot studies were conducted to estimate the expected variance between instrument, within-run, between-run and total precision of a new lot of BioPlex® 2200 APLS IgG and IgA reagents. Results are within acceptance criteria.

b. Linearity/assay reportable range:

Three APLS aCL and aβ2GPI IgG and IgA positive patient samples were tested to demonstrate linearity. These samples were diluted with immunodepleted serum according to CLSI EP06-A. Each sample and dilution was evaluated in replicates of four using one APLS IgG and IgA lot on one instrument. Linear and polynomial regression analysis of APLS IgG and IgA recovery vs. sample dilution was performed to determine if the dilution curves exhibit statistically significant non-linear regression based on the CLSI guideline EP06-A.

The regression parameters (slope, intercept and r^2) of the observed values vs. predicted values are show below.

APLS Assays	Conc.	Slope	Intercept	r^2	Dilution range
aCL IgG (GPL-U/mL)	50.8	0.9998	0.0056	0.9999	50.8-0.5
	56.1	1.0001	0.0105	0.9994	56.1-0.1
	43.3	1.0009	-0.0182	0.9964	43.3-0.3
	104.5	1.0004	-0.0033	0.9991	104.5-0.5
	89.3	1.0008	-0.0307	0.9982	89.3-0.5
	92.7	1.0003	-0.0112	0.9999	92.7-1.9
aβ2GPI IgG (U/mL)	56.8	0.9996	0.0104	0.9999	56.8-0.1
	45.3	0.9995	0.0104	0.9978	45.3-0.4
	54.9	1.0000	0.0010	0.9758	54.9-1.5
	95.1	1.0003	-0.0113	0.9991	95.1-0.6
	98.4	1.0001	-0.0038	0.9958	98.4-0.6
	100.4	1.0008	-0.0049	0.9997	100.4-1.5
aCL IgA (APL-U/mL)	26.4	0.9999	0.0012	0.9932	26.4-0.3
	27.1	1.0014	0.0102	0.9958	27.1-0.3
	30.2	1.0011	-0.0169	0.9836	30.2-0.1
aβ2GPI IgA (U/mL)	33.2	1.0001	0.0009	0.9900	33.2-0.1
	33.9	1.0022	-0.0356	0.9937	33.9-0.1
	28.1	1.0017	-0.0251	0.9758	28.1-0.1

The assay measuring range reported by each APLS IgG and IgA assays is shown below.

BioPlex® 2200 APLS Assay	Assay reportable range
aCL IgG	1.6 to 112.0 GPL-U/mL
aβ2GPI IgG	1.4 to 112.0 U/mL
aCL IgA	0.5 to 28.0 APL-U/mL
aβ2GPI IgA	0.6 to 28.0 U/mL

Over-Range (OR) results may be generated for values greater than the reportable measuring range and results are reported as > 112 GPL-U/mL and > 28 APL-U/mL for aCL IgG and IgA, respectively; and >112 U/mL for aβ2GPI IgG and > 28 U/mL IgA.

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

Traceability:

There is no international or certified reference material available for APLS aCL and aβ2GPI IgG and IgA. The calibrators are assigned relative arbitrary units (U/mL for aβ2GPI, and GPL-U/mL and APL-U/mL for aCL IgG and IgA).

Value Assignment:

The calibrators are manufactured independently from the controls, and are stabilized with <0.3% ProClin® 300, <0.1% sodium benzoate, and <0.1% sodium azide. Calibrator assignment is established for matched lots of BioPlex® 2200 APLS IgG or IgA kit and calibrators using a master set of calibrators as reference and replicate analyses on multiple BioPlex® 2200 instruments. The BioPlex® 2200 APLS IgG Reagent Kit is calibrated using a set of seven (7) distinct serum based calibrators for aCL and aβ2GPI IgG; three (3) distinct serum based calibrators for aCL and aβ2GPI IgA, which are used to establish points of reference for determining the presence of APLS IgG, or IgA in human specimens.

The negative control has been tested to give results with values below the cut-off for each assay. The positive control is prepared by blending human disease state serum with negative serum matrix and is manufactured to give results with values above the assay cut-off. The value assignment of the Control Set is derived by testing each control on three BioPlex® 2200 Analyzers with at least two kit lots. For each control level, three vials are tested in replicates of five using each of the kit lots and each analyzer. This testing is performed on three analyzers for a total of 45 replicates per reagent lot. The total number of replicates for each control level is 90 when two reagent lots are used and 135 when three reagent lots are used. The mean value of the control is calculated using data from all reagent lots, and the acceptable range of ±30% is based on the inter-assay precision specification of 15% (i.e. 2x inter-assay precision).

The target values and ranges (in parenthesis) for the BioPlex® 2200 APLS IgG and

IgA Calibrator and Control sets are listed below.

Calibrator Level	APLS IgG		APLS IgA	
	aCL IgG GPL-U/mL	aβ2GPI IgG U/mL	aCL IgA APL-U/mL	aβ2GPI IgA U/mL
1	≤ 6	≤ 6	≤ 6	≤ 6
2	14 (10 – 18)	14 (10 – 18)	28 (20 – 36)	28 (20 – 36)
3	28 (20 – 36)	28 (20 – 36)	Not Applicable	Not Applicable
4	112 (80 – 144)	112 (80 – 144)	Not Applicable	Not Applicable

Control Level	aCL IgG GPL-U/mL	aβ2GPI IgG U/mL	aCL IgA APL-U/mL	aβ2GPI IgA U/mL
Negative	≤ 10	≤ 10	≤ 10	≤ 10
Positive	56 (36 – 76)	56 (36 – 76)	46 (36 – 56)	46 (36 – 56)

Stability:

Stability studies have been performed to support the following claims:

BioPlex® 2200 APLS IgG and IgA Control and Calibrator Sets: Calibrator Open Vial Stability (2 to 8°C), 30 days from first opening; Control Open Vial Stability (2 to 8°C), 60 days from first opening; Calibration Curve On-board Stability, 30 days; Calibrators and Controls Real Time Stability (2 to 8°C), 13 months; labeled as until expiration date; Calibrators and Controls Accelerated Stability (2 to 8°C), 2.5 years predicted; Calibrators and Controls Freeze-thaw (-20 or -80°C), 5-freeze thaw cycles.

BioPlex® 2200 APLS IgG and IgA Kit: Real Time (unopened) Kit Stability, 12 months or until the date of expiration when stored unopened on the instrument or at 2 to 8°C; The Open kit claim is 60 days.

Sample stability studies were also performed: Sample stability fresh (2 to 8°C), 7 days; Sample stability frozen (-20 or -80°C), 8 months; Sample Freeze-thaw (-20 or -80°C), up to 3-freeze thaw cycles acceptable.

d. Detection limit:

The Limit of Detection (LoD) of BioPlex® 2200 IgG and IgA kits was determined by assaying three low negative serum samples and a negative serum (blank) sample in replicates of 50. The LoD was calculated according to CLSI EP17-A. The samples were prepared from a high titer positive control which was then diluted in negative serum spanning the range in analyte concentration below the cutoff. Each dilution was assayed daily in replicates of ten for a period of five days. The LoD was calculated using the equation $LoD = LoB + c_{\beta}SD_s$. The LoB was calculated at the 95th percentile of 50 negative samples. c_{β} is the 95th percentile of the standard Gaussian distribution with a correction factor applied to account for the biased estimate of the population standard deviation. The results of LoD and LoB are summarized in the table below.

BioPlex® 2200 APLS Assay	LoD	LoB
aCL IgG	1.6 GPL-U/mL	1.4 GPL-U/mL
aβ ₂ GPI IgG	1.4 U/mL	1.2 U/mL
aCL IgA	0.5 APL-U/mL	0.3 APL-U/mL
aβ ₂ GPI IgA	0.6 U/mL	0.5 U/mL

e. *Analytical specificity:*

Interfering Substances:

An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex® 2200 APLS IgG and IgA assay according to CLSI EP7-A2. Samples were prepared by blending a pool of negative human serum with samples positive for aCL IgG or IgA and aβ₂GPI IgG or IgA to achieve approximate values of 10, 20, 60 and 100 GPL for aCL IgG and 10, 20, 60, 100 U/mL for aβ₂GPI IgG and 10, 20 APL-U/mL and U/mL for aCL and aβ₂GPI IgA with interferent or blank. Test and control samples were evaluated in alternating order in replicates of ten each. Substances are considered interfering if their presence in a sample results in more than ± 20% deviation in quantitation relative to the value determined in the absence of the substance. No interference was observed with any of the substances tested. The substances and the maximum levels tested are shown in the table below:

Substance	Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin, Unconjugated	≤ 20 mg/dL
Bilirubin, Conjugated	≤ 30 mg/dL
Cholesterol	≤ 500 mg/dL
Red Blood Cells	≤ 0.4% (v/v)
Gamma Globulin	≤ 6 g/dL
Triglycerides	≤ 3300 mg/dL
Protein (total)	≤ 12 g/dL
Beta-Carotene	≤ 0.6 mg/dL
Ascorbic Acid	≤ 3 mg/dL
Lithium Heparin	≤ 8000 units/dL
Sodium Heparin	≤ 8000 units/dL
Sodium Citrate	≤ 1000 mg/dL
EDTA	≤ 800 mg/dL

Cross-Reactivity:

A cross-reactivity study was performed to determine if samples from individuals with various disease states and other potentially interfering factors interfere with test results from the BioPlex® 2200 APLS IgG or IgA kit. Samples from individual with known disease states for potential cross reactivity listed in the table below were evaluated with the BioPlex® 2200 APLS IgG, or IgA kit. The table below shows the

number (N) of samples containing potential cross reactants as disease state evaluated by the BioPlex® APLS IgG and IgA. The cross reactivity was obtained as the positivity rate from the ratio of the number of samples scored positive by the BioPlex® APLS IgG or IgA assays to the total number of cross reactant samples evaluated.

Cross Reactive Disease State	N	aCL IgG		aβ2GPI IgG		aCL IgA		aβ2GPI IgA	
		# Pos	% Pos	# Pos	% Pos	# Pos	% Pos	# Pos	% Pos
Systemic Lupus Erythematosus	34	2	5.9%	2	5.9%	2	5.9%	2	5.9%
Scleroderma	20	0	0.0%	0	0.0%	1	5.0%	2	10.0%
Sjogrens	22	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Crohn's Disease	21	1	4.8%	0	0.0%	1	4.8%	1	4.8%
Ulcerative Colitis	20	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Rheumatoid Arthritis	12	0	0.0%	0	0.0%	1	8.3%	0	0.0%
Syphilis	15*	0	0.0%	0	0.0%	0	0.0%	0	0.0%

*One sample exhibiting repeated instrument errors was excluded from the IgG data analysis

High dose hook effect:

Not applicable

f. Assay cut-off:

The cutoff value and assignment of the calibrators are determined by performing concordance testing and Receiver Operator Characteristic (ROC) analysis. The study to determine the APLS IgG or IgA assay cutoff is comprised of two sample groups – one clinical cohort has 103 samples from patients diagnosed as primary and secondary APS and 208 from normal healthy and 123 from non-APS cardiac donors.

The cut-off was established to achieve a clinical specificity of 99% while accepting the resultant clinical sensitivity. The criteria for choosing a cutoff at the 99th percentile of a normal healthy population is derived from the “International Consensus Statement on an Update of the Classification Criteria for Definite Antiphospholipid Syndrome (APS)”, Journal of Thrombosis and Haemostasis (2006) 4, 295.

A cutoff of 20.0 GPL- or APL-U/mL for aCL IgG or IgA and 20 U/mL for a β ₂GPI IgG or IgA was established by optimizing for clinical accuracy.

2. Comparison studies:

a. *Method comparison with predicate device:*

The performance of the BioPlex® 2200 APLS IgG and IgA kits was evaluated using a total of 804 specimens, including 300 apparently healthy blood donors, 302 patients previously diagnosed with primary or secondary APS and 202 patients with other rheumatic or non-APS diseases. Results in the measuring range and 10% of diluted total samples of both the new and the predicate immunoassays are compared. Results are summarized in the tables below:

BioPlex® 2200 APLS IgG

		Predicate IgG EIA Kit (aCL: 0-100 GPL U/mL) (a β ₂ GPI: 0-200 U/mL)		
		Positive	Negative	Total
aCL IgG (1.6-112 GPL-U/mL)	Positive	99	14	13
	Negative	32	112	144
	Total	131	126	257
a β ₂ GPI IgG (1.4-112 U/mL)	Positive	109	7	116
	Negative	13	130	143
	Total	122	137	259

aCL IgG Positive Agreement (95% CI) = 75.6% (99/131) (67.6 – 82.1%)

aCL IgG Negative Agreement (95% CI) = 88.9% (112/126) (82.2 – 93.3%)

aCL IgG Total Agreement (95% CI) = 82.1% (211/257) (77.0 – 86.3%)

a β ₂GPI IgG Positive Agreement (95% CI) = 89.3% (109/122) (82.6 – 93.7%)

a β ₂GPI IgG Negative Agreement (95% CI) = 94.9% (130/137) (89.8 – 97.5%)

a β ₂GPI IgG Total Agreement (95% CI) = 92.3% (239/259) (88.4 – 94.9%)

BioPlex® 2200 APLS IgA

		Predicate IgA EIA Kit (aCL: 0-80 APL-U/mL) (a β ₂ GPI: 0-200 U/mL)		
		Positive	Negative	Total
aCL IgA (0.5-28 APL-U/mL)	Positive	39	24	63
	Negative	5	416	421
	Total	44	440	484
a β ₂ GPI IgA (0.6-28 U/mL)	Positive	57	1	58
	Negative	85	271	356
	Total	142	272	414

aCL IgA Positive Agreement (95% CI) = 88.6% (39/44) (76.0 – 95.0%)

aCL IgA Negative Agreement (95% CI) = 94.5% (416/440) (92.0 – 96.3%)

aCL IgA Total Agreement (95% CI) = 94.0% (455/484) (91.5 – 95.8%)

a β 2GPI IgA Positive Agreement (95% CI) = 40.1% (57/142) (32.4– 48.4%)
a β 2GPI IgA Negative Agreement (95% CI) = 99.6% (271/272) (97.9 – 99.9%)
a β 2GPI IgA Total Agreement (95% CI) = 79.2% (328/414) (75.1 – 82.9%)

b. *Matrix comparison:*

Testing for matrix effects was conducted using more than 30 matched sets of serum and sodium citrate, lithium heparin, and sodium heparin plasma samples drawn from the same donor in accordance with CLSI EP9-A2. The samples were spiked with aCL IgG or IgA and a β 2GPI IgG or IgA positive sera as necessary in order to assemble a panel of samples to cover the measuring range of the assay. All samples were evaluated in replicates of two. Plasma values were compared to matched serum values. Anticoagulants were considered non-interfering if the linear regression of a β 2GPI-G or aCL-G values from matched serum *versus* plasma samples has a slope of 1.00 ± 0.2 , a y-intercept of 0.0 ± 6.0 and a correlation coefficient between 0.980 and 1.000. The regression correlation parameters for the slopes, intercepts and correlation coefficient (r) are summarized below:

Matrix Comparison	N	BioPlex® APLS Assay	Slope (95% CI)	Intercept (95% CI)	R
Lithium Heparin vs. Serum	32	aCL IgG	0.9720 (0.9457, 0.9984)	0.3788 (-1.0552, 1.8128)	0.9974
	32	a β 2GPI IgG	0.9756 (0.9488, 1.0023)	0.4377 (-1.1789, 2.0543)	0.9973
	36	aCL IgA	0.9767 (0.9090, 1.0445)	0.6309 (-0.3103, 1.5721)	0.9808
	36	a β 2GPI IgA	0.9865 (0.9249, 1.0480)	0.4698 (-0.2643, 1.2039)	0.9844
Sodium Heparin vs. Serum	32	aCL IgG	0.9885 (0.9531, 1.0239)	0.1921 (-1.7335, 2.1177)	0.9954
	32	a β 2GPI IgG	0.9889 (0.9555, 1.0222)	0.3559 (-1.6615, 2.3732)	0.9959
	36	aCL IgA	1.0244 (0.9641, 1.0847)	0.0753 (-0.7627, 0.9134)	0.9860
	36	a β 2GPI IgA	1.0150 (0.9520, 1.0779)	0.1714 (-0.5799, 0.9228)	0.9845
Sodium Citrate vs. Serum	32	aCL IgG	0.9398 (0.8757, 1.0039)	0.8087 (-2.6816, 4.2990)	0.9837
	32	a β 2GPI IgG	0.9351 (0.8730, 0.9972)	1.1299 (-2.6264, 4.8862)	0.9845
	36	aCL IgA	1.0096 (0.9480, 1.0713)	0.1181 (-0.7384, 0.9746)	0.9850
	36	a β 2GPI IgA	1.0061 (0.9500, 1.0622)	0.1801 (-0.4895, 0.8497)	0.9874

3. Clinical studies:

a. *Clinical Sensitivity and Specificity:*

The clinical studies involved testing 504 specimens including 202 non-APS disease control patients and 302 diagnosed primary or secondary APS patients. The BioPlex® 2200 APLS IgG and IgA sensitivity and specificity are shown below:

BioPlex® 2200 APLS IgG

		Clinical Diagnosis		
		Positive	Negative	Total
aCL IgG	Positive	188	3	191
	Negative	98	198	296
	Total	286	201	487*
aβ2GPI IgG	Positive	186	2	188
	Negative	100	199	299
	Total	286	201	487*

* 17 Samples exhibiting repeated instrument errors were excluded from the data analysis

aCL IgG Sensitivity (95% CI) = 65.7% (188/286) (60.1 – 71.0%)

aCL IgG Specificity (95% CI) = 98.5% (198/201) (95.7 – 99.5%)

aβ2GPI IgG Sensitivity (95% CI) = 65.0% (186/286) (59.3 – 70.3%)

aβ2GPI IgG Specificity (95% CI) = 99.0% (199/201) (96.4 – 99.7%)

BioPlex® 2200 APLS IgA

		Clinical Diagnosis		
		Positive	Negative	Total
aCL IgA	Positive	167	7	174
	Negative	135	195	330
	Total	302	202	504
aβ2GPI IgA	Positive	157	6	163
	Negative	145	196	341
	Total	302	202	504

aCL IgA Sensitivity (95% CI) = 55.3% (167/302) (49.7 – 60.8%)

aCL IgA Specificity (95% CI) = 96.5% (195/202) (93.0 – 98.3%)

aβ2GPI IgA Sensitivity (95% CI) = 52.0% (157/302) (46.4 – 57.6%)

aβ2GPI IgA Specificity (95% CI) = 97.0% (196/202) (93.7 – 98.6%)

The results of the BioPlex APLS IgG and IgA in each of disease category are shown below.

Disease Category	Number Enrolled	aCL IgG	aβ2GPI IgG	aCL IgA	aβ2GPI IgA
Primary APS (PAPS)	207*	119 (61.0%)	119 (61.0%)	108 (52.2%)	104 (50.2%)
Secondary APS (SAPS)	95*	67 (73.6%)	67 (73.6%)	59 (62.1%)	53 (55.8%)
Apparently Healthy Subject	300	0 (0.0%)	0 (0.0%)	2 (0.7%)	2 (0.7%)
Systemic Lupus Erythematosus	34	2 (5.9%)	2 (5.9%)	2 (5.9%)	2 (5.9%)
Scleroderma	20	0 (0.0%)	0 (0.0%)	1 (5.0%)	2 (10.0%)
Sjogrens	22	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Crohn's Disease	21	1 (4.8%)	0 (0.0%)	1 (4.8%)	1 (4.8%)
Ulcerative Colitis	20	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rheumatoid Arthritis	12	0 (0.0%)	0 (0.0%)	1 (8.3%)	0 (0.0%)
Syphilis	15^	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CREST	3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fibromyalgia	20	0 (0.0%)	0 (0.0%)	1 (5.0%)	0 (0.0%)
Gout	14	0 (0.0%)	0 (0.0%)	1 (7.0%)	1 (7.0%)
Inflammatory Arthritis	4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Osteoarthritis	12	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Wegeners Granulomatosis	5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

*195 PAPS and 91 SAPS patient sample results were included in the data analysis for APLS IgG.

^One sample exhibiting repeated instrument errors were excluded from the IgG data analysis.

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

Not applicable.

4. **Clinical cut-off:**

See Assay Cutoff

5. Expected values/Reference range:

Three hundred samples from apparently healthy donors including 132 males ranging in age from 7 to 85 and 168 females ranging in age from 14 to 83 were tested with BioPlex® 2200 APLS IgG and IgA kits. The number of positive, mean value and 99th percentile of the BioPlex® APLS IgG and IgA results are shown below. Results of <20.0 GPL- or APL-U/mL for aCL IgG or IgA and < 20.0 U/mL for aβ2GPI IgG or IgA are reported as negative and results > 20.0 GPL- or APL-U/mL for aCL IgG or IgA and > 20.0 U/mL for aβ2GPI IgG or IgA are reported as positive.

APLS Assay	N (%Positive)	Mean	99 th percentile
aCL IgG	0 (0.0%)	<1.6 GPL-U/mL	8.5 GPL-U/mL
aβ ₂ GPI IgG	0 (0.0%)	<1.4 U/mL	6.0 U/mL
aCL IgA	2 (0.7%)	1.4 APL-U/mL	14.5 APL-U/mL
aβ ₂ GPI IgA	2 (0.7%)	1.3 U/mL	12.1 U/mL

Each laboratory should establish its own reference range pertinent to their specific patient populations.

N. Instrument Name:

The BioPlex® 2200 System, software version 4.0 review

O. System Descriptions:

The BioPlex® 2200 System consists of the BioPlex® 2200 Instrument, the BioPlex® 2200 family of multiplexed assays, and the BioPlex® 2200 software. The BioPlex® 2200 Instrument is an automated, self-contained, floor standing analyzer that provides an integrated method for random access heterogeneous, multiplexed, immunodiagnostic assays. Reactions occur in the heated incubation unit. Reagents necessary for multiplexed assays are contained within assay-specific reagent packs that are stored onboard with refrigeration.

The BioPlex® 2200 software consists of the BioPlex® Control Module (BCM), which includes user interface/instrument control, results analysis, assay protocols, error reporting, maintenance scheduling, Medical Decision Support Software (MDSS), and internal quality control. The BioPlex® 2200 system was first cleared as part of k041658 (BioPlex® 2200 ANA Screen on the BioPlex® 2200 Multi-Analyte Detection System). BioRad’s MDSS for use with the BioPlex® was reviewed as part of k043341 for the same analyte detection system. BioPlex® System Software, version 2.0 was reviewed in k063866.

1. Modes of Operation:

The BioPlex® 2200 is a fully-automated, random access, multiplex testing platform.

2. Software: Bio-Rad BioPlex® 2200 software version 4.0 review

FDA has reviewed applicant’s Hazard Analysis and software development processes for this line of product types:

Yes or No

The Device Hazard Analysis was reviewed by FDA under that submission. As indicated in the Product Classification section, BioPlex® 2200 System Software is now at version 4.0.

3. Specimen Identification:

Samples are identified on the BioPlex® 2200 instrument by barcodes on each sample tube, corresponding to the sample's accession identification number.

4. Specimen Sampling and Handling:

The Instructions For Use for the BioPlex® 2200 APLS IgG and IgA kit instructs the user to thoroughly mix thawed specimens before testing and also recommends that users centrifuge thawed specimens prior to loading specimens on the instrument to remove gross particulate matter. As described in BioPlex® 2200 Operation Manual, the instrument samples specimens directly from open sample tubes.

5. Calibration:

The APLS IgG or APLS IgA Calibrator Set should be loaded and assayed at minimum in duplicate every 30 days or with each new Reagent Pack lot. A point-to-point curve fit algorithm, using 4 calibrators for each analyte of the APLS IgG kit and 2 calibrators for each analyte of the APLS IgA kit, is used to establish a separate calibration curve for each assay. Refer to the BioPlex® 2200 System Operation Manual for more information.

6. Quality Control:

Reagent Bead Quality Control: There are three quality control beads in every BioPlex® 2200 assay. These beads serve to evaluate samples as they are processed and report any control issues as they occur and are described below:

Reagent Blank Bead (RBB): The Reagent Blank Bead is a non-antigen coated bead that serves to identify sample problems arising from non-specific binding.

Internal Standard Bead (ISB): The Internal Standard Bead performs fluorescence intensity data-correction. The inherent fluorescent signal of the Internal Standard Bead is used to detect and compensate for Detector Module fluctuations that may occur during sample analysis.

Serum Verification Bead (SVB): The Serum Verification Bead ensures that serum or plasma is present.

In-Kit Quality Control

BioPlex® 2200 APLS IgG (or IgA) Control Set: At the beginning of each day that the APLS IgG or APLS IgA kit is to be used, load and process the corresponding APLS IgG or APLS IgA Control Set as indicated in the BioPlex® 2200 System Operation Manual. Each of the APLS IgG and APLS IgA Control Sets includes a negative control and a positive control for each aCL IgG (or IgA) and α 2GPI IgG (or IgA) in a human serum matrix made from defibrinated plasma, containing antibodies present for analytes within the APLS IgG (or IgA) kit. The positive controls are manufactured to give positive results, with values above the cutoff for each specific bead. The negative control is manufactured to give negative results, with values below the cutoff for each specific

bead. The negative control must have a negative result, and the positive control must have a positive result.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:

Not applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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