

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

**A. 510(k) Number:**

K090409

**B. Purpose for Submission:**

New device.

**C. Measurand:**

Herpes Simplex Virus (HSV-1 and HSV-2) type specific IgG antibodies to the HSV glycoprotein G (gG) 1 antigen and gG2 antigen.

**D. Type of Test:**

Multiplexed micro particle immunoassay based on Luminex technology

**E. Applicant:**

Bio-Rad Laboratories

**F. Proprietary and Established Names:**

BioPlex™ 2200 HSV 1 & 2 Kit

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.3305 - Herpes Simplex Virus Serological Reagents

2. Classification:

Class II (Special Controls)

3. Product code:

MXJ and MYF

4. Panel:

Microbiology (83)

## **H. Intended Use:**

### 1. Intended use(s):

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.

### 2. Indication(s) for use:

Same as Intended Use

### 3. Special conditions for use statement(s):

For prescription use only

### 4. Special instrument requirements:

Bio-Rad BioPlex 2200 System.

## **I. Device Description:**

The BioPlex 2200 HSV-1 & HSV-2 IgG kit is a multiplexed micro particle bead based immunoassay for the qualitative detection of IgG antibodies to HSV glycoprotein G (gG) 1 and 2 in human serum and EDTA or heparinized plasma using the Luminex flow cytometry technology

## **J. Substantial Equivalence Information:**

### 1. Predicate device name(s):

Reference Method for clinical evaluation: HerpeSelect® 1 and 2 immunoblot,

### 2. Predicate K number(s):

K000238

3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended Use	<p>The BioPlex™ 2200 HSV-1 &amp; 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.</p> <p>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.</p>	same
matrix	serum	same
antigen	<ol style="list-style-type: none"> <li>1. Recombinant gG1 antigen (molecular weight 55 KD)</li> <li>2. Recombinant gG2 antigen (molecular weight 31 KD)</li> </ol>	<ol style="list-style-type: none"> <li>1. HSV native virus antigens</li> <li>2. Recombinant gG1 antigen 35-45 KD</li> <li>3. Recombinant gG2 antigen 80-110 KD</li> </ol>

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Method	Multiplexed microparticle flow cytometry immunoassay	Immunoblot assay

**K. Standard/Guidance Document referenced (if applicable):**

CLSI EP5: Evaluation of Precision Performance of Clinical Chemistry Devices-  
Second Edition, Villanova PA

CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline, 2nd  
Ed. (2005).

**L. Test Principle:**

The BioPlex 2200 HSV-1 & HSV-2 IgG kit is an automated system, it uses the following procedure.

The kit contains two different populations of dyed beads are each coated with HSV 1 & 2 gG1 and gG2 antigens. 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.

The instrument is calibrated using a set of 4 distinct calibrator vials, supplied separately by Bio-Rad Laboratories. The 4 vials representing 4 different antibody concentrations are 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:*

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 below.

Precision: BioPlex 2200 HSV-1 IgG Serum

HSV-1 IgG Panel Members	BioPlex 2200 HSV-1 IgG									
	Sample N	Mean AI	Within Run		Between		Between		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%

Precision: BioPlex 2200 HSV-2 IgG Serum

HSV-2 IgG Panel Members	BioPlex 2200 HSV-2 IgG									
	Sample N	Mean AI	Within Run		Between		Between		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%

The assays reproducibility was assessed at three sites using serum, EDTA and heparinized plasma samples. A reproducibility panel was prepared at Bio-Rad Laboratories and consisted of 8 panel members and the HSV-1 & HSV-2 IgG positive control. Reproducibility testing was performed 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 percent coefficient of variation (% CV) were calculated. Results for the serum reproducibility study are shown below.

HSV-1 IgG Panel Members	BioPlex 2200 HSV-1 IgG											
	Sample N	Mean AI	Within-Run		Between-		Between-		Between-		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.

HSV-2 IgG Panel Members	BioPlex 2200 HSV-2 IgG											
	Sample N	Mean AI	Within-Run		Between-		Between-		Between-		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.

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:*

Potential cross-reactivity was evaluated as follows: Samples known to be positive for one of the twenty potential cross-reactants, as determined by FDA cleared devices, 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. 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.

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
<i>Candida albicans</i>	8	8/8	9	9/9
CMV IgG	8	8/8	8	8/8
<i>E. coli</i>	2	2/2	8	8/8
<i>Toxoplasma gondii</i> 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
<i>N. gonorrhoea</i>	4	4/4	10	10/10
HPV IgG	10	10/10	10	10/10
<i>C. trachomatis</i>	5	5/5	9	9/9
HIV	10	10/10	5	5/5
Rheumatoid Factor	7	7/7	9	9/9
Bacterial Vaginosis				
- <i>Bacteroides sp.</i>	N/A	N/A	6	4/6**
- <i>Trichomonis</i>	10	10/10	10	10/10
- <i>Mobiluncus sp.</i>	1	1/1	4	4/4
- <i>Gardenella vaginalis</i>	10	10/10	10	10/10

\* One 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 *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

Testing for interfering substances was conducted according to CLSI Protocol EP7-A2 (Vol. 25, No. 27). Samples were pre-prepared by blending a pool of negative human serum with samples positive for HSV-1 and HSV-2 IgG to achieve values of 3.0 to 5.0 AI. Interferent or solvent (negative control) was added exogenously at levels indicated in the Table below. Test and control samples were evaluated in replicates of ten. Changes in signal ranged from - 8.3 to 10.3%. No significant interference was observed in any of the substances tested.

#### Interfering Substances

Substance	Concentration
Hemoglobin	500 mg/dL
Bilirubin (unconjugated)	20 mg/dL
Bilirubin (conjugated)	30 mg/dL
Cholesterol	500 mg/dL
Red Blood Cells	0.4% (v/v)
Gamma Globulin	6 g/dL
Triglyceride	3300 mg/dL

Beta Carotene	0.6 mg/dL
Total Protein (albumin)	12 g/dL
Ascorbic Acid	3 mg/dL
Heparin Lithium	8000 units/dL
Heparin Sodium	8000 units/dL
EDTA	800 mg/dL
Sodium Citrate	1000 mg/dL

*f. Assay cut-off:*

The cut-off value and assignment of the calibrators were determined by performing concordance and Receiver Operator Characteristic (ROC) analysis, using predicate results as the standard. Analyze-it software is used for the ROC analysis.

Based on the results, calibrator values are adjusted such that the cut-off value at time of market is equal to 1.0 AI for HSV-1 and HSV-2 IgG assay. Samples with AI values <0.9 are considered negative, samples with AI values >1.1 AI are considered positive while samples with an AI value between >0.9 and <1.1 are considered equivocal. Testing was conducted internally at Bio-Rad Laboratories.

A total of 662 samples were evaluated to confirm cut-off values established in early development. All samples were confirmed positive, negative or equivocal by the Focus HerpeSelect®1 and HerpeSelect®2 ELISA IgG predicate kits. ROC Analysis was performed for each analyte using this population of samples.

BioPlex 2200 HSV-1 and HSV-2 IgG assays met or exceeded the concordance requirements of  $\geq 96\%$  and  $\geq 94\%$  positive agreement as well as  $\geq 95$  and  $\geq 97\%$  negative agreement respectively. The results of concordance testing and ROC analysis validate the cut-off that was established for each of the analytes in the BioPlex HSV-1 and HSV-2 IgG assays.

2. Comparison studies:

*a. Method comparison with reference method:*

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 leftover 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 the Tables below.

**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				

**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 leftover serum samples from expectant mothers (N=399). Results are shown in the Tables below.

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

		BioPlex 2200 HSV-1 IgG							
		Positive	Equivocal	Negative	Total	% Sensitivity	95% Confidence Interval	% Specificity	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				

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

		BioPlex 2200 HSV-2 IgG							
		Positive	Equivocal	Negative	Total	% Sensitivity	95% Confidence Interval	% Specificity	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 below.

**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%)
	Equivocal	0	0	0	0				
	Negative	0	2	48	50				
	Total	50	2	48	100				

**BioPlex 2200 HSV-2 IgG vs. CDC HSV Panel (N = 50)**

		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%)
	Equivocal	0	0	0	0				
	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 leftover 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 the following tables.

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

		BioPlex 2200 HSV-1 IgG							
		Positive	Equivocal	Negative	Total	% Sensitivity	95% Confidence Interval	% Specificity	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				

**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)	NA*	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*

b. *Matrix comparison:*

Matched serum and plasma (EDTA and heparin) samples drawn from 87 individual donors were acquired from commercial sources. All samples were evaluated in replicates of two. Plasma AI values were compared to matched serum AI values. All samples correlated well, the corresponding slopes of regression and square of correlation ( $R^2$ ) was 0.99.

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable

b. *Clinical specificity:*

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

See 1 f

5. Expected values/Reference range:

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). The observed and the hypothetical positive and negative predicted values were also calculated for HSV1 &2 in both of the study populations.

**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
<b>Total</b>		207	71.6%	5	1.7%	77	26.6%	289

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

**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
<b>Total</b>		109	38.1%	1	0.4%	176	61.5%	286

**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
<b>Total</b>	288	72.2%	2	0.5%	109	27.3%	399

**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
<b>Total</b>	157	39.3%	0	0.0%	242	60.7%	399

**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%

*N/A = Not applicable*

**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%	98.8%
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%

**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%

**N. Proposed Labeling:**

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

**O. Conclusion:**

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