510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k062213

B. Purpose for Submission:

This is an original bundled application for a new multiplexed flow immunoassay for the qualitative detection of two (2) separate analytes; Epstein-Barr Virus Viral Capsid Antigen (EBV VCA) IgM antibodies and Heterophile antibodies in human serum to aid in the diagnosis of infectious mononucleosis.

C. Measurand:

Epstein-Barr Virus Viral Capsid Antigen (EBV VCA) IgM antibodies and Heterophile antibodies

D. Type of Test:

Multiplexed flow immunoassay

E. Applicant:

BIO-RAD LABORATORIES, INC.

F. Proprietary and Established Names:

BioPlex 2200 EBV IgM kit, Controls and Calibrators on the BioPlex 2200 Multi-Analyte Detection System

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LJN	I	866.3235 – Epstein-Barr virus serological reagents	Microbiology (83)
KTN	II	866.5640 Infectious mononucleosis immunological test system	Immunology

H. Intended Use:

1. Intended use(s):

   The BioPlex 2200 EBV IgM kit is a multiplex flow immunoassay intended for the qualitative detection of two (2) separate analytes; Epstein-Barr Virus Viral Capsid Antigen (EBV VCA) IgM antibodies and Heterophile antibodies in human serum. The test system can be used in conjunction with the BioPlex 2200 EBV IgG kit as an aid in the laboratory diagnosis of infectious mononucleosis (IM).

   The EBV IgM kit is intended for use with the Bio-Rad BioPlex 2200 System.

   Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, neonatal specimens, or infants. Assay performance characteristics have not been established for the diagnosis of nasopharyngeal carcinoma, Burkitt's lymphoma, and other EBV-associated lymphomas.

2. Indication(s) for use:

See above

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

The BioPlex 2200 EBV IgM kit is intended for use with the BioPlex 2200 System instrument and software.

I. Device Description:

The BioPlex 2200 EBV IgM kit is a multiplex flow immunoassay for the qualitative detection of two (2) separate analytes; Epstein-Barr Virus Viral Capsid Antigen (EBV VCA) IgM antibodies and Heterophile antibodies in human serum. See test principle below for more details.

J. Substantial Equivalence Information:

Predicate Device 1: Wampole Monolatex Agglutination test.

510k number: K862008

Component	Similarities	
	Device	Predicate
Intended Use	Aid in diagnosis of infectious mononucleosis	Aid in diagnosis of infectious mononucleosis
	Differences	
	Device	Predicate
Technology	Multiplexed flow immunoassay	Agglutination Assay
Intended Use	Qualitative detection	Qualitative or Semi-quantitative detection
Matrices	Serum	Serum or plasma

J. Substantial Equivalence Information:

Predicate Device 2: Diasorin EBV VCA IgM Capture EIA.

510k number: K946157

Component	Similarities	
	Device	Predicate
Intended Use	Aid in diagnosis of infectious mononucleosis	Aid in diagnosis of infectious mononucleosis
Matrices	Serum	Serum
	Differences	
	Device	Predicate
Technology	Multiplexed flow immunoassay	Traditional EIA
Intended Use	Qualitative detection	Qualitative or Semi-quantitative detection

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

STANDARDS
Title and Reference Number
Interference Testing in Clinical Chemistry; Approved Guideline (EP 7-A)
Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (EP5-A2)

Other Standards

GUIDANCE			
Document Title	**Office**	**Division**	**Web Page**
Review Criteria for In Vitro Diagnostic Devices for Detection of IGM Antibodies to Viral Agents	**OIVD**	**DIHD**	**http://www.fda.gov/cdrh/ode/527.pdf**
Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff	**CBER/ OIVD**		**http://www.fda.gov/cdrh/oivd/guidance/1588.html**

L. Test Principle:

The BioPlex 2200 EBV IgM kit uses multiplex flow immunoassay, a methodology that greatly resembles traditional EIA, but permits simultaneous detection and identification of many antibodies in a single tube. Two (2) different populations of dyed beads are coated with proteins associated with infectious mononucleosis. One (1) is coated with an *E. coli* derived recombinant fusion protein, EBV VCA p18 (40kD), and the other is coated with horse erythrocyte stromal extract (heterophile antigen). The BioPlex 2200 System combines an aliquot of patient sample, sample diluent containing goat anti-human IgG, and bead reagent into a reaction vessel. The mixture is incubated at 37°C. After a wash cycle, anti-human IgM 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 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 PE.

Three additional dyed beads, an Internal Standard Bead (ISB), a 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 respectively. The instrument is calibrated using a set of two (2) distinct calibrator vials, supplied separately by Bio-Rad Laboratories. A combination of two (2) vials representing two (2) different antibody concentrations is used for calibration. The result for each of these antibodies is expressed as an antibody index (AI).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Precision Studies:
   A precision panel, consisting of six (6) panel members was prepared by Bio-Rad Laboratories. Two (2) of the six (6) panel members had high levels of the antibodies contained in the BioPlex 2200 EBV IgG kit EBV IgM kit (EBV VCA IgM and Heterophile) and two (2) of the six (6) panel members had antibody levels near the cutoff, both prepared from positive patient samples. Two (2) of the six (6) panel members were negative (one high negative and one low negative) for both of the analytes. Precision testing was performed at Bio-Rad Laboratories on one lot of the EBV IgM kit, one lot of the EBV IgM Calibrator Set and one lot of the EBV IgM Control Set. Each of the six (6) panel members was tested in duplicate (x2) on two (2) runs per day for ten (10) days using one (1) lot of EBV IgM kit, one (1) lot of EBV IgM Calibrator Set and one (1) lot of EBV IgM Control Set (2 times x 2 runs x 10 days = 40 replicates per panel member). The data were analyzed for intra-assay and inter-assay precision according to the principles described in the Clinical Laboratory Standards Institute guidance EP5-A2, revised November 2004 and ISO/TR 22971:2205. The standard deviation (SD) and percent coefficient of variation (%CV) were calculated. Results can be found in Tables U and V.

Table U. Precision Results; BioPlex 2200 EBV VCA IgM

EBV VCA IgM Panel Members	Sample N*	AI Mean	Within-Run		Between-Day		Between-Run		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive 1	42	2.5	0.2	8.8%	0.1	2.4%	0.2	6.6%	0.3	11.2%
High Positive 2	43	2.7	0.2	5.6%	0.2	6.9%	0.1	1.8%	0.2	9.1%
Low Positive 1	42	1.6	0.1	6.5%	0.0	0.0%	0.1	4.3%	0.1	7.8%
Low Positive 2	42	1.9	0.1	4.4%	0.1	2.9%	0.1	4.8%	0.1	7.1%
High Negative	43	0.7	0.0	6.4%	0.0	0.0%	0.0	2.7%	0.0	7.0%
Low Negative	43	0.1	0.0	0.0%	0.0	0.0%	0.0	0.0%	0.0	0.0%

**Additional samples were run.*

Table V. Precision Results; BioPlex 2200 Heterophile

Heterophile Panel Members	Sample N*	AI Mean	Within-Run		Between-Day		Between-Run		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive 1	42	2.8	0.1	3.7%	0.2	8.6%	0.1	1.8%	0.3	9.5%
High Positive 2	43	2.8	0.1	4.7%	0.3	9.9%	0.1	5.3%	0.3	12.2%
Low Positive 1	42	2.1	0.1	3.9%	0.1	3.7%	0.2	9.0%	0.2	10.5%
Low Positive 2	42	1.9	0.1	3.9%	0.1	4.6%	0.1	7.5%	0.2	9.6%
High Negative	43	0.7	0.0	7.0%	0.0	4.6%	0.0	0.0%	0.1	8.4%
Low Negative	43	0.0	0.0	0.0%	0.0	0.0%	0.0	0.0%	0.0	0.0%

**Additional samples were run.*

Reproducibility Studies

A reproducibility panel, consisting of six (6) panel members was prepared by Bio-Rad Laboratories. Two (2) of the six (6) panel members had high levels of the antibodies contained in the BioPlex 2200 EBV IgM kit (EBV VCA IgM and Heterophile) and two (2) of the six (6) panel members had antibody levels near the cutoff, both prepared from positive patient samples. Two (2) of the six (6) panel members were negative (one high negative and one low negative) for both of the analytes. In addition, a positive control (antibody positive for both analytes) and a negative control (antibody negative for both analytes) were also tested. Reproducibility testing was performed at each of three (3) US testing facilities on a total of three (3) lots of the EBV IgM kit, three (3) lots of the EBV IgM Calibrator Set and three (3) lots of the EBV IgM Control Set. The panels were provided to each of the testing sites. Each of the six (6) panel members and positive and negative controls was tested in quadruple (x4) on each day for three (3) days at each of three (3) US testing facilities using one (1) lot of EBV IgM kit, one (1) lot of EBV IgM Calibrator Set and one (1) lot of EBV IgM Control Set (4 times x 3 days x 3 sites = 36 replicates per panel member and controls). The data were analyzed for intra-assay and inter-assay reproducibility according to the

principles described in the Clinical Laboratory Standards Institute guidance EP5-A2, revised November 2004 and ISO/TR 22971:2205. The standard deviation (SD) and percent coefficient of variation (%CV) were calculated. Positive results can be found in Tables S and T.

Table S. Reproducibility Results; BioPlex 2200 EBV VCA IgM

EBV VCA IgM Panel Members	Sample N	Grand Mean AI	Within-Run		Between-Day		Between-Run		Between-Site*		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive 1	36	1.9	0.1	5.9%	0.1	4.5%	0.1	3.8%	0.0	0.0%	0.2	8.4%
High Positive 2	36	2.0	0.1	3.5%	0.0	0.0%	0.1	5.8%	0.0	2.2%	0.1	7.1%
Low Positive 1	35**	1.2	0.1	4.4%	0.1	5.6%	0.0	1.4%	0.0	3.9%	0.1	8.3%
Low Positive 2	36	1.4	0.1	5.8%	0.1	4.8%	0.0	0.0%	0.0	2.4%	0.1	7.9%
Positive Control	36	2.0	0.1	5.5%	0.1	2.8%	0.1	3.0%	0.3	15.9%	0.3	17.2%

**Between site variance includes between lot variance.*
***1 replicate missing due to insufficient sample volume.*

Table T. Reproducibility Results; BioPlex 2200 Heterophile

Heterophile Panel Members	Sample N	Grand Mean AI	Within-Run		Between-Day		Between-Run		Between-Site*		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive 1	36	2.8	0.1	2.8%	0.0	0.0%	0.1	5.2%	0.1	5.1%	0.2	7.8%
High Positive 2	36	2.7	0.1	3.2%	0.0	0.0%	0.1	4.4%	0.0	0.7%	0.1	5.5%
Low Positive 1	35**	1.9	0.1	5.0%	0.0	0.0%	0.0	0.0%	0.0	2.3%	0.1	5.5%
Low Positive 2	36	1.8	0.1	4.7%	0.0	1.0%	0.0	0.0%	0.1	5.6%	0.1	7.4%
Positive Control	36	2.5	0.1	5.3%	0.1	2.6%	0.0	0.0%	0.0	0.0%	0.1	5.9%

**Between site variance includes between lot variance.*
***1 replicate missing due to insufficient sample volume.*

b. *Linearity/assay reportable range:*

Not Applicable.

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

Not Applicable.

d. *Detection limit:*

Not applicable.

e. *Analytical specificity:*
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 BioPlex 2200 EBV IgM kit. A panel of at least ten (10)

specimens* positive for each cross reactant were evaluated for possible cross reactivity with the BioPlex 2200 EBV IgM kit for both EBV IgM antibody assays. The test specimens were also evaluated on corresponding commercially available microplate EIA and latex agglutination tests. Due to the number of VCA IgM positive results obtained with the initial 10 Toxoplasmosis and CMV samples, an additional 33 Toxoplasmosis and 42 CMV positive samples were tested with the BioPlex 2200 EBV IgM kit. This study was performed to demonstrate that the BioPlex 2200 VCA IgM assay does not exhibit cross reactivity with Toxoplasmosis or CMV IgM samples. For these additional samples, only those that exhibited positive reactivity were tested on corresponding commercially available microplate EIA and latex agglutination tests. Most of the samples evaluated were high positive for each disease state. The majority of all samples that elicited a positive result were also confirmed positive by the corresponding commercially available test, indicating reactivity to EBV IgM antibodies rather than cross reactivity with a potentially interfering factor. Results can be found in Table W.
**Due to limited availability of samples, only four E. coli specimens were evaluated.*

Table W. Cross-Reactivity

Cross Reactives	N	Method	BioPlex 2200 EBV IgM	
			EBV VCA	Heterophile
ANA	10	BioPlex 2200	1	0
		Commercial Assay	1	0
		Discrepants	0	0
Rubella IgM	10	BioPlex 2200	0	0
		Commercial Assay	0	0
		Discrepants	0	0
HSV IgM	10	BioPlex 2200	0	0
		Commercial Assay	0	0
		Discrepants	0	0
E. Coli	4*	BioPlex 2200	0	0
		Commercial Assay	N/A	N/A
		Discrepants	N/A	N/A
Toxo IgM		BioPlex 2200 (N)	43	43
		BioPlex 2200 (+)	14	0
		Commercial Assay (N)	14†	10††
		Commercial Assay (+)	9	0
		Discrepants	5	0

Cross Reactives	N	Method	BioPlex 2200 EBV IgM	
			EBV VCA	Heterophile
Rheumatoid Factor	10	BioPlex 2200	0	0
		Commercial Assay	0	0
		Discrepants	0	0
VZV IgM	10	BioPlex 2200	0	0
		Commercial Assay	0	0
		Discrepants	0	0
HIV	10*	BioPlex 2200	0	0
		Commercial Assay	N/A	N/A
		Discrepants	N/A	N/A
Pregnant women	10	BioPlex 2200	0	0
		Commercial Assay	0	0
		Discrepants	0	0
CMV IgM		BioPlex 2200 (N)	52	52
		BioPlex 2200 (+)	25	1
		Commercial Assay (N)	25†	10††
		Commercial Assay (+)	22	0
		Discrepants	3	1

**Commercially available assay data was not obtained, due to low sample volume.*
†*Commercially available assay testing was performed on BioPlex 2200 positive samples only.*
††*Commercially available assay testing was performed on the initial ten samples evaluated.*

Interfering Substances:

Testing for interfering substances was conducted according to NCCLS Protocol EP7-A (Vol. 22, No. 27). No significant interference was observed in any of the substances tested. The following substances, listed in Table X, were tested (N=10) at maximum levels on one reagent lot.

Table X. Interfering Substances

Substance	Concentration
Hemoglobin	≤ 500 mg/dL
Bilirubin (unconjugated)	≤ 20 mg/dL
Bilirubin (conjugated)	≤ 20 mg/dL
Triglycerides	≤ 3000 mg/dL
Protein (total)	≤ 12 g/dL
Cholesterol	≤ 500 mg/dL
Red Blood Cells	≤ 0.4% Concentrate
Gamma-globulin	≤ 2.5 g/dL
Ascorbic Acid	≤ 3 mg/dL

f. Assay cut-off:

A final cut-off of 1 AI was established for all BioPlex 2200 EBV IgM kit assays based on an evaluation of 548 serum samples with the BioPlex 2200 EBV IgM kit assays and corresponding commercially available microplate EIA and latex agglutination tests. ROC analysis was performed for each BioPlex 2200 EBV IgM assay using this population of samples. Samples that were equivocal on the commercially available tests were excluded from the analysis. This analysis was used to optimize sensitivity and specificity for the BioPlex 2200 EBV IgM kit assays. A final cut-off of 1 AI was established for all BioPlex 2200 EBV IgM kit assays based on the data collected.

2. Comparison studies:

a. Method comparison with predicate device:

Performance of the EBV IgM kit was tested against corresponding commercially available microplate EIA/agglutination tests. A total of 621 banked serum samples from patients for which an EBV test was ordered were tested at 3 U.S. clinical testing sites. The EBV IgG kit was run in conjunction with the EBV IgM kit to allow for a complete antibody response profile. The characterization by antibody response was not compared with clinical data regarding presence, absence or status of disease. Two (2) samples were excluded due to RBB analysis error messages during BioPlex 2200 EBV IgM testing. One (1) sample was excluded due to RBB analysis error messages

during BioPlex 2200 EBV IgG testing. Using Table A as a guideline, results were analyzed by BioPlex 2200 EBV IgM analytes and corresponding EBV IgM reference assays according to serological characterization based on reference assay results. For the purpose of percent agreement calculations, BioPlex 2200 EBV IgM equivocal results were assigned to the opposite clinical interpretation than that of the corresponding reference assay result. Results from all sites are shown and summarized in Tables F - I.

Table F. BioPlex 2200 EBV VCA IgM vs. EIA: Comparison by Serological Pattern Characterization

EBV Serological Status	Reference EBV VCA IgM Interpretation						Total
	Positive			Negative			
	BioPlex 2200 EBV VCA IgM			BioPlex 2200 EBV VCA IgM			
	Pos	Eqv	Neg	Pos	Eqv	Neg	
	N	N	N	N	N	N	N
Primary Acute	30	1	0	0	0	0	31
Late Acute	31	1	16	1	4	57	110
Recovering	0	0	0	1	0	3	4
Previous Infection	0	0	0	6	6	293	305
Susceptible	0	0	0	4	0	123	127
Inconclusive	4	0	0	6	0	31	41
Overall	65	2	16	18	10	507	618

Table G. BioPlex 2200 EBV VCA IgM vs. EIA: Percent Agreement & Confidence Intervals by Serological Pattern Characterization

EBV Serological Status	Positive Agreement		95% CI	Negative Agreement		95% CI
Primary Acute	(30/31)	96.8%	83.8 - 99.4%	(0/0)	N/A*	N/A*
Late Acute	(31/48)	64.6%	50.4 - 76.6%	(57/62)	91.9%	82.5 - 96.5%
Recovering	(0/0)	N/A*	N/A*	(3/4)	75.0%	30.1 - 95.4%
Previous Infection	(0/0)	N/A*	N/A*	(293/305)	96.1%	93.2 - 97.7%
Susceptible	(0/0)	N/A*	N/A*	(123/127)	96.9%	92.2 - 98.8%
Inconclusive	(4/4)	100%	51.0-100%	(31/37)	83.8%	68.9 - 92.3%
Overall	(65/83)	78.3%	68.3 - 85.8%	(507/535)	94.8%	92.5 - 96.4%

**In cases where agreement resulted in (0/0) samples, percent agreement and 95% confidence interval could not be calculated.*

Table H. BioPlex 2200 Heterophile vs. Agglutination Test: Comparison by Serological Pattern Characterization

EBV Serological Status	Reference Heterophile Interpretation						Total
	Positive			Negative			
	BioPlex 2200 Heterophile			BioPlex 2200 Heterophile			
	Pos	Eqv	Neg	Pos	Eqv	Neg	
	N	N	N	N	N	N	N
Primary Acute	16	1	2	2	0	10	31
Late Acute	3	0	1	1	1	104	110
Recovering	0	0	0	0	0	4	4
Previous Infection	0	0	0	0	3	302	305
Susceptible	0	0	0	0	0	127	127
Inconclusive	4	0	23	0	0	14	41
Overall	23	1	26	3	4	561	618

Table I. BioPlex 2200 Heterophile vs. Agglutination Test: Percent Agreement & Confidence Intervals by Serological Pattern Characterization

EBV Serological Status	Positive Agreement		95% CI	Negative Agreement		95% CI
Primary Acute	(16/19)	84.2%	62.4 - 94.5%	(10/12)	83.3%	55.2 - 95.3%
Late Acute	(3/4)	75.0%	30.1 - 95.4%	(104/106)	98.1%	93.4 - 99.5%
Recovering	(0/0)	N/A*	N/A*	(4/4)	100%	51.0 - 100%
Previous Infection	(0/0)	N/A*	N/A*	(302/305)	99.0%	97.1 - 99.7%
Susceptible	(0/0)	N/A*	N/A*	(127/127)	100%	97.1 - 100%
Inconclusive	(4/27)	14.8%	5.9 - 32.5%	(14/14)	100%	78.5 - 100%
Overall	(23/50)	46.0%	33.0 - 59.6%	(561/568)	98.8%	97.5 - 99.4%

**In cases where agreement resulted in (0/0) samples, percent agreement and 95% confidence interval could not be calculated.*

Comparison of EBV Serological Status

Using Table A as a guideline, samples characterized into serological status associated with EBV disease, using the commercially available microplate EIA and agglutination tests, were compared with characterizations using BioPlex 2200 EBV IgG and IgM kits. The BioPlex 2200 EBV IgM kit was run in conjunction with the BioPlex 2200 EBV IgG kit to allow for a complete antibody response profile. The characterization by antibody response was not compared with clinical data regarding presence, absence or status of disease. Results from 618 serum samples tested at 3 U.S. clinical testing sites are shown in Table N.

Table N. Comparison of EBV Serological Status

EBV Serological status		BioPlex 2200 EBV IgG & IgM Profile								
		Primary Acute	Late Acute	Recovering	Previous Infection	Susceptible	Inconclusive	Total	% Serological Agreement	95% Confidence Interval
Commercially Available Assays	Primary Acute	30	0	0	0	0	1	31	96.8%	83.8 - 99.4%
	Late Acute	5	90	1	13	0	1	110	81.8%	73.6 - 87.9%
	Recovering	1	0	3	0	0	0	4	75.0%	30.0 - 95.4%
	Previous Infection	0	31	2	263	4	5	305	86.2%	81.9 - 89.7%
	Susceptible	4	0	0	0	122	1	127	96.1%	91.1 - 98.3%
	Inconclusive	6	10	0	7	11	7	41	17.1%	8.5 - 31.3%
	Overall	46	131	6	283	137	15	618	83.3%	80.2 - 86.1%

Note: Calculations are performed for unshaded areas only.

b. Matrix comparison:

Not Applicable.

3. Clinical studies:

Not Applicable

4. Clinical cut-off**:**

Not Applicable

5. Expected values/Reference range:
Expected values for the EBV IgM kit are presented by age and gender in the following tables for serum samples from unselected hospitalized pediatric and adult patients (N=302) and patients for which an EBV test was ordered (N=619). A total of 303 serum samples from unselected hospitalized pediatric and adult patients and a total of 621 serum samples from patients for which an EBV test was ordered were tested. One (1) sample from the unselected hospitalized population, and two (2) samples from the patients for which an EBV test was ordered population were excluded due to RBB analysis error messages during BioPlex 2200 EBV IgM testing. For all analytes, results of ≤0.8 AI are negative, 0.9 and 1.0 AI are equivocal, and ≥1.1 AI are reported as positive.

Table B. Hospitalized Patient Samples: EBV VCA IgM

Age	Gender	BioPlex 2200 EBV VCA IgM						Total
		Positive		Equivocal		Negative		
		N	%	N	%	N	%	N
< 5 years of age	F	3	11%	0	0%	24	89%	27
	M	1	5%	0	0%	19	95%	20
5-12 years of age	F	2	9%	0	0%	20	91%	22
	M	1	3%	1	3%	32	94%	34
13-20 years of age	F	5	14%	1	3%	29	83%	35
	M	0	0%	1	7%	14	93%	15
21-30 years of age	F	0	0%	0	0%	6	100%	6
	M	0	0%	0	0%	2	100%	2
31-40 years of age	F	0	0%	0	0%	10	100%	10
	M	0	0%	0	0%	11	100%	11
41-50 years of age	F	1	8%	0	0%	12	92%	13
	M	1	14%	0	0%	6	86%	7
51-60 years of age	F	0	0%	0	0%	23	100%	23
	M	0	0%	1	5%	18	95%	19
61-70 years of age	F	0	0%	0	0%	11	100%	11
	M	0	0%	0	0%	11	100%	11
71-80 years of age	F	1	9%	0	0%	10	91%	11
	M	0	0%	0	0%	6	100%	6
81-90 years of age	F	0	0%	0	0%	11	100%	11
	M	0	0%	0	0%	6	100%	6
91-100 years of age	F	0	0%	0	0%	0	0%	0
	M	0	0%	0	0%	2	100%	2
Total		15	5%	4	1%	283	94%	302

Table C. Hospitalized Patient Samples: Heterophile

Age	Gender	BioPlex 2200 Heterophile						Total
		Positive		Equivocal		Negative		
		N	%	N	%	N	%	N
< 5 years of age	F	1	4%	0	0%	26	96%	27
	M	0	0%	0	0%	20	100%	20
5-12 years of age	F	0	0%	0	0%	22	100%	22
	M	1	3%	0	0%	33	97%	34
13-20 years of age	F	0	0%	0	0%	35	100%	35
	M	0	0%	0	0%	15	100%	15
21-30 years of age	F	0	0%	0	0%	6	100%	6
	M	0	0%	0	0%	2	100%	2
31-40 years of age	F	0	0%	0	0%	10	100%	10
	M	0	0%	0	0%	11	100%	11
41-50 years of age	F	0	0%	0	0%	13	100%	13
	M	0	0%	0	0%	7	100%	7
51-60 years of age	F	0	0%	0	0%	23	100%	23
	M	0	0%	0	0%	19	100%	19
61-70 years of age	F	0	0%	0	0%	11	100%	11
	M	0	0%	0	0%	11	100%	11
71-80 years of age	F	0	0%	0	0%	11	100%	11
	M	0	0%	0	0%	6	100%	6
81-90 years of age	F	0	0%	0	0%	11	100%	11
	M	0	0%	0	0%	6	100%	6
91-100 years of age	F	0	0%	0	0%	0	0%	0
	M	0	0%	0	0%	2	100%	2
Total		2	1%	0	0%	300	99%	302

Table D. Samples from Patients for which an EBV Test was Ordered: EBV VCA IgM

Age	Gender	BioPlex 2200 EBV VCA IgM						Total
		Positive		Equivocal		Negative		
		N	%	N	%	N	%	N
< 5 years of age	F	3	10%	0	0%	27	90%	30
	M	6	18%	0	0%	27	82%	33
5-12 years of age	F	9	15%	1	2%	52	84%	62
	M	6	10%	1	2%	55	89%	62
13-20 years of age	F	17	22%	2	3%	59	76%	78
	M	10	26%	1	3%	27	71%	38
21-30 years of age	F	5	11%	1	2%	40	87%	46
	M	7	21%	1	3%	25	76%	33
31-40 years of age	F	5	10%	1	2%	46	88%	52
	M	1	4%	0	0%	23	96%	24
41-50 years of age	F	3	9%	1	3%	30	88%	34
	M	4	13%	1	3%	26	84%	31
51-60 years of age	F	4	15%	1	4%	22	81%	27
	M	2	8%	1	4%	23	88%	26
61-70 years of age	F	1	8%	0	0%	12	92%	13
	M	0	0%	0	0%	21	100%	21
71-80 years of age	F	0	0%	0	0%	2	100%	2
	M	0	0%	0	0%	3	100%	3
81-90 years of age	F	0	0%	0	0%	2	100%	2
	M	0	0%	0	0%	2	100%	2
91-100 years of age	F	0	0%	0	0%	0	0%	0
	M	0	0%	0	0%	0	0%	0
Total		83	13%	12	2%	524	85%	619

Table E. Samples from Patients for which an EBV Test was Ordered: Heterophile

Age	Gender	BioPlex 2200 Heterophile						Total
		Positive		Equivocal		Negative		
		N	%	N	%	N	%	N
< 5 years of age	F	0	0%	0	0%	30	100%	30
	M	0	0%	0	0%	33	100%	33
5-12 years of age	F	3	5%	0	0%	59	95%	62
	M	3	5%	0	0%	59	95%	62
13-20 years of age	F	8	10%	1	1%	69	88%	78
	M	7	18%	1	3%	30	79%	38
21-30 years of age	F	0	0%	2	4%	44	96%	46
	M	4	12%	0	0%	29	88%	33
31-40 years of age	F	0	0%	0	0%	52	100%	52
	M	1	4%	1	4%	22	92%	24
41-50 years of age	F	0	0%	0	0%	34	100%	34
	M	0	0%	0	0%	31	100%	31
51-60 years of age	F	0	0%	0	0%	27	100%	27
	M	0	0%	0	0%	26	100%	26
61-70 years of age	F	0	0%	0	0%	13	100%	13
	M	0	0%	0	0%	21	100%	21
71-80 years of age	F	0	0%	0	0%	2	100%	2
	M	0	0%	0	0%	3	100%	3
81-90 years of age	F	0	0%	0	0%	2	100%	2
	M	0	0%	0	0%	2	100%	2
91-100 years of age	F	0	0%	0	0%	0	0%	0
	M	0	0%	0	0%	0	0%	0
Total		26	4%	5	1%	588	95%	619

The distribution of BioPlex 2200 EBV VCA IgM and Heterophile AI values for serum samples from adult and pediatric unselected hospitalized patients and from patients for which an EBV test was ordered are presented in the following histograms.

Figure 1. Hospitalized Patient Samples: EBV VCA IgM

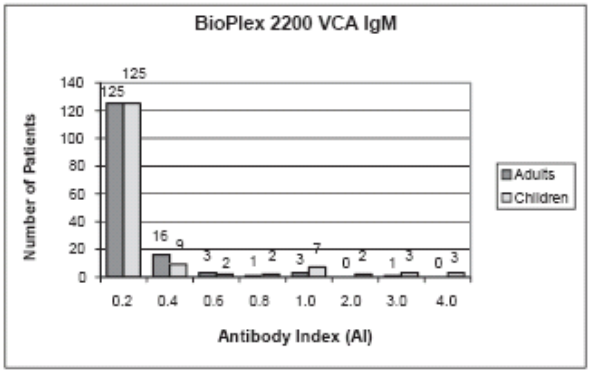


Figure 2. Hospitalized Patient Samples: Heterophile

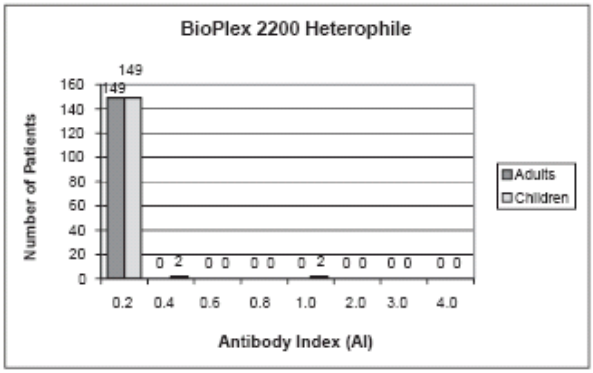


Figure 3. Samples from Patients for which an EBV Test was Ordered: EBV VCA IgM

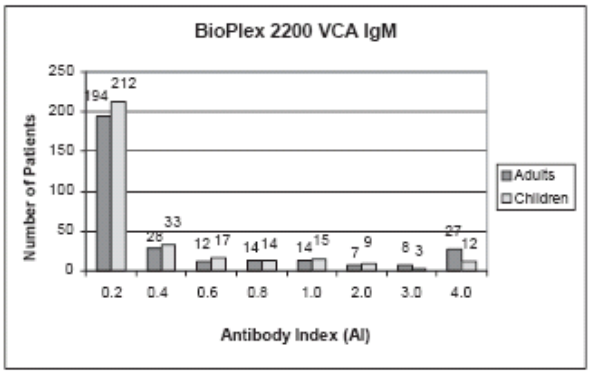
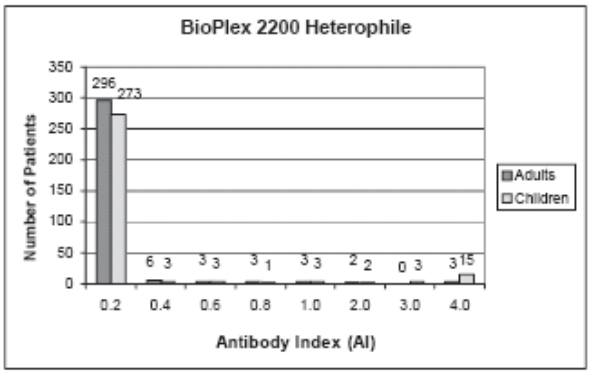


Figure 4. Samples from Patients for which an EBV Test was Ordered: Heterophile



N. Proposed Labeling:

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

O. Conclusion:

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