

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

A. 510(k) Number: K062543

B. Purpose for Submission: New device clearance

C. Measurand: Herpes Simplex Virus

D. Type of Test: Chemiluminescent technology for antibody technology

E. Applicant: Focus Diagnostics

F. Proprietary and Established Names: Plexus™ HerpeSelect®1 and 2 IgG

G. Regulatory Information:

1. Regulation section: 866.3305
2. Classification: II
3. Product code: MXJ/MYF
4. Panel: Microbiology

H. Intended Use:

Focus Diagnostics' Plexus™ HerpeSelect®1 and 2 IgG is intended for qualitatively detecting the presence or absence of human IgG class antibodies to HSV-1 and HSV-2 in human sera. The test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV-1 and HSV-2 infection. The predictive value of a positive or negative result depends on the population's prevalence and the pretest likelihood of HSV-1 and HSV-2 infection. The performance of this assay has not been established for use in a pediatric population, for neonatal screening, for testing of immunocompromised patients, for use by a point of care facility or for use with automated equipment.

2. Indication(s) for use: NA
3. Special conditions for use statement(s): NA
4. Special instrument requirements: Luminex xMAP® or Bio-rad BioPlex® 2200

I. Device Description:

The Focus Diagnostics Plexus HerpeSelect®1 and 2 IgG uses an Antigen Bead suspension that contains two distinct HSV antigen bead types that fluoresce at different wavelengths and/or intensities: gG1 beads and gG2 beads.

The Focus Diagnostics Plexus HerpeSelect®1 and 2 IgG is a three step procedure.

1. Patient sera are diluted, and the diluted sera are incubated with Antigen Beads. If HSV antibodies are present, then the antibodies bind to the corresponding antigen beads.
2. Phycoerythrin—conjugated goat anti-human IgG, (Conjugate) is added, and the Conjugate binds to the bound HSV antibody (if present), and forms a Conjugate-HSV antibody-antigen bead sandwich.
3. Fluorescence from each distinct HSV antigen bead type is measured and compared against a Cut-off Calibrator.

J. Substantial Equivalence Information:

1. Predicate device name(s): HerpeSelect 1 and 2 Immunoblot IgG, HerpeSelect 1 ELISA IgG, HerpeSelect 2 ELISA IgG
2. Predicate 510(k) number(s): K000238, K02129, K021486
3. Comparison with predicate:

Item	Device	Predicate
	Focus Plexus HerpeSelect 1 and 2 IgG	Focus HerpeSelect 1 and 2 Immunoblot IgG
Similarities		
Same intended use	Qualitatively detecting the presence or absence of human IgG class antibodies to HSV-1 and HSV-2 in human sera.	Qualitatively detecting the presence or absence of human IgG class antibodies to HSV-1 and HSV-2 in human sera.
Same indications for use	The test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV-1 and HSV-2 infection.	The test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV-1 and HSV-2 infection.
Same type specific HSV-1 antigen	Recombinant gG1 antigen	Recombinant gG1 antigen
Same type specific HSV-2 antigen	Recombinant gG2 antigen	Recombinant gG2 antigen
Same immunoglobulin type	IgG	IgG
Same sample matrix	Serum	Serum
Differences		
Methodology	Luminex-based fluorescent bead assay	Immunoblot assay
CLIA complexity	High	Moderate

- K. Standard/Guidance Document Referenced (if applicable):** Class II Special Controls Guidance Document: Herpes Simplex Virus Types 1 and 2 Serological Assays (<http://www.fda.gov/cdrh/oivd/guidance/1305.pdf>)

L. Test Principle:

The Focus Diagnostics Plexus HerpeSelect®1 and 2 IgG uses an Antigen Bead suspension that contains two distinct HSV antigen bead types that fluoresce at different wavelengths and/or intensities: gG1 beads and gG2 beads.

The Focus Diagnostics Plexus HerpeSelect® 1 and 2 IgG is a three step procedure.

1. Patient sera are diluted, and the diluted sera are incubated with Antigen Beads. If HSV antibodies are present, then the antibodies bind to the corresponding antigen beads.
2. Phycoerythrin—conjugated goat anti-human IgG, (Conjugate) is added, and the Conjugate binds to the bound HSV antibody (if present), and forms a Conjugate-HSV antibody-antigen bead sandwich.
4. Fluorescence from each distinct HSV antigen bead type is measured and compared against a Cut-off Calibrator.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility

Inter-laboratory Reproducibility and Inter/Intra-assay Reproducibility

Focus, a clinical laboratory located in Southern California, and a university laboratory located in Northern California assessed the device's inter-laboratory reproducibility and inter/intra-assay reproducibility. Each of the three laboratories tested eleven samples in triplicate on five different days.

Inter-laboratory Reproducibility and Inter/Intra-assay Reproducibility^a

Sample	HerpeSelect 1 Plexus IgG Results					HerpeSelect 2 Plexus IgG Results				
	Intra- and Inter-assay			Inter-Lab		Intra- and Inter-assay			Inter-Lab	
	Mean Index	Intra-assay % CV	Inter-assay % CV	Mean Index	% CV	Mean Index	Intra-assay % CV	Inter-assay % CV	Mean Index	% CV
9	4.93	3.6	10.3	4.94	3.7	3.88	3.4	10	3.87	2.5
6	4.24	3.8	8.7	4.22	3.3	4.9	2.6	8.5	4.89	2.1
2	3.87	4.8	7.9	3.86	1.3	3.36	4.3	7.7	3.35	2
8	3.27	4.9	9.1	3.25	3	4.56	3.1	8.3	4.55	1.5
4	3.24	4.9	7.4	3.22	2.1	2.55	4.5	8.9	2.54	5.8

1	3.04	4.3	8.9	3.02	2.3	2.71	3.8	9.3	2.7	2.1
12 ^b	2.13	7.9	8.7	2.13	4.1	1.87	7.2	8.8	1.87	3.4
3	0.34	9.1	14.9	0.34	6.8	0.06	8.7	28.3	0.06	22.6
10 ^c	0.19	9.9	213.1	0.19	59	0.12	11.4	334.2	0.4	103.8
10 ^d	0.13	10	15.8	0.12	1.9	0.06	11.5	41.7	0.06	38.3
7	0.18	8.3	16.3	0.17	9.4	0.06	8.1	23.7	0.06	17.3
5	0.14	9	16	0.14	2.7	0.06	8.3	39.8	0.06	38.1

- a. Excludes two runs at one site that were invalid because the Negative Control index was beyond the acceptable QC criteria (it appears that the Positive Control was run in those wells since the indices were about 1.9 for both gG1 and gG2)
- b. Samples 12 (inter-lab reproducibility) and t4 (inter-lot reproducibility below) were separate samples, but they were made with the same sera Samples 11 did not have sufficient volume to be sent to investigators.
- c. This line includes all data for Sample 10, including one run at Lab 2, where it appears that Sample I may have been run instead since the indices were about 2.7 for both gG1 and gG 2 .
- d. This line includes all data for Sample 10. except for one run at Lab 2, where it appears that Sample I may have been run instead since the indices were about 2.7 for both gGI and gG2

Inter-Lot Reproducibility

Focus assessed the device's Inter-lot Reproducibility by testing eleven samples with three separate lots. The samples were run in triplicate. Each lot had a different set of gG-I and gG2 beads, a different lot of conjugate (made from 2 different stock conjugates), and a different lot of calibrator (made from 2 different combinations of positive and negative sera). The results of the studies are summarized in the tables below:

Sample	HSV-1		HSV-2	
	Mean	Inter-Lot	Mean	Inter-Lot
	Index	%CV	Index	%CV
9	5.2	7.4	3.9	12.8
6	4.36	8.5	4.76	9.2
2	3.6	7.3	3.19	9.3
4	3.29	7.9	2.54	6.4
8	3.23	11.3	4.45	9.4
1	3.14	5.8	2.73	4.8
12/14*	2.22	10.5	1.86	7.8
3	0.31	17	0.11	50.9
7	0.15	31.3	0.08	21.8
5	0.1	45.6	0.06	24.9
10	0.09	50.6	0.06	26.9

*Samples 12 (inter-lab reproducibility above) and 14 (inter-lot reproducibility) were separate samples, but they were made with the same sera. Samples II and 13 did not have sufficient volume to be sent to investigators.

- 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*
 - i. *Cross-reactivity*

Cross-reactivity (n = 51)

Focus assessed cross-reactivity with two groups of samples: a "HSV ELISA dual negative" group (n=37), and a "HSV ELISA mixed sero-reactivity" group (n=14).

The HSV ELISA dual negative group (n=37) included samples that were sero-negative with both the HerpeSelect-1 ELISA IgG and HerpeSelect 2 ELISA IgG, and were sero-positive by at least one of a FDA cleared CMV ELISA IgG (n = 18), a home brew VZV ACIF (n=32), a FDA cleared EBV VCA IgG (n=31). The HerpeSelect 1 and 2 Plexus IgG was HSV-1 negative with all but one of the HSV ELISA dual negatives, and equivocal with one sample (the one sample was CMV+ VZV+ and EBV+). The HerpeSelect 1 and 2 Plexus IgG was HSV-2 negative with all but one of the HSV ELISA dual negatives, and equivocal with one sample (the one sample was CMV- VZV+ and EBV+).

The HSV ELISA mixed reactivity group (n=14) included samples that were sero-positive with either the HerpeSelect-1 ELISA IgG or HerpeSelect 2 ELISA IgG, and were sero-positive by at least one of a FDA cleared CMV ELISA IgG (HSV-1 neg n = 2, HSV-2 neg n = 9), a home brew VZV ACIF (HSV-1 neg n = 1, HSV-2 neg n = 2), a FDA cleared EBV VCA IgG (HSV-1 neg n = 1, HSV-2 neg n = 0). The HerpeSelect 1 and 2 Plexus IgG was HSV-1 negative with all of the HSV-1 ELISA negatives in the mixed reactivity group. The HerpeSelect 1 and 2 Plexus IgG was HSV-2 negative with all of the HSV-2 ELISA negatives in the mixed reactivity group.

Cross-reactant	HSV ELISAs	HerpeSelect- 1 Plexus					HerpeSelect-2 Plexus				
		n	Neg	Eqv*	Pos	% POS	n	Neg	Eqv*	Pos	% POS
CMV IgG +	Dual Neg	18	17	1	0	5.6% (1/18) 95%CI 0.1-27.3%	18	18	0	0	0.0% (0/18) 95%CI 0.0-18.5%
	+/- or -/+	2	2	0	0	0.0% (0/2) 95%CI 0.0-84.2%	9	9	0	0	0.0% (0/9) 95%CI 0.0-33.6%
	Total	20	19	1	0	5.0% (1/20) 95%CI 0.1-24.9%	27	27	0	0	0.0% (0/27) 95%CI 0.0-12.8%

VZV IgG +	Dual Neg	32	31	I	0	3.1% (1/32) 95%CI 0.1-16.2%	32	31	I	0	3.1% (1/32) 95%CI 0.1-16.2%
	+/-or-/+	I	I		0	0.0% (0/1) na	2	2		0	0.0% (0/2) 95%CI 0.0-84.2%
	Total	33	32	I	0	3.0% (1/33) 95%CI 0.1-15.8%	34	33		1	2.9% (1/34) 95%CI 0.1 15.3%
EBV IgG +	Dual Neg	31	30		1	3.2% (1/31) 95%CI 0.1-16.7%	31	30		1	3.2% (1/31) 95%CI 0.1-16.7%
	+/-or-/+	I	1		0	0.0% (0/1) na	0	0		0	na
	Total	32	31		1	3.1% (1/32) 95%CI 0.1-16.2%	31	30		1	3.2% (1/31) 95%CI 0.1-16.7%

ii. *Interfering substances:* not applicable

f. *Assay cut-off*

2. Comparison studies:

a. *Method comparison with predicate device:* Immunoblot IgG as the reference method, see clinical studies

b. *Matrix comparison:* not applicable

3. Clinical studies:

PERFORMANCE CHARACTERISTICS

Summary of Studies (see details below)

Study	HerpeSelect 1 Plexus IgG Results	HerpeSelect 2 Plexus IgG Results
Expectant Mothers (Indicated population)	Agreement with positives 96.5% Agreement with negatives 92.2%	94.3% 95.5%
Sexually Active Adults (Indicated population)	Agreement with positives 91.0% Agreement with negatives 96.5%	96.3% 97.4%
CDC HSV/CMV Panel	Agreement with positives 100% Agreement with negatives 100%	100% 100%
Low Prevalence Population	Agreement with negatives 97.9%	100%
Cross-reactivity with CMV, EBV and VZV.	Cross-reactivity 0-5%	0-3%
Reproducibility	%CV of positives ≤10%	≤10%

Reactivity with Expectant Mothers (n = 300)

Focus (n = 150) and an external investigator (n = 150) assessed the device's reactivity with sera from Expectant Mothers. The sera were sequentially submitted to the laboratory, archived, and masked. The external investigator was an University laboratory located in Northern California, and the sera were collected in the Pacific Northwestern United States. The HerpeSelect Plexus results were compared to the HerpeSelect 1 ELISA IgG and the HerpeSelect 2 ELISA IgG, using the Focus HerpeSelect 1 and 2 Immunoblot IgG as the reference method.

HSV-1 Reactivity

The Focus HerpeSelect 1 Immunoblot IgG was: HSV-1 positive for 170 samples, HSV-1 negative with 128 samples, and HSV Common Antigen band positive for two samples. The Plexus HerpeSelect 1 agreed with: 96.5% (164/170) of Immunoblot positives, and 92.2% (118/128) of Immunoblot negatives. The two Immunoblot HSV Common Antigen band positives were both negative in the Plexus.

HSV-2 Reactivity

The Focus HerpeSelect 2 Immunoblot IgG was: HSV-2 positive for 122 samples, HSV-2 negative with 176 samples, and HSV Common Antigen band positive for two samples. The Plexus HerpeSelect 2 agreed with: 94.3% (115/122) of Immunoblot positives, and 95.5% (168/176) of Immunoblot negatives. The two Immunoblot HSV Common Antigen band positives were both negative in the Plexus.

Plexus HerpeSelect 1 IgG Reactivity with Expectant Mothers (n = 300)

Lab	Herpe - Select Immu noblo t	Plexus HerpeSelect-1					HerpeSelect-1 ELISA				
		n	Ne g	Eqv	Pos	% Agreement	n	Ne g	Eqv	Pos	% Agreement
Site 1	Pos	84	6	0	78	92.9% (78/84) 95%CI 85.1- 97.3%	84	5	1	78	92.9% (78/84) 95%CI 85.1- 97.3%
Focus	Pos	86	0	0	86	100% (86/86) 95%CI 95.8- 100%	86	0	0	86	100% (86/86) 95%CI 95.8- 100%
Combined Labs	Pos	170	6	0	164	96.5% (164/170) 95%CI 92.5- 98.7%	170	5	1	164	96.5% (164/170) 95%CI 92.5- 98.7%
Site 1	Neg	66	61	1	4	92.4% (61/66) 95%CI 83.2- 97.5%	66	59	2	5	89.4% (59/66) 95%CI 79.4- 95.6%
Focus	Neg	62	57	2	3	91.9% (57/62) 95%CI 82.2- 97.3%	62	59	1	2	95.2% (59/62) 95%CI 86.5- 99.0%
Combined Labs	Neg	128	118	3	7	92.2% (118/128) 95%CI 86.1- 96.2%	128	118	3	7	92.2% (118/128) 95%CI 86.1- 96.2%
Site 1	Com	0	0	0	0	Na	0	0	0	0	Na
Focus	Com	2	2	0	0	Na	2	2	0	0	Na

Combined Labs	Com	2	2	0	0	Na	2	2	0	0	Na
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Plexus HerpeSelect 2 IgG Reactivity with Expectant Mothers (n = 300)

Lab	Herpe-Select Immunoblot	Plexus HerpeSelect-2					HerpeSelect-2 ELISA				
		n	Neg	Eqv	Pos	% Agreement	n	Neg	Eqv	Pos	% Agreement
Site 1	Pos	60	3	1	56	93.3% (56/60) 95%CI 83.8-98.2%	60	2	0	58	96.7% (58/60) 95%CI 88.5-99.6%
Focus	Pos	62	2	1	59	95.2% (59/62) 95%CI 86.5-99.0%	62	1	0	61	98.4% (61/62) 95%CI 91.3-100%
Combined Labs	Pos	122	5	2	115	94.3% (115/122) 95%CI 88.5-97.7%	122	3	0	119	97.5% (119/122) 95%CI 93.0-99.5%
Site 1	Neg	90	88	0	2	97.8% (88/90) 95%CI 92.2-99.7%	90	86	0	4	95.6% (86/90) 95%CI 89.0-98.8%
Focus	Neg	86	80	3	3	93.0% (80/86) 95%CI 85.4-97.4%	86	80	1	5	93.0% (80/86) 95%CI 85.4-97.4%
Combined Labs	Neg	176	168	3	5	95.5% (168/176) 95%CI 91.2-98.0%	176	166	1	9	94.3% (166/176) 95%CI 89.8-97.2%
Site 1	Com	0	0	0	0	na	0	0	0	0	na
Focus	Com	2	2	0	0	Na	2	2	0	0	Na
Combined Labs	Com	2	2	0	0	Na	2	2	0	0	Na

Reactivity with Sexually Active Adults (n = 300)

Focus (n = 150) and an external investigator (n = 150) assessed the device's reactivity with sera from sexually active adults. The sera were sequentially submitted to the laboratory, archived, and masked. The external investigator was a clinical laboratory located in Southern California, and the sera were collected in the Pacific Northwestern United States. The HerpeSelect Plexus results were compared to the HerpeSelect 1 ELISA IgG and the HerpeSelect 2 ELISA IgG, using the Focus HerpeSelect 1 and 2 Immunoblot IgG as the reference method.

HSV-1 Reactivity

The Focus HerpeSelect 1 Immunoblot IgG was: HSV-1 positive for 157 samples, HSV-1 negative with 142 samples, and HSV Common Antigen band positive for one sample. The Plexus HerpeSelect 1 agreed with: 91.0% (142/156) of Immunoblot positives (one sample was not run on the Plexus device), and 96.5% (137/142) of Immunoblot negatives.

HSV-2 Reactivity

The Focus HerpeSelect 2 Immunoblot IgG was: HSV-2 positive for 109 samples, HSV-2 negative with 190 samples, and HSV Common Antigen band positive for one sample. The Plexus HerpeSelect 2 agreed with: 96.3% (105/109) of Immunoblot positives, and 97.4% (184/189) of Immunoblot negatives (one sample was not run on the Plexus device).

Plexus HerpeSelect 1 IgG Reactivity with Sexually Active Adults (n = 300)

Lab	Herpe-Select Immunoblot	Plexus HerpeSelect-1					HerpeSelect-1 ELISA				
		n	Neg	Eqv	Pos	% Agreement	n	Neg	Eqv	Pos	% Agreement
Site 2	Pos	71	4	2	65	91.5% (65/71) 95%CI 82.5-96.8%	71	3	0	68	95.8% (68/71) 95%CI 88.1-99.1%
Focus	Pos	85*	5	3	77	90.6% (77/85) 95%CI 82.3-95.9%	86	4	2	80	93.0% (80/86) 95%CI 85.4-97.4%
Combined Labs	Pos	156	9	5	142	91.0% (142/156) 95%CI 85.4-95.0%	157	7	2	147	93.6% (147/157) 95%CI 88.6-96.9%
Site 2	Neg	79	78	1	0	98.7% (78/79) 95%CI 93.1-100%	79	77	1	1	97.5% (77/79) 95%CI 91.2-99.7%
Focus	Neg	63	59	2	2	93.7% (59/63) 95%CI 84.5-98.2%	63	60	0	3	95.2% (60/63) 95%CI 86.7-99.0%
Combined Labs	Neg	142	137	3	2	96.5% (137/142) 95%CI 92.0-98.9%	142	137	1	4	96.5% (137/142) 95%CI 92.0-98.9%
Site 2	Com	0	0	0	0	na	0	0	0	0	na
Focus	Com	1	1	0	0	na	1	1	0	0	na
Combined Labs	Com	1	1	0	0	na	1	1	0	0	na

*One of 300 samples was not run in the Plexus HerpeSelect, and that one sample was HSV-1 negative/HSV-2 positive in the Immunoblot.

Plexus HerpeSelect 2 IgG Reactivity with Sexually Active Adults (n = 300)

Lab	Herpe-Select Immunoblot	Plexus HerpeSelect-2					HerpeSelect-2 ELISA				
		n	Neg	Eqv	Pos	% Agreement	n	Neg	Eqv	Pos	% Agreement
Site 2	Pos	47	3	1	43	91.5% (43/47) 95%CI 79.6-97.6%	47	1	0	46	97.9% (46/47) 95%CI 88.7-99.9%
Focus	Pos	62	0	0	62	100%(62/62) 95%CI 94.2-100%	62	0	1	61	98.4%(61/62) 95%CI 91.3-100%

Combined Labs	Pos	109	3	1	105	96.3% (105/109) 95%CI 90.9-99.0%	109	1	1	107	98.2% (107/109) 95%CI 93.5-99.8%
Site 2	Neg	103	100	1	2	97.1% (100/103) 95%CI 91.7-99.4%	103	102	0	1	99.0% (102/103) 95%CI 94.7-100%
Focus	Neg	86*	84	0	2	97.7% (84/86) 95%CI 91.8-99.7%	87	84	1	2	96.6% (84/87) 95%CI 90.3-99.3%
Combined Labs	Neg	189	184	1	4	97.4% (184/189) 95%CI 93.9-99.1%	190	186	1	3	97.9% (186/190) 95%CI 94.7-99.4%
Site 2	Com	0	0	0	0	na	0	0	0	0	na
Focus	Com	1	1	0	0	na	1	1	0	0	na
Combined Labs	Com	1	1	0	0	na	1	1	0	0	na

*One of 300 samples was not run in the Plexus HerpeSelect, and that one sample was HSV-1 negative/HSV-2 positive in the Immunoblot.

Agreement with CDC Panel (n = 100)

The following information is from a serum panel obtained from the CDC and tested by Focus Diagnostics. The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply an endorsement of the assay by the CDC.

The test panel consists of 100 samples. This panel contains duplicate samples of 50 test sera. The duplicates serve to test for reproducibility. There are 16 HSV-1 positive, 7 HSV-2 positive, 11 double-positive and 16 double-negative sera resulting in 54 HSV-1 positive and 36 HSV-2 positive specimens.

Determination of positive and negative samples

Of the 54 HSV-1 positive samples, the HerpeSelect[®] Plexus IgG correctly identified 100% (54/54).

Of the 36 HSV-2 positive samples, the HerpeSelect[®] Plexus IgG correctly identified 100% (36/36).

Of the 22 double positive samples, the HerpeSelect[®] Plexus IgG correctly identified 100% (22/22).

Of the 32 double negative samples, the HerpeSelect[®] Plexus IgG correctly identified 100% (32/32).

Agreement with CDC Panel (n = 100)

Sample Type	CDC Result		n	HerpeSelect-1 Plexus Results				HerpeSelect-2 Plexus Results			
	HSV1	HSV2		Neg	Eqv	Pos	% Agreement	Neg	Eqv	Pos	% Agreement
HSV-1 Positive	Pos	Neg	32	0	0	32	100% (32/32) 95%CI 89.1-100%	32	0	0	100% (32/32) 95%CI 89.1-100%
HSV-2 Positive	Neg	Pos	14	14	0	0	100% (14/14) 95%CI 76.8-100%	0	0	14	100% (14/14) 95%CI 76.8-100%
Dual	Pos	Pos	22	0	0	22	100% (22/22)	0	0	22	100% (22/22)

Positive							95%CI 84.6-100%				95%CI 84.6-100%
Dual Negative	Neg	Neg	32	32	0	0	100% (32/32) 95%CI 89.1-100%	32	0	0	100% (32/32) 95%CI 89.1-100%

CDC Panel Reproducibility

All paired sera were correctly identified: The Focus Diagnostics HerpeSelect® 1 and 2 Plexus IgG identified 16 out of 16 paired HSV-1 positive and HSV-2 negative (100%), 7 out of 7 paired HSV-2 positive and HSV-1 negative (100%), 11 out of 11 paired double-positive (100%) and 16 out of 16 paired double-negative (100%) samples.

Specificity with a Low Prevalence Population (n = 77)

Focus (n = 77) assessed the device's reactivity with sera from a low prevalence population. Focus selected sera from patients aged 18 and 19 years, and that had been submitted to a clinical laboratory in Southern California from states having a history of low sexually transmitted disease prevalence. Focus excluded sera that were submitted for sexually transmitted diseases, herpesvirus testing, and tests indicating the patient may be immunocompromised. The sera were sequentially selected, archived and masked. The HerpeSelect Plexus results were compared to the Focus HerpeSelect 1 and 2 Immunoblot IgG.

HSV-1 Reactivity

The Focus HerpeSelect 1 Immunoblot IgG was: HSV-1 positive for 28 samples, HSV-1 negative with 47 samples, and HSV Common Antigen band positive for two samples.

The Plexus HerpeSelect 1 agreed with: 96.4% (27/28) of Immunoblot positives (one HSV-1 Immunoblot positive was equivocal in the Plexus device), and 97.9% (46/47) of Immunoblot negatives (one HSV-1 Immunoblot negative was positive in the Plexus device). One Immunoblot HSV Common Antigen band positive was equivocal in the Plexus, and the other sample was Plexus negative.

HSV-2 Reactivity

The Focus HerpeSelect 2 Immunoblot IgG was: HSV-2 positive for four samples, HSV-2 negative with 71 samples, and HSV Common Antigen band positive for two samples.

The Plexus HerpeSelect 2 agreed with: 75.0% (3/4) of Immunoblot positives (one HSV-1 Immunoblot positive was equivocal in the Plexus device), and 100% (71/71) of Immunoblot negatives (one HSV-1 Immunoblot negative was positive in the Plexus device). Both Immunoblot HSV Common Antigen band positives were negative in the Plexus.

Specificity with Low Prevalence Population (n = 77)

HerpeSelect Immunoblot	Plexus HerpeSelect-1					Plexus HerpeSelect-2				
	n	Ne g	Eq v	Pos	% Agreement	n	Ne g	Eq v	Pos	% Agreement
Pos	28	0	1	27	96.4% (27/28) 95%CI 81.6-99.9%	4	0	1	3	75.0% (3/4) 95%CI 19.4-99.4%
Neg	47	46	0	1	97.9% (46/47) 95%CI 88.7-99.9%	71	71	0	0	100% (71/71) 95%CI 94.9-100%
Com	2	1	1	0	Na	2	2	0	0	na

4. Clinical cut-off:

5. Expected values/Reference range:

EXPECTED VALUES

An outside investigator assessed the device with masked, archived and unselected sera from 1) sexually active adults (n = 300), and 2) from expectant mothers (n = 300). The reference methods were Focus Diagnostics HerpeSelect 1 ELISA IgG and HerpeSelect 2 ELISA IgG. The observed prevalences and the hypothetical predictive values for the two populations are shown below. The positive predictive value will decrease proportionally to the prevalence of HSV infection as reflected in the table below. The calculations are based on **HerpeSelect 1 and 2 Plexus IgG** having

- 1) HSV-1 sensitivity of 96.5% and a HSV-1 specificity of 92.2% (expectant mothers), and
- 2) HSV-2 sensitivity of 94.3% and a HSV-2 specificity of 95.5% (expectant mothers).
- 3) HSV-1 sensitivity of 91.0% and a HSV-1 specificity of 96.5% (Sexually Active Adults), and
- 4) HSV-2 sensitivity of 96.3% and a HSV-2 specificity of 97.4% (Sexually Active Adults).

Observed Prevalence with Sexually Active Adults

Sero-status	Observed Prevalence		
	HerpeSelect ELISA	HerpeSelect Immunoblot	HerpeSelect Plexus
HSV-1 neg	48.3% (145/300)	47.3% (142/300)	49.2% (147/299)
HSV-1 +	50.3% (151/300)	52.0% (156/300)	48.2% (144/299)
HSV-2 neg	62.7% (188/300)	63.0% (189/300)	62.9% (188/299)
HSV-2 +	36.7% (110/300)	36.3% (109/300)	36.4% 9109/299)

Observed Prevalence with Expectant Mothers

Sero-status	Observed Prevalence		
	HerpeSelect ELISA	HerpeSelect Immunoblot	HerpeSelect Plexus
HSV-1 neg	41.7% (125/300)	42.6% (128/300)	42.0% (126/300)
HSV-1 +	57.0% (171/300)	56.7% (170/300)	57.0% (171/300)
HSV-2 neg	57.0% (171/300)	58.7% (176/300)	58.3% (175/300)
HSV-2 +	42.7% (128/300)	40.7% (122/300)	40.0% (120/300)

Expectant Mothers Prevalence vs. Hypothetical Predictive Values

Prevalence	HSV-1		HSV-2	
	PPV	NPV	PPV	NPV
50%	92.5	92.2	95.4	95.5
40%	89.2	94.7	93.3	97.0
30%	84.1	96.5	90.0	98.0
25%	80.5	97.3	87.5	98.5
20%	75.6	97.9	84.0	98.8
15%	68.6	98.5	78.7	99.2
10%	57.9	99.1	70.0	99.5
5%	39.4	99.6	52.4	99.8

Sexually Active Adults Prevalence vs. Hypothetical Predictive Values

Prevalence	HSV-1		HSV-2	
	PPV	NPV	PPV	NPV
50%	96.3	96.5	97.4	97.4
40%	94.5	97.6	96.1	98.3
30%	91.8	98.5	94.1	98.9
25%	89.7	98.8	92.5	99.1

20%	86.7	99.1	90.3	99.3
15%	82.1	99.4	86.7	99.5
10%	74.3	99.6	80.5	99.7
5%	57.8	99.8	66.1	99.9

Note: Sexually active adult and expectant mother populations in different geographic areas may produce different frequency distributions from the table above. Each laboratory should establish frequency distributions for their specific patient populations.

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.