MAY - 8 2009

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BIOPLEX 2200 HSV-1 AND HSV-2 IgG 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
k090409	May 1, 2009

MANUFACTURER INFORMATION

Manufacturer	
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CLASSIFICATION INFORMATION

Classification Name	Enzyme Linked Immunosorbent Assay, Herpes Simplex Virus, HSV-1
Common Name:	Multi-Analyte Detection System HSV-1 and HSV-2 IgG
Product Trade Name	BioPlex 2200 HSV-1 and HSV-2 IgG on the BioPlex 2200 Multi-Analyte Detection System
Device Class	Class II
Classification Panel	Microbiology
Regulation Number	866.3305
Product Code	MXJ

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Classification Name	Enzyme Linked Immunosorbent Assay, Herpes Simplex Virus, HSV-2
Common Name:	Multi-Analyte Detection System HSV-1 and HSV-2 IgG
Product Trade Name	BioPlex 2200 HSV-1 and HSV-2 IgG on the BioPlex 2200 Multi-Analyte Detection System
Device Class	Class II
Classification Panel	Microbiology
Regulation Number	866.3305
Product Code	MYF

LEGALLY MARKETED EQUIVALENT (SE) DEVICES

Comparative FDA Cleared PREDICATE DEVICE	510(k) Number	Decision Date
Focus HerpesSelect 1 ELISA IgG	k021429	7/29/2002
Focus HerpesSelect 2 ELISA IgG	k021486	8/1/2002
Focus HerpesSelect 1 and 2 Immunoblot IgG	k000238	4/14/2000

DEVICE DESCRIPTION

The BioPlex 2200 HSV-1 & HSV-2 IgG 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 different populations of dyed beads are each coated with antigens associated with herpes simplex virus, types 1 and 2. The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead set reagent into a reaction vessel. The mixture is incubated at 37°C. After a wash cycle, 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 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. Raw data is calculated in relative fluorescence intensity (RFI).

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 to the reaction vessel and the absence of significant non-specific binding in serum. Refer to the BioPlex 2200 System Operation Manual for more information.

The instrument is calibrated using a set of 4 distinct calibrator vials, supplied separately by Bio-Rad Laboratories.

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KIT COMPONENTS

BioPlex 2200 HSV-1 & HSV-2 IgG Reagent Pack (665-3350). The reagent pack contains supplies sufficient for 100 tests.

Vial	Description
Bead Set	One (1) 10 mL vial, containing dyed beads coated with HSV-1 and HSV-2 IgG antigens, an Internal Standard bead (ISB), a Serum Verification bead (SVB), and a Reagent Blank bead (RBB) in buffer with Glycerol and protein stabilizers (bovine). ProClin™ 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
Conjugate	One (1) 5 mL vial, containing phycoerythrin conjugated murine monoclonal anti-human IgG antibody and phycoerythrin conjugated murine monoclonal anti-human FXIII antibody*, in buffer with protein stabilizers (bovine). ProClin™ 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives. **The phycoerythrin conjugated anti-human FXIII antibody is used to verify the presence of serum or plasma in the reaction vessel.*
Sample Diluent	One (1) 10 mL vial, containing buffer with protein stabilizers (bovine and murine). ProClin™ 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.

ADDITIONAL REQUIRED ITEMS, AVAILABLE FROM BIO-RAD

Catalog #	Description
663-3300	BioPlex 2200 HSV-1 & HSV-2 IgG Calibrator Set: Four (4) 0.5 mL vials, each containing human antibodies to HSV-1 and HSV-2 IgG derived from human disease state plasma, in a human serum matrix made from defibrinated plasma. All calibrators contain ProClin™ 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
663-3330	BioPlex 2200 HSV-1 & HSV-2 IgG Control Set: Two (2) 1.5 mL Positive Control serum vials, each containing human antibodies to HSV-1 and HSV-2 IgG derived from human disease state plasma, in a human serum matrix made from defibrinated plasma, and two (2) 1.5 mL Negative Control serum vials, in a human serum matrix made from defibrinated plasma. All controls contain ProClin™ 300 (0.3%), sodium benzoate (0.1%) and sodium azide (<0.1%) as preservatives.
660-0817	BioPlex 2200 System Sheath Fluid: Two (2) 4 L bottles containing Phosphate Buffered Saline (PBS). ProClin® 300 (0.3%) and Sodium azide (0.1%) as preservatives.
660-0818	BioPlex 2200 System Wash Solution: One (1) 10 L bottle containing Phosphate Buffered Saline (PBS) and Tween 20. ProClin® 300 (0.3%) and Sodium azide (0.1%) as preservatives.
660-0000	BioPlex 2200 Instrument and Software.

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INTENDED USE / INDICATIONS FOR USE

The BioPlex™ 2200 HSV-1 & HSV-2 IgG kit is a multiplex flow immunoassay intended for the qualitative detection and differentiation of IgG antibodies to herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) in human serum and EDTA or heparinized plasma. The test is indicated for sexually active individuals and expectant mothers as an aid for the presumptive diagnosis of HSV-1 or HSV-2 infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1 and HSV-2.

The test is not FDA cleared for screening blood or plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates and immunocompromised patients or for use at point of care facilities.

The BioPlex 2200 HSV-1 & HSV-2 IgG kit is intended for use with the Bio-Rad BioPlex 2200 System.

TECHNOLOGICAL CHARACTERISTICS

The following tables summarize similarities and differences between the BioPlex 2200 HSV-1 and HSV-2 IgG Kit and the predicate device used in comparative studies with the BioPlex 2200 HSV-1 and HSV-2 IgG Kit.

BioPlex 2200 HSV-1 and HSV-2 IgG Assay vs. Predicate HSV 1 and 2 Immunoblot IgG

Table 1: Similarities between reagents and materials

Similarities between Components / Materials	**BioPlex 2200 HSV-1 and HSV-2 IgG Kit**	**Predicate HSV 1 and 2 Immunoblot IgG**
Reagents	Wash Solution, Sample Diluent.	Wash Buffer, Diluent.
Controls	Negative Control and multi-analyte Positive Control.	Negative Control and Positive/Cutoff Control.

Table 2: Similarities between reagents with regard to function and use

Similarities between Function and Use	**BioPlex 2200 HSV-1 and HSV-2 IgG Kit**	**Focus HerpesSelect 1 and 2 Immunoblot IgG**
Analyte Detection	Qualitative detection of IgG antibodies to HSV-1 and HSV-2.	Qualitative detection of IgG antibodies to HSV-1 and HSV-2.

Table 3: Differences between reagents and materials

Differences between Components / Materials	**BioPlex 2200 HSV-1 and HSV-2 IgG Kit**	**Focus HerpesSelect 1 and 2 Immunoblot IgG**
Solid Phase	Bead reagent - dyed antigen coated beads.	Treated nitrocellulose membrane strips containing antigen bands.
Reagents	Conjugate: Anti-human IgG / Phycoerythrin.	Conjugate: goat anti-human IgG / alkaline phosphatase, Blotting Powder, Substrate.
Sheath Fluid	Sheath Fluid is used to suspend the bead reagent and introduce it into the detector.	Not similar; not utilized in blot assays.
Calibrator(s)	Calibrators.	None.

Table 4: Differences between reagents with regard to function and use

Differences between Function and Use	BioPlex 2200 HSV-1 and HSV-2 IgG Kit	Focus HerpesSelect 1 and 2 Immunoblot IgG
Technique	Flow immunoassay.	Immunoblot.
Matrices	Serum and plasma.	Serum.

PERFORMANCE SUMMARY

A. Expected Values

Prevalence
The observed prevalence and expected values for the BioPlex 2200 HSV-1 & HSV-2 IgG kit are presented by age and gender for serum samples from sexually active individuals where an HSV-1 test was ordered (N=289); sexually active individuals where an HSV-2 test was ordered (N=286); and for expectant mothers (N=399). Results are shown in Tables 5 - 11.

Table 5: Sexually Active Individuals With an HSV-1 Test Ordered: BioPlex 2200 HSV-1 IgG (N = 289)

Age in Years	Gender	BioPlex 2200 HSV-1 IgG						Total
		Positive		Equivocal		Negative		
		N	%	N	%	N	%	N
18-20	F	6	85.7%	0	0.0%	1	14.3%	7
	M	8	66.7%	0	0.0%	4	33.3%	12
21-30	F	15	62.5%	0	0.0%	9	37.5%	24
	M	21	58.3%	0	0.0%	15	41.7%	36
31-40	F	19	86.4%	1	4.5%	2	9.1%	22
	M	23	71.9%	1	3.1%	8	25.0%	32
41-50	F	17	81.0%	0	0.0%	4	19.0%	21
	M	38	74.5%	1	2.0%	12	23.5%	51
51-60	F	8	61.5%	0	0.0%	5	38.5%	13
	M	23	74.2%	2	6.5%	6	19.4%	31
61-70	F	11	68.8%	0	0.0%	5	31.3%	16
	M	15	75.0%	0	0.0%	5	25.0%	20
71-80	F	1	50.0%	0	0.0%	1	50.0%	2
	M	2	100%	0	0.0%	0	0.0%	2
81-89	F	0	0.0%	0	0.0%	0	0.0%	0
	M	0	0.0%	0	0.0%	0	0.0%	0
Total		207	71.6%	5	1.7%	77	26.6%	289

Note: Due to rounding numbers across columns may not total 100%.

Table 6:Sexually Active Individuals With an HSV-2 Test Ordered: BioPlex 2200 HSV-2 IgG (N = 286)

Age in Years	Gender	BioPlex 2200 HSV-2 IgG						Total
		Positive		Equivocal		Negative		
		N	%	N	%	N	%	N
18-20	F	2	50.0%	0	0.0%	2	50.0%	4
	M	2	22.2%	0	0.0%	7	77.8%	9
21-30	F	10	38.5%	0	0.0%	16	61.5%	26
	M	15	36.6%	0	0.0%	26	63.4%	41
31-40	F	9	69.2%	0	0.0%	4	30.8%	13
	M	16	32.0%	1	2.0%	33	66.0%	50
41-50	F	9	52.9%	0	0.0%	8	47.1%	17
	M	21	40.4%	0	0.0%	31	59.6%	52
51-60	F	7	46.7%	0	0.0%	8	53.3%	15
	M	10	37.0%	0	0.0%	17	63.0%	27
61-70	F	4	50.0%	0	0.0%	4	50.0%	8
	M	4	20.0%	0	0.0%	16	80.0%	20
71-80	F	0	0.0%	0	0.0%	0	0.0%	0
	M	0	0.0%	0	0.0%	3	100%	3
81-89	F	0	0.0%	0	0.0%	1	100%	1
	M	0	0.0%	0	0.0%	0	0.0%	0
Total		109	38.1%	1	0.4%	176	61.5%	286

Table 7: Sexually Active Individuals With an HSV-1 Test Ordered: BioPlex 2200 HSV-1 IgG and HSV-2 IgG Dual Positive (N = 289)

Age in Years	Gender	BioPlex 2200 HSV-1 & HSV-2 IgG Dual Positive		Total
		N	%	N
18-20	F	3	42.9%	7
	M	3	25.0%	12
21-30	F	10	41.7%	24
	M	10	27.8%	36
31-40	F	14	63.6%	22
	M	12	37.5%	32
41-50	F	10	47.6%	21
	M	9	17.6%	51
51-60	F	3	23.1%	13
	M	8	25.8%	31
61-70	F	3	18.8%	16
	M	5	25.0%	20
71-80	F	1	50.0%	2
	M	0	0.0%	2
81-89	F	0	0.0%	1
	M	0	0.0%	0
Total		91	31.5%	289

Table 8. Sexually Active Individuals With an HSV-2 Test Ordered: BioPlex 2200 HSV-1 IgG and HSV-2 IgG Dual Positive (N = 286)

Age in Years	Gender	BioPlex 2200 HSV-1 & HSV-2 IgG Dual Positive		Total
		N	%	N
18-20	F	1	25.0%	4
	M	1	11.1%	9
21-30	F	7	26.9%	26
	M	9	22.0%	41
31-40	F	4	30.8%	13
	M	10	20.0%	50
41-50	F	6	35.3%	17
	M	13	25.0%	52
51-60	F	4	26.7%	15
	M	7	25.9%	27
61-70	F	4	50.0%	8
	M	4	20.0%	20
71-80	F	0	0.0%	0
	M	0	0.0%	3
81-89	F	0	0.0%	1
	M	0	0.0%	0
Total		70	24.5%	286

Table 9: Expectant Mothers: BioPlex 2200 HSV-1 IgG (N = 399)

Age in Years	BioPlex 2200 HSV-1 IgG						Total
	Positive		Equivocal		Negative		
	N	%	N	%	N	%	N
14-20	35	58.3%	0	0.0%	25	41.7%	60
21-30	133	70.7%	2	1.1%	53	28.2%	188
31-40	98	76.0%	0	0.0%	31	24.0%	129
41-50	21	100%	0	0.0%	0	0.0%	21
Unknown	1	100%	0	0.0%	0	0.0%	1
Total	288	72.2%	2	0.5%	109	27.3%	399

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Table 10: Expectant Mothers: BioPlex 2200 HSV-2 IgG (N = 399)

Age in Years	BioPlex 2200 HSV-2 IgG						Total
	Positive		Equivocal		Negative		
	N	%	N	%	N	%	N
14-20	12	20.0%	0	0.0%	48	80.0%	60
21-30	66	35.1%	0	0.0%	122	64.9%	188
31-40	68	52.7%	0	0.0%	61	47.3%	129
41-50	11	52.4%	0	0.0%	10	47.6%	21
Unknown	0	0.0%	0	0.0%	1	100%	1
Total	157	39.3%	0	0.0%	242	60.7%	399

Table 11: Expectant Mothers: BioPlex 2200 HSV-1 IgG & HSV-2 IgG Dual Positive (N = 399)

Age in Years	BioPlex 2200 HSV-1 & HSV-2 IgG Dual Positive		Total
	N	%	N
14-20	9	15.0%	60
21-30	46	24.5%	188
31-40	56	43.4%	129
41-50	11	52.4%	21
Unknown	0	0.0%	1
Total	122	30.6%	399

Prevalence of HSV-1 or HSV-2 infection may vary by geographical area, age, or gender. The predictive value of the assay is dependent on the prevalence of HSV infection. Tables 12 - 14 present the observed prevalence and predictive values as well as hypothetical predictive values for decreasing prevalence rates. The hypothetical HSV-1 predictive values presented are based on BioPlex 2200 HSV-1 IgG 97.6% sensitivity and 90.1% specificity in sexually active individuals with an HSV-1 test ordered and 96.3% sensitivity and 99.0% specificity in expectant mothers. The hypothetical HSV-2 predictive values presented are based on BioPlex 2200 HSV-2 IgG sensitivity of 90.6% and specificity 98.2 % in sexually active adults with an HSV-2 test ordered and a 96.9% sensitivity and 100% specificity in expectant mothers.

Table 12: Summary of Observed Prevalence, Positive Predictive Value (PPV), Negative Predictive Value (NPV)

Population	N	BioPlex 2200 HSV-1 IgG			BioPlex 2200 HSV-2 IgG		
		Prevalence	PPV	NPV	Prevalence	PPV	NPV
Sexually Active Individuals with an HSV-1 Test ordered	289	71.6%	96.2%	93.6%	N/A	N/A	N/A
Sexually Active Individuals with an HSV-2 Test ordered	286	N/A	N/A	N/A	38.1%	97.3%	93.8%
Expectant Mothers	399	72.2%	99.7%	90.1%	39.3%	100%	97.9%

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Table 13: HSV-1 Hypothetical Predictive Values by Prevalence

Prevalence	Sexually Active Individuals		Expectant Mothers	
	PPV	NPV	PPV	NPV
80%	97.5%	90.4%	99.7%	87.0%
70%	95.8%	94.1%	99.6%	92.0%
60%	93.7%	96.2%	99.3%	94.7%
50%	90.8%	97.4%	99.0%	96.4%
40%	86.8%	98.3%	98.5%	97.6%
30%	80.9%	98.9%	97.6%	98.4%
25%	76.7%	99.1%	97.0%	98.6%
20%	71.1%	99.3%	96.0%	99.1%
15%	63.5%	99.5%	94.4%	99.3%
10%	52.3%	99.7%	91.5%	99.6%
5%	34.2%	99.9%	83.5%	99.8%

Table 14: HSV-2 Hypothetical Predictive Values by Prevalence

Prevalence	Sexually Active Individuals		Expectant Mothers	
	PPV	NPV	PPV	NPV
80%	99.5%	72.3%	100%	89.0%
70%	99.2%	81.7%	100%	93.3%
60%	98.7%	87.4%	100%	95.6%
50%	98.1%	91.3%	100%	97.0%
40%	97.1%	94.0%	100%	98.0%
30%	95.6%	96.1%	100%	98.7%
25%	94.4%	96.9%	100%	99.0%
20%	92.6%	97.7%	100%	99.2%
15%	89.9%	98.3%	100%	99.5%
10%	84.8%	98.9%	100%	99.7%
5%	72.6%	99.5%	100%	99.8%

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B. Comparative Testing

Table 15 summarizes the performance of the BioPlex 2200 HSV-1 and HSV-2 IgG kit observed during comparative testing. Refer to Tables 16 - 23 for detailed performance testing summaries.

Table 15: Summary Performance of the BioPlex 2200 HSV-1 and HSV-2 IgG Assay

Population	BioPlex 2200 HSV-1 IgG				BioPlex 2200 HSV-2 IgG			
	% Sensitivity	95% Confidence Interval	% Specificity	95% Confidence Interval	% Sensitivity	95% Confidence Interval	% Specificity	95% Confidence Interval
Sexually Active Individuals With an HSV-1 Test Ordered (N = 289)	97.6% (202/207)	94.5 - 99.0%	90.1% (73/81)	81.7 - 94.9%	N/A	N/A	N/A	N/A
Sexually Active Individuals With an HSV-2 Test Ordered (N = 286)	N/A	N/A	N/A	N/A	90.6% (106/117)	83.9 - 94.7%	98.2% (166/169)	94.9 - 99.4%
Expectant Mothers (N = 399)	96.3% (287/298)	93.5 - 97.9%	99.0% (100/101)	94.6 - 99.8%	96.9% (157/162)	93.0 - 98.7%	100% (237/237)	98.4 - 100%
CDC Panel (N = 100)	100%* (50/50)	92.8 - 100%	96.0%** (48/50)	86.5 - 98.9%	100%* (50/50)	92.8 - 100%	100%** (50/50)	92.8 - 100%
Low Prevalence [16-19 years] (N = 200)	93.3% (97/104)	86.7 - 96.7%	97.9% (94/96)	92.7 - 99.4%	N/A	N/A	97.8% (181/185)	94.6 - 99.2%

** % Positive Agreement*
*** % Negative Agreement*
N/A = Not applicable

Performance of the BioPlex 2200 HSV-1 & HSV-2 IgG kit in the intended use populations was tested against a commercially available immunoblot test in a prospective study conducted at a total of 3 U.S. clinical sites. For purposes of sensitivity and specificity calculations, the BioPlex 2200 equivocal results were assigned to the opposite clinical interpretation than that of the corresponding immunoblot result. Likewise, immunoblot equivocal results were assigned to the opposite clinical interpretation than that of the BioPlex 2200 result.

Performance in Sexually Active Individuals

The sensitivity and specificity of the HSV-1 & HSV-2 IgG kit was assessed using remnant serum samples from sexually active individuals where an HSV-1 test was ordered (N=289) and sexually active individuals where an HSV-2 test was ordered (N=286). Samples were tested at 3 U.S. clinical sites. Combined results from all sites are shown in Tables 16 & 17.

Table 16: Sexually Active Individuals With an HSV-1 Test Ordered: BioPlex 2200 HSV-1 IgG vs.Immunoblot (N = 289)

		BioPlex 2200 HSV-1 IgG							
		Positive	Equivocal	Negative	Total	% Sensitivity	95% Confidence Interval	% Specificity	95% Confidence Interval
Commercially Available HSV-1 IgG Immunoblot	Positive	202	1	1	204	97.6% (202/207)	(94.5 - 99.0%)	90.1% (73/81)	(81.7 - 94.9%)
	Equivocal	1	1	3	5				
	Negative	4	3	73	80				
	Total	207	5	77	289				

Table 17: Sexually Active Individuals With an HSV-2 Test Ordered: BioPlex 2200 HSV-2 IgG vs. Immunoblot (N = 286)

		BioPlex 2200 HSV-2 IgG							
		Positive	Equivocal	Negative	Total	% Sensitivity	95% Confidence Interval	% Specificity	95% Confidence Interval
Commercially Available HSV-2 IgG Immunoblot	Positive	106	1	10	117	90.6% (106/117)	(83.9 - 94.7%)	98.2% (166/169)	(94.9 - 99.4%)
	Equivocal	0	0	0	0				
	Negative	3	0	166	169				
	Total	109	1	176	286				

Performance in Expectant Mothers

The sensitivity and specificity of the HSV-1 & HSV-2 IgG kit was assessed using remnant serum samples from expectant mothers (N=399). Results are shown in Tables 18 & 19.

Table 18: Expectant Mothers: BioPlex HSV-1 IgG vs. Immunoblot (N = 399)

		BioPlex 2200 HSV-1 IgG							
		Positive	Equivocal	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval
Commercially Available HSV-1 IgG Immunoblot	Positive	287	2	8	297	96.3% (287/298)	(93.5 - 97.9%)	99.0% (100/101)	(94.6 - 99.8%)
	Equivocal	0	0	1	1				
	Negative	1	0	100	101				
	Total	288	2	109	399				

Table 19: Expectant Mothers: BioPlex HSV-2 IgG vs. Immunoblot (N = 399)

		BioPlex 2200 HSV-2 IgG							
		Positive	Equivocal	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval
Commercially Available HSV-2 IgG Immunoblot	Positive	157	0	4	161	96.9% (157/162)	(93.0 - 98.7%)	100% (237/237)	(98.4 - 100%)
	Equivocal	0	0	1	1				
	Negative	0	0	237	237				
	Total	157	0	242	399				

Agreement with CDC Panel

The performance of the BioPlex 2200 HSV-1 & HSV-2 IgG kit was assessed using a masked, well characterized HSV serum panel from the CDC. The panel consists of 24% HSV-1 and HSV-2 dual-positive samples, 50% HSV-1 positive and 50% HSV-1 negative samples and 48% HSV-2 positive and 52% HSV-2 negative samples. The results are presented to convey further information on the performance of the test kit and do not imply endorsement of the assay by the CDC. Results are shown in Tables 20 & 21.

Table 20: BioPlex 2200 HSV-1 IgG vs. CDC HSV Panel (N = 100)

		BioPlex 2200 HSV-1 IgG							
		Positive	Equivocal	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval
CDC HSV-1 Result	Positive	50	0	0	50	100% (50/50)	(92.8 - 100%)	96.0% (48/50)	(86.5 - 98.9%)
	Negative	0	2	48	50				
	Total	50	2	48	100				

Table 21: BioPlex 2200 HSV-2 IgG vs. CDC HSV Panel (N = 100)

		BioPlex 2200 HSV-2 IgG							
		Positive	Equivocal	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval
CDC HSV-2 Result	Positive	50	0	0	50	100% (50/50)	(92.8 - 100%)	100% (50/50)	(92.8 - 100%)
	Negative	0	0	50	50				
	Total	50	0	50	100				

Performance in a Low Prevalence Population

The sensitivity and specificity of the HSV-1 & HSV-2 IgG kit was assessed using remnant serum samples from a low-prevalence population, collected in a non-STD setting, in people age 16-19 (N=200). Samples were tested at 2 U.S. clinical testing sites. Results are shown in Tables 22 & 23.

Table 22: Low-Prevalence Population, Non-STD Setting:
BioPlex 2200 HSV-1 IgG vs.Immunoblot (N = 200)

		BioPlex 2200 HSV-1 IgG							
		Positive	Equivocal	Negative	Total	Positive (+) % Agreement	95% Confidence Interval	Negative (-) % Agreement	95% Confidence Interval
Commercially Available HSV-1 IgG Immunoblot	Positive	97	1	4	102	93.3% (97/104)	(86.7 - 96.7%)	97.9% (94/96)	(92.7 - 99.4%)
	Equivocal	0	0	2	2				
	Negative	2	0	94	96				
	Total	99	1	100	200				

Table 23: Low-Prevalence Population, Non-STD Setting:
BioPlex 2200 HSV-2 IgG vs. Immunoblot (N = 200)

		BioPlex 2200 HSV-2 IgG							
		Positive	Equivocal	Negative	Total	% Sensitivity	95% Confidence Interval	% Specificity	95% Confidence Interval
Commercially Available HSV-2 IgG Immunoblot	Positive	11	0	2	13	73.3% (11/15)	N/A	97.8% (181/185)	(94.6 - 99.2%)
	Equivocal	0	0	2	2				
	Negative	3	1	181	185				
	Total	14	1	185	200				

N/A = Not applicable. There are insufficient positive samples to calculate a statistically meaningful % sensitivity for the low-prevalence population.

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C. Reproducibility Studies

To assess reproducibility of each of the assays in the BioPlex 2200 HSV-1 & HSV-2 IgG kit, a reproducibility panel was prepared at Bio-Rad Laboratories. The reproducibility panel consisted of 8 panel members and the HSV-1 & HSV-2 IgG positive control. The reproducibility panel members were made from diluted patient sera. Reproducibility testing was performed at 2 external evaluation sites and internally at Bio-Rad Laboratories using 3 lots of the HSV-1 & HSV-2 IgG Reagent Pack, 3 lots of the HSV-1 & HSV-2 IgG Calibrator set and 3 lots of the HSV-1 & HSV-2 IgG Control set (one lot at each site). Each of the reproducibility panel members were tested in duplicate on two runs per day, for 5 days, on 3 lots (2 replicates x 2 runs x 5 days x 3 lots = 60 replicates per panel member). The data were analyzed for intra-assay and inter-assay reproducibility according to the principles described in the Clinical Laboratory Standards Institute (CLSI) guidance EP15-A2 (Vol. 25, No. 17). The standard deviation (SD) and prevent coefficient of variation (% CV) were calculated. Results are shown in Tables 24 & 25.

Table 24: Reproducibility: BioPlex 2200 HSV-1 IgG Serum

HSV-1 IgG Panel Members	BioPlex 2200 HSV-1 IgG											
	Sample N	Mean AI	Within-Run		Between-Run		Between-Day		Between-Site*		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive	60	3.6	0.159	4.4%	0.000	0.0%	0.178	4.9%	0.081	2.2%	0.252	6.9%
High Positive	60	3.8	0.132	3.5%	0.095	2.5%	0.125	3.3%	0.413	10.9%	0.461	12.2%
Low Positive	60	1.5	0.090	6.2%	0.000	0.0%	0.073	5.0%	0.167	11.4%	0.203	13.9%
Low Positive	60	1.3	0.058	4.5%	0.034	2.7%	0.058	4.5%	0.113	8.9%	0.144	11.3%
Near Cutoff	60	1.0	0.050	5.2%	0.018	1.9%	0.047	4.9%	0.128	13.4%	0.146	15.3%
Near Cutoff	60	0.9	0.047	5.1%	0.052	5.6%	0.030	3.2%	0.099	10.7%	0.124	13.5%
High Negative	59**	0.6	0.013	2.3%	0.000	0.0%	0.018	3.2%	0.053	9.5%	0.058	10.3%
High Negative	60	0.6	0.034	5.9%	0.000	0.0%	0.023	3.9%	0.024	4.2%	0.048	8.3%
Positive Control	60	3.0	0.127	4.2%	0.092	3.0%	0.108	3.5%	0.137	4.5%	0.235	7.7%

**Between site variance includes between lot variance.*
*** One replicate lost due to laboratory error.*

Table 25: Reproducibility: BioPlex 2200 HSV-2 IgG Serum

HSV-2 IgG Panel Members	BioPlex 2200 HSV-2 IgG											
	Sample N	Mean AI	Within-Run		Between-Run		Between-Day		Between-Site*		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive	59**	3.0	0.149	5.0%	0.124	4.1%	0.000	0.0%	0.155	5.2%	0.249	8.2%
High Positive	60	3.5	0.121	3.4%	0.135	3.8%	0.093	2.6%	0.226	6.4%	0.304	8.6%
Low Positive	60	1.8	0.111	6.1%	0.000	0.0%	0.074	4.1%	0.145	7.9%	0.197	10.7%
Low Positive	60	1.5	0.061	4.0%	0.047	3.1%	0.059	3.9%	0.117	7.8%	0.151	10.1%
Near Cutoff	60	1.2	0.052	4.3%	0.034	2.9%	0.059	4.9%	0.063	5.3%	0.106	8.9%
Near Cutoff	60	1.2	0.034	2.9%	0.072	6.0%	0.040	3.4%	0.069	5.8%	0.113	9.4%
High Negative	60	0.7	0.039	5.2%	0.000	0.0%	0.037	5.1%	0.058	7.9%	0.079	10.7%
High Negative	60	0.6	0.037	6.3%	0.000	0.0%	0.029	5.0%	0.027	4.7%	0.054	9.3%
Positive Control	60	2.8	0.097	3.4%	0.092	3.3%	0.088	3.1%	0.056	2.0%	0.170	6.0%

**Between site variance includes between lot variance.*
*** One replicate lost due to laboratory error.*

D. Precision Studies

A Precision panel, consisting of 8 panel members was prepared by Bio-Rad Laboratories. For each analyte, 2 of the 8 panel members had high positive levels of the antibodies, 2 had low positive levels of the antibodies, and 2 had antibody levels near the cutoff; additionally there were 2 high negative panel members. Precision testing was performed at Bio-Rad Laboratories on one lot of the HSV-1 & HSV-2 IgG Reagent Pack, one lot of the HSV-1 & HSV-2 IgG Calibrator Set and one lot of the HSV-1 & HSV-2 IgG Control Set. Each of the 8 panel members was tested in duplicate (x2) on 2 runs per day for 20 days (2 times x 2 runs x 20 days = 80 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. The standard deviation (SD) and percent coefficient of variation (%CV) were calculated. Results are shown in Tables 26 & 27.

Table 26: Precision: BioPlex 2200 HSV-1 IgG Serum

HSV-1 IgG Panel Members	BioPlex 2200 HSV-1 IgG									
	Sample N	Mean AI	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive	80	3.2	0.14	4.4%	0.16	5.0%	0.00	0.0%	0.21	6.6%
High Positive	80	3.6	0.16	4.3%	0.08	2.2%	0.10	2.7%	0.20	5.5%
Low Positive	80	1.3	0.05	3.7%	0.02	1.5%	0.03	2.5%	0.06	4.7%
Low Positive	80	1.7	0.08	4.9%	0.09	5.5%	0.03	1.7%	0.13	7.6%
Near Cutoff	80	1.0	0.03	2.7%	0.03	3.4%	0.03	2.9%	0.05	5.2%
Near Cutoff	80	1.1	0.04	3.9%	0.03	2.7%	0.02	2.2%	0.06	5.2%
High Negative	80	0.7	0.04	5.8%	0.00	0.0%	0.01	2.0%	0.04	6.1%
High Negative	80	0.5	0.02	4.5%	0.02	3.2%	0.01	2.6%	0.03	6.1%

Table 27: Precision: BioPlex 2200 HSV-2 IgG Serum

HSV-2 IgG Panel Members	BioPlex 2200 HSV-2 IgG									
	Sample N	Mean AI	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Positive	80	5.5	0.17	3.0%	0.20	3.6%	0.03	0.5%	0.26	4.8%
High Positive	80	4.4	0.17	3.8%	0.07	1.5%	0.11	2.4%	0.21	4.8%
Low Positive	80	1.8	0.09	5.2%	0.02	1.2%	0.05	2.9%	0.11	6.1%
Low Positive	80	2.4	0.09	3.8%	0.09	3.6%	0.09	3.6%	0.15	6.3%
Near Cutoff	80	1.3	0.05	3.8%	0.04	2.7%	0.02	1.4%	0.06	4.9%
Near Cutoff	80	1.1	0.06	5.2%	0.04	3.2%	0.02	2.1%	0.07	6.5%
High Negative	80	0.8	0.05	5.8%	0.03	3.4%	0.01	1.3%	0.05	6.8%
High Negative	80	0.6	0.03	4.6%	0.00	0.0%	0.02	2.9%	0.03	5.4%

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E. Cross-Reactivity

A cross-reactivity study was performed to determine if samples from various disease states and other potentially cross-reacting agents interfere with test results when tested with the BioPlex 2200 HSV-1 & HSV-2 IgG kit. Samples known to be positive for one of the twenty potential cross-reactants listed in the table below were evaluated with the BioPlex 2200 HSV-1 & HSV-2 IgG assays. All samples were pre-tested by a commercially available HSV-1 and HSV-2 IgG immunoblot assay and only those that tested negative by the immunoblot assay were further tested by the BioPlex 2200 HSV-1 & HSV-2 IgG kit. Table 28 summarizes negative agreement between the BioPlex 2200 HSV-1 & HSV-2 IgG assays and the corresponding commercially available HSV-1 and HSV-2 IgG immunoblot assay within each of the twenty cross-reactant panels. The results demonstrate that the various disease state samples evaluated do not cross-react with the 2 antigens in the BioPlex 2200 HSV-1 & HSV-2 IgG kit.

Table 28: Cross-Reactivity

Potential Cross-Reactant	HSV-1 IgG		HSV-2 IgG	
	N	BioPlex 2200 Negative Agreement	N	BioPlex 2200 Negative Agreement
ANA IgG	5	5/5	10	10/10
Candida albicans	8	8/8	9	9/9
CMV IgG	8	8/8	8	8/8
E. coli	2	2/2	8	8/8
Toxoplasma gondii IgG	8	8/8	8	8/8
HCV IgG	7	7/7	10	9/10*
VZV IgG	10	10/10	10	10/10
Rubella IgG	6	6/6	7	7/7
HBs Antibody	8	8/8	9	9/9
EBV-VCA IgG	7	7/7	7	7/7
Syphilis IgG	4	4/4	7	7/7
N. gonorrhea	4	4/4	10	10/10
HPV IgG	10	10/10	10	10/10
C. trachomatis	5	5/5	9	9/9
HIV	10	10/10	5	5/5
Rheumatoid Factor	7	7/7	9	9/9
Bacterial Vaginosis				
- *Bacteroides sp.*	N/A	N/A	6	4/6**
- *Trichonomis*	10	10/10	10	10/10
- *Mobiluncus sp.*	1	1/1	4	4/4
- *Gardenella vaginalis*	10	10/10	10	10/10

** One (1) HCV sample was identified as low positive for HSV-2 by the BioPlex 2200 HSV-2 IgG assay with an AI value of 1.3.*

*** Two (2) Bacteroides sp. samples were identified HSV-2 equivocal and low positive with AI values of 1.0 and 1.1, respectively, by the BioPlex 2200 HSV-2 IgG assay.*

N/A = Not available

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY - 8 2009

David V. Bhend
Regulatory Affairs Representative
Bio-Rad Laboratories
6565 185th Ave. NE
Redmond, WA 98052

Re: K090409
Trade/Device Name: BioPlex™ 2200 HSV-1 and HSV-2 IgG Kit
Regulation Number: 21 CFR 866.3305
Regulation Name: Herpes simplex virus serological reagents
Regulatory Class: Class II
Product Code: MXJ,MYF
Dated: February 17, 2009
Received: February 18, 2009

Dear Mr. Bhend:

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 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); 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 Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. 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 (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): k090409

Device Name: BioPlex 2200 HSV-1 and HSV-2 IgG kit on the
BioPlex 2200 Multi-Analyte Detection System

Indication For Use:

The BioPlex™ 2200 HSV-1 & HSV-2 IgG kit is a multiplex flow immunoassay intended for the qualitative detection and differentiation of IgG antibodies to herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) in human serum and EDTA or heparinized plasma. The test is indicated for sexually active individuals and expectant mothers as an aid for the presumptive diagnosis of HSV-1 or HSV-2 infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1 and HSV-2.

The test is not FDA cleared for screening blood or plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates and immunocompromised patients or for use at point of care facilities.

The BioPlex 2200 HSV-1 & HSV-2 IgG kit is intended for use with the Bio-Rad BioPlex 2200 System.

Prescription Use X And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

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

510(k) k090409