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BIOPLEX 2200 ANA SCREEN 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

510(k) Number	510(k) Summary Report Date
K041658	December 13, 2004

MANUFACTURER INFORMATION

Manufacturer	
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CLASSIFICATION INFORMATION

Classification Name	Antinuclear Antibody (Enzyme-Labeled), Antigen, Controls
Common Name:	Multi-Analyte Detection System ANA Screen
Product Trade Name	BioPlex 2200 ANA Screen on the BioPlex 2200 Multi-Analyte Detection System
Device Class	Class II
Classification Panel	Immunology and Microbiology
Regulation Number	866.5100

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LEGALLY MARKETED EQUIVALENT (SE) DEVICES

Instrument

BioPlex2200 System	Comparative FDA Cleared PREDICATE DEVICE	510(k) Number	Product Code	Decision Date
BioPlex 2200 ANA Screen on the BioPlex 2200 System	Zeus Athena Multi-Lyte ANA Test System	K011244	LKJ	12/10/2001
	Diagnostic Products Corporation (DPC) Immulite 2000 Automated Immunoassay Analyzer	K970227	JJE	4/8/1997

Assay

BioPlex2200 ANA Screen	Comparative FDA Cleared Device	510(k) Number	Product Code	Decision Date
ANA Screen (based on results of all analytes listed below)	Bio-Rad (Helix) Autoimmune EIA ANA Screening Test	954723	LKJ	12/15/1995

	BioPlex2200 ANA Screen Analyte	Comparative FDA Cleared PREDICATE DEVICE	510(k) Number	Product Code	Decision Date
1.	SSA (SSA 60 and SSA 52)	Inova Diagnostics, Inc. QUANTA Lite™ SSA	922830	LLL	9/18/1992
2.	SSB	Bio-Rad (Helix) Autoimmune EIA SS-B / La Test	932419	LLL	8/5/1993
3.	Sm	Inova Diagnostics, Inc. QUANTA Lite™ Sm	922831	LLL	9/18/1992
4.	SmRNP	Inova Diagnostics, Inc. QUANTA Lite™ RNP (Sm/RNP)	922833	LLL	9/18/1992
5.	RNP (RNP 68 and RNP A)	Pharmacia Varelisa® RNP Antibodies	993589	LKO	11/26/1999
6.	Ribosomal Protein	Inova Diagnostics, Inc. QUANTA Lite™Ribosome P	981237	MQA	6/5/1998
7.	Chromatin	Inova Diagnostics, Inc. QUANTA Lite™ Chromatin ELISA	982603	LLL	10/7/1998
8.	dsDNA (quant. / semi-quant.)	Pharmacia Varelisa® ds-DNA ANTIBODY EIA Kit	950031	LRM	3/10/1995
9.	Centromere	Bio-Rad (Helix) Autoimmune EIA Anti-Centromere Test	000489	LLL	4/15/2000
10.	Scl-70	Bio-Rad (Helix) Autoimmune EIA Anti-Scl-70 Test	951798	LJM	7/17/1995
11.	Jo-1	Bio-Rad (Helix) Autoimmune EIA Anti-Jo-1 Test	951850	LJM	7/18/1995

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DEVICE DESCRIPTION

The ANA Screen detects the presence of clinically relevant circulating autoantibodies in serum or plasma. These autoantibodies may be useful as an aid in the diagnosis of systemic rheumatic diseases such as Systemic Lupus Erythematosus (SLE), Mixed Connective Tissue Disease (MCTD), Undifferentiated Connective Tissue Disease (UCTD), Sjogren's Syndrome (SS), Scleroderma (Systemic Sclerosis), Dermatomyositis, Polymyositis, Rheumatoid Arthritis (RA), CREST Syndrome, and Raynaud's Phenomenon. Bio-Rad's ANA Screen uses a comprehensive group of autoantigens. Beads are individually coated with individual antigens, so that the presence of each antinuclear and autoimmune antibody can be individually determined. Fluorescence detection facilitates the differentiation of normal and abnormal antibody concentrations.

The ANA Screen uses multiplex flow immunoassay, a methodology that resembles traditional EIA, but permits simultaneous detection and identification of many antibodies in a single tube. Thirteen (13) different populations of dyed beads are coated with antigens associated with systemic autoimmune disease (dsDNA, Chromatin, Ribosomal Protein, SS-A 60, SS-A 52, SS-B, Sm, SmRNP, RNP A, RNP 68, Scl-70, Jo-1 and Centromere B)*. The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead reagent into a reaction vessel. The mixture is incubated at 37°C. After a wash cycle, murine monoclonal anti-human IgG antibody, conjugated to phycoerythrin (PE), is added to the dyed beads and this mixture is incubated at 37°C. The excess conjugate is removed in another wash cycle, and the beads are re-suspended in wash buffer.

The bead mixture is suspended in sheath fluid and then passes through the detector and the identity of the dyed beads is determined by the fluorescence of the dyes. Individually dyed with combinations of two different fluorescent dyes (red and orange), a bead may have one of many possible levels of classifier dye fluorescent intensities. Based on it's fluorescent signature, each bead is classified to it's own unique region. Bio-Rad has used the various combinations of dyes to create 25 uniquely color-coded regions that are associated with 25 unique sets of beads (more can be added if needed). The detector measures at least 200 beads for each analyte, per specimen. The BioPlex 2200 ANA Screen utilizes one of these regions for each of the 13 analytes it detects. Three additional regions are assigned to beads used for quality control purposes. The bead regions used by the BioPlex 2200 ANA Screen are defined in the table below.

Bead Region	Assay Name	Description
17	dsDNA	Antigen coated bead - dsDNA
21	Chromatin (DNP)	Antigen coated bead - Chromatin
34	ISB	Internal Standard Bead – verifies detector response and corrects for fluctuations in laser intensity due to voltage fluctuation and/or temperature.
36	RNP-A	Antigen coated bead – RNP-A
38	SSB	Antigen coated bead – SSB
52	SSA-52	Antigen coated bead – SSA-52
54	Reagent Blank Bead	Blank bead – verifies absence of significant non-specific binding in serum or plasma
56	Scl-70	Antigen coated bead – Scl-70
71	Sm	Antigen coated bead – Sm
75	Centromere B	Antigen coated bead – Centromere B
79	Sm/RNP	Antigen coated bead – Sm/RNP
81	Ribosomal P	Antigen coated bead – Ribosomal P
92	RNP-68	Antigen coated bead – RNP-68
94	SSA-60	Antigen coated bead – SSA-60
96	Jo-1	Antigen coated bead – Jo-1
100	SVB (FXIII)	Serum Verification Bead (coated with a monoclonal antibody to Factor XIII) – verifies the addition of serum or plasma to the reaction vessel

While the identity of the dyed beads is determined by the fluorescence of the dyes, the amount of antibody captured by the antigen is determined by the fluorescence of the attached PE. Raw data is calculated in relative fluorescence intensity (RFI) and fluorescence ratio (FR).

Three additional dyed beads, Internal Standard Bead (ISB), Serum Verification Bead (SVB) and a Blank Bead (BB) are present in each reaction mixture to verify detector response, the addition of serum or plasma to the reaction vessel and the absence of significant non-specific binding in serum or plasma. Refer to the BioPlex 2200 System Operation Manual for more information. The instrument is calibrated using a set of six (6) distinct calibrator vials, supplied separately by Bio-Rad Laboratories. For dsDNA, six (6) vials, representing six (6) different levels of antibody concentrations, are used for quantitative calibration, and results for patient samples are expressed in IU/mL. Results of ≤4 IU/mL are negative, 5 - 9 IU/mL are indeterminate, and results of 10 IU/mL or higher are considered positive for dsDNA antibody. For the other twelve (12) beads, four (4) vials representing four (4) different antibody concentrations are used for semi-quantitative calibration. The result for each of these antibodies is expressed as an antibody index (AI). An AI of 1.0 indicates an antibody cut-off concentration that corresponds to approximately the 99th percentile of values obtained from a non-diseased population; results of 1.0 or higher are reported as positive. Results of <1.0 are reported as negative.

* In cases where either SS-A 60 and/or SS-A 52 are positive, results are reported as positive for SS-A, and when either RNP A and/or RNP 68 are positive, results are reported as positive for RNP.

INTENDED USE

The Bio-Plex 2200 ANA Screen is intended for the qualitative screening of specific antinuclear antibodies (ANA), the quantitative detection of antibody to dsDNA, and the semi-quantitative detection of ten (10) separate antibody assays (Chromatin, Ribosomal Protein, SS-A, SS-B, Sm, SmRNP, RNP, Scl-70, Jo-1, and Centromere B,) in human serum and/or EDTA or heparinized plasma. The test system is used as an aid in the diagnosis of systemic rheumatic diseases. The ANA Screen is intended for use with the Bio-Rad BioPlex 2200 System.

INDICATIONS FOR USE

The Bio-Plex 2200 ANA Screen is intended for the qualitative screening of specific antinuclear antibodies (ANA), the quantitative detection of antibody to dsDNA, and the semi-quantitative detection of ten (10) separate antibody assays (Chromatin, Ribosomal Protein, SS-A, SS-B, Sm, Sm/RNP, RNP, Scl-70, Jo-1, and Centromere B,) in human serum and/or EDTA or heparinized plasma.

The ANA Screen is intended for use with the Bio-Rad BioPlex 2200 System.

Uses:
The test system is used to screen serum or plasma (EDTA, heparin) samples and detect the presence of antinuclear antibodies as an aid in the diagnosis of systemic rheumatic diseases (Systemic Lupus Erythematosus [SLE], Mixed Connective Tissue Disease [MCTD], Undifferentiated Connective Tissue Disease [UCTD], Sjögren's Syndrome [SS], Scleroderma [Systemic Sclerosis], Dermatomyositis, Polymyositis, Rheumatoid Arthritis [RA], CREST Syndrome, and Raynaud's Phenomenon) in conjunction with clinical findings and other laboratory tests.

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TECHNOLOGICAL CHARACTERISTICS

The following table summarize similarities and differences between the BioPlex 2200 System, the Zeus Athena Multi-Lyte™ System, and the Immulite® 2000 Automated Immunoassay Analyzer.

Table 1: Similarities and differences between instruments

Similarities and Differences between Instruments	**BioPlex 2200 System**	**Zeus Athena Multi-Lyte™ System**	**Immulite® 2000 Automated Immunoassay Analyzer**
Detection	Based on Luminex Corporation's multiplex, bead-based technology.	Based on Luminex Corporation's multiplex, bead-based technology.	Not similar: luminometer (photomultiplier tube) to detect chemiluminescence.
Sample Handling / Processing Capabilities	Automated sample handling and processing.	Not similar: no automated sample handling or processing capabilities.	Automated sample handling and processing.
Reagent Storage	On-board, refrigerated reagent storage.	Not similar: off-line reagent storage.	On-board, refrigerated reagent storage.

The following tables summarize similarities and differences between the BioPlex 2200 ANA Screen and the predicate Autoimmune EIA devices used in comparative studies with the BioPlex 2200 ANA Screen.

Table 2(a:) Similarities between reagents and materials

Similarities between Components / Materials	**BioPlex 2200 ANA Screen**	**Predicate Autoimmune EIA's**
Reagents	Wash Buffer, Sample Diluent	Wash Buffer, Sample Diluent
Calibrators	Calibrators (quantitative and semi-quantitative analytes)	Calibrators (quantitative and semi-quantitative analytes)
Controls	Single Negative Control	Single Negative Control

Table 2(b): Differences between reagents and materials

Differences between Components / Materials	**BioPlex 2200 ANA Screen**	**Predicate Autoimmune EIA's**
Solid Phase	Bead reagent - dyed antigen coated beads	96 well microplate – antigen coated microwells
Reagents	Conjugate: Anti-human IgG / Phycoerythrin	Conjugate: Anti-Human IgG / Horse-radish Peroxidase, Substrate (TMB)
Calibrators	Calibrators (qualitative and semi-quantitative analytes)	Cut-off / Low Positive Controls (qualitative analytes)
Controls	One multi-analyte positive control covering all 11 analytes.	One positive control per analyte.
Sheath Fluid	Sheath Fluid is used to suspend the bead reagent and introduce it into the detector.	Not similar; not utilized in EIA's.

Table 3(a): Similarities between reagents with regard to function and use

Similarities between Function and Use	BioPlex 2200 ANA Screen	Predicate Autoimmune EIA's
Intended Use	Quantitative (dsDNA only) and semi-quantitative/qualitative autimmune antibody detection	Quantitative (dsDNA only) and semi-quantitative/qualitative autimmune antibody detection
Matrices	Serum and Plasma (EDTA and Heparin) for all analytes	Serum and Plasma (Jo-1, dsDNA, RNP, SSB)

Table 3(b): Differences between reagents with regard to function and use

Differences between Function and Use	BioPlex 2200 ANA Screen	Predicate Autoimmune EIA's
Matrices	Serum and Plasma (EDTA and Heparin) for all analytes	Serum (ANA Screen, SSA, Sm, Sm/RNP, Ribosome P, Chromatin, Centromere, Scl-70)

PERFORMANCE SUMMARY

A. Expected Values

The following testing was tested internally at Bio-Rad Laboratories:

Expected values for the ANA Screen test are presented in the following table for a U.S. population of normal blood donors (N=222). For dsDNA, results of ≤4 IU/mL are negative, 5 – 9 IU/mL are indeterminate, and ≥10 IU/mL or higher are reported as positive. For the other assays, results of <1.0 are negative and results of ≥1.0 AI are reported as positive.

Result	Positive		Negative		Indeterminate	
N = 222	#	(%)	#	(%)	#	(%)
ANA Screen*	15	6.8	207	93.2	N/A	N/A
dsDNA	3	1.4	211	95.0	8	3.6
Chromatin	2	0.9	220	99.1	N/A	N/A
Ribosomal Protein	0	0	222	100.0		
SS-A	2	0.9	220	99.1		
SS-B	0	0	222	100		
Sm	1	0.5	221	99.5		
SmRNP	2	0.9	220	99.1		
RNP	6	2.7	216	97.3		
Scl-70	1	0.5	221	99.5		
Jo-1	0	0.0	222	100.0		
Centromere B	3	1.4	219	98.6		

*results calculated based on testing of all analytes.

Expected values for the ANA Screen test are presented in the following table for patients from the BioPlex 2200 ANA Screen prospective study conducted at three clinical sites (N=908). For dsDNA, results of ≤4 IU/mL are negative, 5 – 9 IU/mL are indeterminate, and ≥10 IU/mL or higher are reported as positive. For the other assays, results of <1.0 are negative and results of ≥1.0 AI are reported as positive.

Result	Positive (%)	Negative (%)	Indeterminate (%)
ANA Screen[1]	390(43.0%)	518 (57.0%)	N/A
dsDNA	119 (13.1)%	741 (81.6%)	48(5.3%)
Chromatin	168 (18.5%)	740 (81.5%)	N/A
Ribosomal Protein	37 (4.1%)	871 (95.9%)	
SS-A	173 (19.0%)	735 (81.0%)	
SS-B	76 (8.4%)	832 (91.6%)	
Sm	60 (6.6%)	848 (93.4%)	
SmRNP	103 (11.3%)	805 (88.7%)	
RNP	112 (12.3%)	796 (87.7%)	
Scl-70	23 (2.5%)	885 (97.5%)	
Jo-1	6 (0.7%)	902 (99.3%)	
Centromere B	38 (4.2%)	870 (95.8%)	

B. Reproducibility Studies

A reproducibility panel, consisting of 11 serum panel members, was prepared at Bio-Rad Laboratories. Each of ten (10) positive panel members was prepared by combining one (1) or more antibody positive patient samples for one (1) or more of the 13 analytes contained in the Bio-Rad BioPlex 2200 ANA Screen (dsDNA, Chromatin, SS-A 52, SS-A 60, SS-B, Sm, RNP 68, RNP A, SmRNP, Centromere, Ribosomal Protein, Scl-70, Jo-1). Five (5) of the ten (10) members had higher levels of the antibodies and five (5) of the ten (10) members had antibody levels near the cutoff. One (1) panel member was negative for all 13 analytes. In addition, three (3) lots of the BioPlex 2200 ANA Screen Control Set [1 positive control (antibody positive for all 13 analytes), 1 diluted positive control, and a negative control (antibody negative for all 13 analytes)] were also tested.

Reproducibility testing was performed at three (3) US testing facilities on a total of three (3) lots of the Bio-Rad ANA Screen. Each testing facility evaluated reproducibility using one (1) kit lot of the Bio-Rad ANA Screen. The eleven (11) panel members were provided to each of the testing sites. Each of the eleven (11) panel members and the Autoimmune Control Set was tested in duplicate (x2) on two (2) runs per day (morning and afternoon) for ten (10) days using one (1) lot of Bio-Rad ANA Screen Reagent Pack and one (1) lot of Bio-Rad ANA Screen Calibrator Set at each of three (3) sites. [2 times x 2 runs x 10 days = 40 replicates per panel member per site. Total replicates at 3 sites = 120 replicates per panel member.] The data were then analyzed for intra-assay and inter-assay reproducibility according to the National Committee for Clinical Laboratory Standards (NCCLS EP5-A, Vol. 19, No. 2, p7, Eq. (1) and p8 Eq. (4)). The mean Antibody Index (AI), standard deviation (SD), and percent coefficient of variation (%CV) for each panel member is presented. For dsDNA, the mean International Units per ml (IU/mL), standard deviation (SD), and percent coefficient of variation (%CV) for each panel member is presented.

Intra-assay and inter-assay reproducibility on the BioPlex 2200 ANA Screen for the serum panel members from three sites and three lots are presented in the tables below.

Reproducibility Results; Intra-assay – Site 1 - Serum

Clinical Site #1 Lot 1		BioPlex2200 ANA Screen Intra-assay												
		dsDNA (IU/ml)	Chromatin (AI)	Ribosomal Protein (AI)	SS-A 52 (AI)	SS-A 60 (AI)	SS-B (AI)	Sm (AI)	SmRNP (AI)	RNP-A (AI)	RNP-68 (AI)	Scl-70 (AI)	Jo-1 (AI)	Centromere (AI)
High Positive Panel	Mean	45.6	2.7	2.4	4.1	3.4	3.6	3.3	4.0	4.1	3.8	3.3	3.9	3.7
	SD*	0.89	0.08	0.07	0.19	0.07	0.07	0.09	0.08	0.10	0.13	0.08	0.10	0.08
	%CV	2.0%	2.9%	2.7%	4.6%	1.9%	2.0%	2.9%	2.0%	2.4%	3.5%	2.4%	2.5%	2.2%
	N=	40	40	40	36	36	36	40	40	40	40	40	40	40
Low Positive Panel	Mean	17.0	1.3	1.2	2.2	1.8	1.7	1.5	2.2	1.9	1.8	1.9	1.9	2.0
	SD*	0.05	0.06	0.04	0.17	0.07	0.05	0.05	0.06	0.05	0.09	0.06	0.09	0.05
	%CV	2.9%	4.4%	3.9%	7.9%	3.9%	3.1%	3.2%	2.6%	2.6%	4.9%	2.9%	5.0%	2.7%
	N=	40	40	40	40	40	40	40	40	40	40	36	40	40
Negative Panel	Mean	0.0	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	SD*	0.00	0.03	0.00	0.00	0.02	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Positive [1] Control	Mean	23.2	2.5	1.7	3.1	2.5	2.7	2.8	3.0	2.7	2.5	2.7	2.7	2.8
	SD*	0.62	0.10	0.04	0.16	0.04	0.07	0.07	0.07	0.08	0.16	0.06	0.08	0.05
	%CV	2.7%	4.0%	2.6%	5.1%	1.7%	2.6%	2.4%	2.2%	3.0%	6.6%	2.0%	2.9%	1.9%
	N=	36	36	40	36	36	36	36	40	36	36	36	36	36
Negative Control	Mean	0.0	0.2	0.1	0.0	0.1	0.1	0.1	0.5	0.2	0.0	0.1	0.0	0.0
	SD*	0.00	0.02	0.00	0.00	0.02	0.02	0.00	0.03	0.03	0.00	0.02	0.02	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	36	40	40

* NCCLS EP5 – A Vol. 19, No. 2, page 7 equation 1

[1] Cumulative results of positive control and diluted positive control.

As can be seen in the above table, the CV% for intra-assay precision ranged from 1.7% to 7.9% for all serum positive panel members for all analytes when tested at Site 1 on the BioPlex 2200 ANA Screen Lot 1.

Reproducibility Results; Intra-assay – Site 2 - Serum

Clinical Site #2 Lot 2		BioPlex2200 ANA Screen Intra-assay												
		dsDNA (IU/ml)	Chromatin (AI)	Ribosomal Protein (AI)	SS-A 52 (AI)	SS-A 60 (AI)	SS-B (AI)	Sm (AI)	SmRNP (AI)	RNP-A (AI)	RNP-68 (AI)	Scl-70 (AI)	Jo-1 (AI)	Centromere (AI)
High Positive Panel	Mean	44.9	2.9	2.7	3.8	3.6	3.5	3.9	3.4	3.8	3.9	3.2	3.1	2.9
	SD*	1.06	0.09	0.07	0.09	0.09	0.07	0.11	0.12	0.10	0.16	0.10	0.12	0.10
	%CV	2.4%	3.2%	2.8%	2.4%	2.6%	2.1%	2.9%	3.4%	2.7%	4.2%	3.3%	4.0%	3.3%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Low Positive Panel	Mean	18.2	1.5	1.6	2.2	1.9	1.6	1.7	1.9	1.8	1.8	1.8	1.4	1.6
	SD*	0.52	0.09	0.07	0.09	0.07	0.05	0.15	0.07	0.08	0.09	0.13	0.07	0.08
	%CV	2.9%	5.5%	4.4%	4.3%	3.9%	3.1%	8.6%	3.5%	4.3%	5.2%	7.1%	5.1%	5.2%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Negative Panel	Mean	0.0	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	SD*	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Positive[1] Control	Mean	24.7	2.3	2.7	2.8	2.8	3.8	3.0	2.7	2.9	3.4	2.4	3.6	2.4
	SD*	0.72	0.09	0.07	0.13	0.10	0.12	0.09	0.07	0.11	0.14	0.08	0.14	0.09
	%CV	2.9%	4.1%	2.5%	4.7%	3.5%	3.1%	3.0%	2.5%	3.8%	4.2%	3.2%	3.8%	3.7%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Negative Control	Mean	1.1	0.2	0.1	0.0	0.0	0.0	0.2	0.1	0.1	0.0	0.1	0.0	0.0
	SD*	0.22	0.02	0.00	0.00	0.02	0.00	0.03	0.02	0.00	0.00	0.02	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40

* NCCLS EP5 – A Vol. 19, No. 2, page 7 equation 1

[1] Cumulative results of positive control and diluted positive control.

As can be seen in the above table, the CV% for intra-assay precision ranged from 2.1% to 8.6% for all serum positive panel members for all analytes when tested at Site 2 on the BioPlex 2200 ANA Screen Lot 2.

Reproducibility Results; Intra-assay – Site 3 - Serum

Clinical Site #3 Lot 3		BioPlex2200 ANA Screen Intra-assay												
		dsDNA (IU/ml)	Chromatin (AI)	Ribosomal Protein (AI)	SS-A 52 (AI)	SS-A 60 (AI)	SS-B (AI)	Sm (AI)	SmRNP (AI)	RNP-A (AI)	RNP-68 (AI)	Scl-70 (AI)	Jo-1 (AI)	Centromere (AI)
High Positive Panel	Mean	52.8	2.8	2.6	4.7	4.2	4.0	3.7	3.7	4.7	4.3	3.8	3.9	4.2
	SD*	1.16	0.11	0.07	0.41	0.11	0.10	0.09	0.11	0.13	0.16	0.09	0.13	0.09
	%CV	2.2%	3.9%	2.9%	8.7%	2.6%	2.4%	2.3%	3.0%	2.7%	3.8%	2.5%	3.4%	2.1%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Low Positive Panel	Mean	19.9	1.4	1.3	2.8	2.2	2.1	1.8	1.9	2.2	2.3	2.3	2.0	2.5
	SD*	0.72	0.07	0.05	0.25	0.10	0.08	0.05	0.05	0.07	0.10	0.06	0.10	0.08
	%CV	3.6%	4.7%	3.5%	9.1%	4.4%	3.7%	3.0%	2.8%	3.1%	4.5%	2.7%	4.8%	3.0%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Negative Panel	Mean	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	SD*	0.00	0.04	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Positive [1] Control	Mean	26.1	2.7	2.5	3.4	3.1	3.1	2.7	3.4	3.5	2.8	2.9	3.1	2.9
	SD*	0.60	0.07	0.08	0.38	0.08	0.08	0.07	0.07	0.10	0.09	0.07	0.11	0.09
	%CV	2.3%	2.7%	3.1%	11.1%	2.8%	2.5%	2.5%	2.2%	3.0%	3.4%	2.5%	3.6%	3.1%
	N=	36	36	40	36	36	36	36	40	36	36	36	36	36
Negative Control	Mean	1.0	0.3	0.1	0.0	0.0	0.1	0.1	0.1	0.2	0.0	0.1	0.0	0.0
	SD*	0.00	0.03	0.00	0.05	0.00	0.02	0.00	0.00	0.02	0.00	0.02	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40

* NCCLS EP5 – A Vol. 19, No. 2, page 7 equation 1

[1] Cumulative results of positive control and diluted positive control.

As can be seen in the above table, the CV% for intra-assay precision ranged from 2.1% to 11.1% for all serum positive panel members for all analytes when tested at Site 3 on the BioPlex 2200 ANA Screen Lot 3.

Reproducibility Results; Inter-assay – Site 1 - Serum

Clinical Site #1 Lot 1		BioPlex2200 ANA Screen Inter-assay												
		dsDNA (IU/ml)	Chromatin (AI)	Ribosomal Protein (AI)	SS-A 52 (AI)	SS-A 60 (AI)	SS-B (AI)	Sm (AI)	SmRNP (AI)	RNP-A (AI)	RNP-68 (AI)	Scl-70 (AI)	Jo-1 (AI)	Centromere (AI)
High Positive Panel	Mean	45.6	2.7	2.4	4.1	3.4	3.6	3.3	4.0	4.1	3.8	3.3	3.9	3.7
	SD*	1.82	0.13	0.16	0.28	0.20	0.21	0.10	0.14	0.14	0.20	0.12	0.20	0.10
	%CV	4.0%	4.8%	6.7%	6.8%	5.8%	5.8%	3.2%	3.5%	3.5%	5.4%	3.7%	5.0%	2.8%
	N=	40	40	40	36	36	36	40	40	40	40	40	40	40
Low Positive Panel	Mean	17.0	1.3	1.2	2.2	1.8	1.7	1.5	2.2	1.9	1.8	1.9	1.9	2.0
	SD*	0.60	0.08	0.06	0.21	0.08	0.08	0.07	0.09	0.08	0.12	0.12	0.12	0.11
	%CV	3.5%	6.1%	5.6%	9.7%	4.6%	5.0%	5.0%	4.0%	4.0%	6.3%	6.3%	6.2%	5.3%
	N=	40	40	40	40	40	40	40	40	40	40	36	40	40
Negative Panel	Mean	0.0	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	SD*	0.00	0.03	0.00	0.00	0.02	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Positive[1] Control	Mean	23.2	2.5	1.7	3.1	2.5	2.7	2.8	3.0	2.7	2.5	2.7	2.7	2.8
	SD*	2.09	0.29	0.10	0.39	0.25	0.29	0.26	0.10	0.26	0.29	0.28	0.27	0.27
	%CV	9.0%	11.7%	5.8%	12.8%	10.0%	10.7%	9.5%	3.2%	9.7%	11.6%	10.5%	10.1%	9.8%
	N=	36	36	40	36	36	36	36	40	36	36	36	36	36
Negative Control	Mean	0.0	0.2	0.1	0.0	0.1	0.1	0.1	0.5	0.2	0.0	0.1	0.0	0.0
	SD*	0.00	0.02	0.00	0.00	0.04	0.05	0.00	0.08	0.05	0.02	0.04	0.02	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	36	40	40

* NCCLS EP5 – A Vol. 19, No. 2, page 8 equation 4

[1] Cumulative results of positive control and diluted positive control.

As can be seen in the above table, the CV% for inter-assay precision ranged from 2.8% to 12.8% for all serum positive panel members for all analytes when tested at Site 1 on the BioPlex 2200 ANA Screen Lot 1.

Reproducibility Results; Inter-assay – Site 2 - Serum

Clinical Site #2 Lot 2		BioPlex2200 ANA Screen Inter-assay												
		dsDNA (IU/ml)	Chromatin (AI)	Ribosomal Protein (AI)	SS-A 52 (AI)	SS-A 60 (AI)	SS-B (AI)	Sm (AI)	SmRNP (AI)	RNP-A (AI)	RNP-68 (AI)	Scl-70 (AI)	Jo-1 (AI)	Centromere (AI)
High Positive Panel	Mean	44.9	2.9	2.7	3.8	3.6	3.5	3.9	3.4	3.8	3.9	3.2	3.1	2.9
	SD*	3.40	0.25	0.19	0.28	0.24	0.30	0.22	0.25	0.24	0.28	0.21	0.28	0.18
	%CV	7.6%	8.8%	7.2%	7.4%	6.8%	8.4%	5.8%	7.2%	6.3%	7.2%	6.5%	9.0%	6.2%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Low Positive Panel	Mean	18.2	1.5	1.6	2.2	1.9	1.6	1.7	1.9	1.8	1.8	1.8	1.4	1.6
	SD*	1.15	0.16	0.10	0.19	0.15	0.14	0.20	0.13	0.15	0.18	0.17	0.12	0.17
	%CV	6.3%	10.2%	6.6%	8.4%	8.1%	8.8%	11.9%	6.8%	8.7%	10.2%	9.5%	9.0%	10.6%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Negative Panel	Mean	0.0	0.1	0.1	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	SD*	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Positive[1] Control	Mean	24.7	2.3	2.7	2.8	2.8	3.8	3.0	2.7	2.9	3.4	2.4	3.6	2.4
	SD*	1.71	0.19	0.19	0.24	0.21	0.32	0.23	0.18	0.24	0.29	0.18	0.30	0.20
	%CV	7.0%	8.3%	7.1%	8.6%	7.3%	8.4%	7.8%	6.8%	8.4%	8.6%	7.3%	8.2%	8.6%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Negative Control	Mean	1.1	0.2	0.1	0.0	0.0	0.0	0.2	0.1	0.1	0.0	0.1	0.0	0.0
	SD*	0.27	0.02	0.00	0.00	0.02	0.03	0.03	0.02	0.00	0.00	0.03	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40

* NCCLS EP5 – A Vol. 19, No. 2, page 8 equation 4

[1] Cumulative results of positive control and diluted positive control.

As can be seen in the above table, the CV% for inter-assay precision ranged from 5.8% to 11.9% for all serum positive panel members for all analytes when tested at Site 2 on the BioPlex 2200 ANA Screen Lot 2.

Reproducibility Results; Inter-assay – Site 3 - Serum

Clinical Site #3 Lot 3		BioPlex2200 ANA Screen Inter-assay												
		dsDNA (IU/ml)	Chromatin (AI)	Ribosomal Protein (AI)	SS-A 52 (AI)	SS-A 60 (AI)	SS-B (AI)	Sm (AI)	SmRNP (AI)	RNP-A (AI)	RNP-68 (AI)	Scl-70 (AI)	Jo-1 (AI)	Centromere (AI)
High Positive Panel	Mean	52.8	2.8	2.6	4.7	4.2	4.0	3.7	3.7	4.7	4.3	3.8	3.9	4.2
	SD*	2.05	0.16	0.15	0.47	0.21	0.20	0.17	0.18	0.20	0.23	0.16	0.24	0.15
	%CV	3.9%	5.6%	5.9%	9.8%	5.1%	5.0%	4.5%	5.1%	4.2%	5.5%	4.3%	6.0%	3.6%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Low Positive Panel	Mean	19.9	1.4	1.3	2.8	2.2	2.1	1.8	1.9	2.2	2.3	2.3	2.0	2.5
	SD*	1.29	0.11	0.09	0.28	0.15	0.15	0.10	0.11	0.13	0.13	0.13	0.15	0.14
	%CV	6.5%	7.9%	7.0%	10.0%	6.8%	7.2%	5.5%	5.8%	5.6%	5.9%	5.7%	7.2%	5.5%
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Negative Panel	Mean	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	SD*	0.00	0.04	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40
Positive[1] Control	Mean	26.1	2.7	2.5	3.4	3.1	3.1	2.7	3.4	3.5	2.8	2.9	3.1	2.9
	SD*	1.06	0.15	0.23	0.41	0.15	0.14	0.12	0.25	0.16	0.18	0.13	0.19	0.14
	%CV	4.1%	5.6%	9.5%	12.0%	5.0%	4.5%	4.5%	7.5%	4.6%	6.4%	4.4%	6.0%	4.8%
	N=	36	36	40	36	36	36	36	40	36	36	36	36	36
Negative Control	Mean	1.0	0.3	0.1	0.0	0.0	0.1	0.1	0.1	0.2	0.0	0.1	0.0	0.0
	SD*	0.00	0.04	0.00	0.05	0.04	0.04	0.00	0.00	0.04	0.00	0.03	0.00	0.00
	%CV	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N=	40	40	40	40	40	40	40	40	40	40	40	40	40

* NCCLS EP5 – A Vol. 19, No. 2, page 8 equation 4
[1] Cumulative results of positive control and diluted positive control.

As can be seen in the above table, the CV% for inter-assay precision ranged from 3.6% to 12.0% for all serum positive panel members for all analytes when tested at Site 3 on the BioPlex 2200 ANA Screen Lot 3.

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C. Clinical Testing

Prospective Testing

Prospective: Comparison of ANA Screen and ANA Microplate EIA
Performance of the ANA Screen was evaluated against a commercially available ANA Microplate EIA. A total of 908 prospective serum samples were tested at 3 U.S. clinical testing sites. The samples were collected from patients seen at a rheumatology clinic and suspected of having systemic autoimmune disease. Results are summarized in the table below.

	Positive ANA Screen[1]	**Negative ANA Screen[1]**	**Total**
Positive EIA*	351	149	500
Negative EIA	39	369	408
Total	390	518	908

The results of comparative prospective testing demonstrated the following:

Positive Agreement: 351/500 = 70.2% (95% CI 66.1 – 74.3 %)
Negative Agreement: 369/708 = 90.4% (95% CI 87.5 – 93.4%)
Overall agreement: 720/908 = 79.3% (95% CI 76.6 – 82%)

Prospective: Comparison of Selected Antibodies to EIA Methods
Of the 908 prospective serum samples tested, samples positive by the ANA Screen for specific autoantibodies were also tested by a corresponding commercially available microplate EIA. Results can be seen in the table below.

Antibody/ Antibody Group	dsDNA	Chromatin	Ribosomal-P	SS-A	SS-B	Sm	SmRNP	RNP	Scl-70	Jo-1	Centromere
N	832*	908	908	908	908	908	908	879**	908	908	908
Bio-Rad and EIA Positive	83	98	18	156	57	35	90	79	9	6	31
Bio-Rad Positive and EIA Negative	25	70	19	17	19	25	13	25	14	0	7
Bio-Rad and EIA Negative	699	680	868	721	820	843	782	759	877	897	869
Bio-Rad Negative and EIA Positive	25	60	3	14	12	5	23	16	8	5	1
% Overall Agreement	94%	86%	98%	97%	97%	97%	96%	95%	98%	99%	99%
95% Confidence Interval	92-96%	83-88%	97-99%	95-98%	95-98%	96-98%	95-97%	94-97%	97-99%	99-100%	99-100%

* 76 BioPlex dsDNA indeterminate or predicate dsDNA equivocal results excluded.
** 29 predicate RNP equivocal results excluded.

Retrospective Testing

Retrospective: Comparison of Selected Antibodies to EIA Methods
Performance of the ANA Screen was further evaluated by testing 440 retrospective serum samples, all known to be positive for ANA and one or more of the autoantibodies listed below. An additional 100 serum sample known to be negative for ANA were also tested. The retrospective specimens were tested by both the ANA Screen and commercially available microplate EIA methods that were specific for the corresponding autoantibodies. Results can be found in the tables below.

Antibody / Antibody Group	dsDNA	Chromatin	Ribosomal-P	SS-A	SS-B	Sm	SmRNP	RNP	Scl-70	Jo-1	Centromere
N	123*†	138†	138†	139†	140	139†	139†	138**	139†	130†	140
Bio-Rad and EIA Positive	19	11	14	37	39	25	38	37	13	30	36
Bio-Rad Positive and EIA Negative	0	2	3	0	1	0	0	2	4	0	3
Bio-Rad and EIA Negative	101	108	118	100	100	104	99	95	118	100	101
Bio-Rad Negative and EIA Positive	3	17	3	2	0	10	2	4	4	0	0
% Overall Agreement	98%	86%	96%	99%	99%	93%	99%	96%	94%	100%	98%
95% Confidence Interval	94-100%	80-92%	92-99.5%	96-100%	98-100%	88-98%	96-100%	92-99.5%	90-99%	99.6-100%	95-100%

* 16 BioPlex dsDNA indeterminate or predicate dsDNA equivocal results excluded.
**2 predicate RNP equivocal results are excluded.
†A total of 19 (1 dsDNA, 2 Chromatin, 2 Ribosomal-P, 1SS-A, 1Sm, 1SmRNP, 1Scl-70, and 10 Jo-1 retrospective study samples with repeatedly low Serum Verification Bead (SVB) results were excluded.

Combined Prospective and Retrospective Testing

Combined Prospective and Retrospective: Comparison of Selected Antibodies to EIA Methods
The combined results from the prospective and retrospective studies were analyzed for performance in comparison to the EIA methods. Results from the combined analysis can be found in the table below.

Antibody/ Antibody Group	dsDNA	Chromatin	Ribosomal-P	SS-A	SS-B	Sm	SmRNP	RNP	Scl-70	Jo-1	Centromere
N	955*†	1046†	1046†	1047†	1048	1047†	1047†	1017**	1047†	1038†	1048
Bio-Rad and EIA Positive	102	109	32	193	96	60	128	116	22	36	67
Bio-Rad Positive and EIA Negative	25	72	22	17	20	25	13	27	18	0	10
Bio-Rad and EIA Negative	800	788	986	821	920	947	881	854	995	997	970
Bio-Rad Negative and EIA Positive	28	77	6	16	12	15	25	20	12	5	1
% Overall Agreement	94%	86%	97%	97%	97%	96%	96%	95%	97%	99.5%	99%
95% Confidence Interval	93-96%	84-88%	96-98 %	96-98%	96-98%	95-97%	95-98%	94-97%	96-98%	99-99.9%	98.6-99.6 %

* 92 BioPlex dsDNA indeterminate or predicate dsDNA equivocal results excluded
** 31 predicate RNP equivocal results are excluded
†A total of 19 (1 dsDNA, 2 Chromatin, 2 Ribosomal-P, 1SS-A, 1Sm, 1SmRNP, 1Scl-70, and 10 Jo-1 retrospective study samples with repeatedly low Serum Verification Bead (SVB) results were excluded.

D. CDC Panel

The Centers for Disease Control (CDC) provides a reference serum panel, which was tested to evaluate characteristics of the ANA Screen. The results are presented as a means to convey further information on the performance of the ANA Screen with a masked, characterized serum panel. This does not imply an endorsement of the ANA Screen by the CDC. A summary of results can be found in the table below.

CENTER FOR DISEASE CONTROL (CDC)* Reference Sera		BioPlex 2200 ANA Screen Results															
	Expected Results	ANA Screen†	dsDNA	Chromatin (DNP)	RNP A	RNP 68	RNP (Compound)	SSB 48	SSA 52	SSA 60	SSA (Compound)	Scl-70	Sm	Sm RNP	Ribosomal P	Centromere B	Jo-1
CDC-1	Homogeneous / rim	+	+	+									+	+			
CDC-2	Speckled/La	+						+	+	+	+						
CDC-3	Speckled	+		+		+	+	+		+	+		+	+			
CDC-4	U1-RNP	+		+	+	+	+							+			
CDC-5	Sm	+		+	+		+						+	+			
CDC-6	Nucleolar	+		+													
CDC-7	SSA/Ro	+								+	+						
CDC-8	Centromere	+														+	
CDC-9	Scl-70	+										+					
CDC-10	Jo-1	+							+		+						+
CDC-11	PM/Scl																

* Committee on ANA Serology of the Arthritis Foundation

† results calculated based on testing of all analytes.

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E. Cross-Reactivity

A cross-reactivity study was performed to determine if samples from various disease states and other potentially interfering factors interfere with test results when tested with the ANA Screen. A panel of ten (10) specimens with potentially interfering disease states was tested with the ANA Screen for each of the eleven (11) autoantibodies. All panel specimens were previously characterized and known to be negative for all autoantibodies detected by the ANA Screen. Samples that elicited a positive response by the BioPlex 2200 ANA Screen were also tested by a corresponding commercially available EIA test method

Cross Reactants	N	Method	Centromere B	Chromatin	dsDNA	Jo1	Ribosomal P	RNP	SCL-70	Smith	Sm-RNP	SSA	SSB
			# of Positive Samples										
Cardiolipin	10	BioPlex	0	3	1	1	0	0	0	1	2	4	0
		EIA	NT	3	1	1	NT	NT	NT	0	2	4	NT
Mitochondrial M2	10	BioPlex	6	3	1	0	0	2	0	0	1	4	1
		EIA	4	2	0	NT	NT	1	NT	NT	1	4	1
Single-stranded DNA (ssDNA)	10	BioPlex	1	4	4	0	2	1	2	1	1	4	2
		EIA	1	4	4*	NT	1	EQ	1	1	1	4	2
Histone	10	BioPlex	0	7	6	0	4	5	1	5	6	3	1
		EIA	NT	7	6	NT	2	5	1	5	6	3	1
Myeloperoxidase (MPO)	10	BioPlex	1	1	2	0	2	0	0	0	0	1	0
		EIA	0	0	0	NT	0	NT	NT	NT	NT	0	NT
Proteinase 3 (PR3)	10	BioPlex	1	1	0	0	0	0	0	0	0	0	0
		EIA	1	0	NT	NT	NT	NT	NT	NT	NT	NT	NT
Gliadin	10	BioPlex	0	0	0	0	0	0	0	0	0	1	0
		EIA	NT	NT	NT	NT	NT	NT	NT	NT	NT	1	NT
Smooth Muscle	10	BioPlex	0	2	2	0	2	1	0	1	2	1	0
		EIA	NT	2	2	NT	2	1	NT	1	2	1	NT
Thyroid Peroxidase (TPO)	10	BioPlex	2	0	0	0	0	0	0	0	0	0	0
		EIA	2	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Thyroglobulin (Tg)	10	BioPlex	2	2	1	0	0	2	0	1	1	1	0
		EIA	2	0	0	NT	NT	1	NT	0	1	0	NT
Rheumatoid Factor (RF)	10	BioPlex	0	0	0	0	0	0	0	0	0	0	0
		EIA	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT

NT= Not Tested

**BioPlex dsDNA indeterminate sample excluded.*

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 20 2004

Bio-Rad Laboratories, Inc
c/o Mr. Christopher Bensten
6565 185th Ave, NE
Redmond, WA 98052

Re: k041658
Trade/Device Name: BioPlex 2200 ANA Screen on the BioPlex 2200 Multi-Analyte Detection System
Regulation Number: 21 CFR 866.5100
Regulation Name: Antinuclear Antibody Immunological Test System
Regulatory Class: Class II
Product Code: LKJ, LRM, MQA, LKO, LJM, LLL
Dated: June 15, 2004
Received: June 18, 2004

Dear Mr Bensten:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

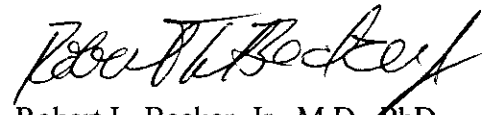
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address
http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,



Robert L. Becker, Jr., M.D., PhD
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known):

Device Name: BioPlex 2200 ANA Screen on the
BioPlex 2200 Multi-Analyte Detection System

Indications for Use:

The Bio-Plex 2200 ANA Screen is intended for the qualitative screening of specific antinuclear antibodies (ANA), the quantitative detection of antibody to dsDNA, and the semi-quantitative detection of ten (10) separate antibody assays (Chromatin, Ribosomal Protein, SS-A, SS-B, Sm, Sm/RNP, RNP, Scl-70, Jo-1, and Centromere B,) in human serum and/or EDTA or heparinized plasma.

The ANA Screen is intended for use with the Bio-Rad BioPlex 2200 System.

Uses:
The test system is used to screen serum or plasma (EDTA, heparin) samples and detect the presence of antinuclear antibodies as an aid in the diagnosis of systemic rheumatic diseases (Systemic Lupus Erythematosus [SLE], Mixed Connective Tissue Disease [MCTD], Undifferentiated Connective Tissue Disease [UCTD], Sjögren's Syndrome [SS], Scleroderma [Systemic Sclerosis], Dermatomyositis, Polymyositis, Rheumatoid Arthritis [RA], CREST Syndrome, and Raynaud's Phenomenon) in conjunction with clinical findings and other laboratory tests.

Prescription Use: ___X___ AND/OR Over-The-Counter Use: _____
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Maria M Chan

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K041658