JUL 9 2012

BioPlex® 2200 ANA Screen with MDSS 510(k) Summary

510(k) Number K113610 Date Prepared: March 2, 2012

Introduction

Bio-Rad Laboratories hereby submits this Special 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides detail as a basis for a determination of substantial equivalence for the BioPlex® 2200 ANA Screen with MDSS.

Submitter name, address and contact

Submitter	Contact Person
Bio-Rad Laboratories, Inc BioPlex Division 5500 E. Second Street Benicia, CA 94510	Juang Wang Regulatory Affairs Representative Phone: (510)741-4609 Fax: (510)741-3941

Device name and Classification

BioPlex 2200 ANA Screen Classification

Classification Name	antinuclear antibody, antigen, control
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
Product Code	LKJ, LRM, MQA,LKO, LJM, LLL, JIX, JJY

BioPlex 2200 Medical Decision Support Software (MDSS) Classification

Classification Name	diagnostic software, k-nearest neighbor algorithm, autoimmune disease
Common Name:	Medical Decision Support Software
Product Trade Name	BioPlex 2200 Medical Decision Support Software(MDSS) on the BioPlex 2200 Multi-Analyte Detection System
Device Class	Class II
Classification Panel	Clinical Toxicology

Regulation Number	862.3100
Product Code	NVI

Legally Marketed Predicate Device

BioPlex® 2200 ANA Screen with MDSS, k043341

Intended Use

The BioPlex® 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 autoimmune diseases.

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

The BioPlex 2200 Medical Decision Support Software (MDSS), used in conjunction with the ANA Screen, is an optional laboratory tool that associates patient antibody results with predefined MDSS profiles that have been correlated with the following systemic autoimmune diseases: Systemic Lupus Erythematosus (SLE), Mixed Connective Tissue Disease (MCTD), Sjögren's Syndrome (SS), Scleroderma (Systemic Sclerosis) and Polymyositis.

Indications For Use

The BioPlex® 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 ANA Screen 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 autoimmune 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.

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

The BioPlex 2200 Medical Decision Support Software (MDSS), used in conjunction with the ANA Screen, is an optional laboratory tool that associates patient antibody results from the ANA Screen with predefined MDSS profiles that have been correlated with the following systemic autoimmune diseases: Systemic Lupus Erythematosus (SLE), Mixed Connective Tissue Disease (MCTD), Sjögren's Syndrome (SS), Scleroderma (Systemic Sclerosis) and Polymyositis.

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 Reagent Blank Bead (RBB) 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 calibrator set, supplied separately by Bio-Rad Laboratories. For dsDNA, 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.

The BioPlex 2200 Medical Decision Support Software (MDSS) is a pattern recognition algorithm that can enhance the performance of the ANA Screen by identifying associated diagnostic patterns among its multiple assay results. The MDSS can suggest one or more possible disease associations after identifying patterns from the eleven (11) individual antibody results. The MDSS is based on the principles of the "k-nearest neighbor"[11] (kNN) statistical technique. Each "unknown" is compared to a pre-established database that contains the results for over 1,400 characterized sera/plasma. Results of MDSS analysis fall into one of the following general outcomes; Negative, No Association, or Association with Disease. When the results of the MDSS analysis fall into the Association with Disease category, the MDSS software will propose a maximum of two disease classifications based upon the similarity of the current analysis to the stored results. The MDSS output can also aid in determining appropriate additional autoimmune serological testing. A description of the BioPlex 2200 ANA Screen with MDSS is included in the pre-market notification submission k043341.

Similarities and Differences

Similarities

Feature	Modified Device
Intended Use/Indications For Use	No Change
Kit components	No Change
Technical Specifications	No Change
Fundamental Scientific Technology	No Change

Differences

The differences are to modify QC testing from each reagent pack to once per day as stated in the Instructions For Use (IFU) of the BioPlex®® 2200 ANA Screen with MDSS, to add sodium azide in kit components for reagent stability enhancement, and to add protein stabilizer and protease inhibitors for microbial contamination prevention.

Feature	Modified	Predicate
Frequency of Reagent Pack QC Testing	QC once per day or per new reagent pack lot	QC once per pack and per day
Reagent Stability Enhancement	Addition of sodium azide in bead, conjugate and sample diluent	None
Microbial Contamination Prevention	Addition of protein stabilizer and protease inhibitors in the particle (bead) diluent	None

Summary of Design Control Activities

A Failure Mode and Effect Analysis (FMEA) was used to facilitate, capture, and quantify potential impacts of false positive or negative patient results. The Risk Priority Number (RPN) is a quantitative measure of the combined effects of severity, occurrence, and detection of potential risks. Specific mitigations are recommended that may include changes to the design or formulation if the RPN score exceeds a chosen threshold.

The Design Control Activities include Risk Analysis method to identify the verification and validation activities required, test used and acceptance criteria.

Based on the conclusion of the risk management report, the modified QC procedure fulfills the requirements of the specifications of the design control process. Therefore, the performance of the modified QC test frequency is substantially equivalent to the current

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

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c/o Juang Wang, Ph.D., RAC
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BioPlex 2200 Division
5500 E. Second Street
Benicia, CA 94510

JUL 9 2012

Re: k113610
Trade Name: BioPlex® 2200 ANA Screen with Medical Decision Support Software (MDSS) for use with 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, JIX, JJY
Dated: June 18, 2012
Received: June 19, 2012

Dear Dr. Wang:

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 class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the

quality systems (QS) regulation (21 CFR Part 820). 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 a 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 Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

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) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan, Ph.D.
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): K113610

Device Name: BioPlex® 2200 ANA Screen with Medical Decision Support Software (MDSS) for use with the BioPlex® 2200 Multi-Analyte Detection System

Indications for Use:

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Prescription Use __x__ AND/OR Over-the-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(Please do not write below this line-Continue on another page of needed)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K113610