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FOCUS technologies

510(k) Summary of Safety and Effectiveness
HerpeSelect® 1 ELISA IgG Catalog No. EL0910G
Prepared July 23, 2002

Applicant	Focus Technologies, Inc. 10703 Progress Way Cypress, California 90630 USA
Establishment Registration No.	2023365
Contact Person	Michael J. Wagner, Esq. tel (714) 220-1900 fax (714) 995-6921 mwagner@focusanswers.com
Summary Date	July 23, 2002
Proprietary Name	HerpeSelect®1 ELISA IgG (automated option)
Generic Name	HSV-1 ELISA IgG
Classification	Herpes Simplex Virus Serological Reagents 21 CFR §866.3305 Class III
Predicate Device	HerpeSelect®1 ELISA IgG (manual option)

Device Description
In the HerpeSelect®1 ELISA IgG IgG assay, the polystyrene microwells are coated with recombinant gG-1 antigen. Diluted serum samples and controls are incubated in the wells to allow specific antibody present in the samples to react with the antigen. Nonspecific reactants are removed by washing, and peroxidase-conjugated anti-human IgG is added and reacts with specific IgG. Excess conjugate is removed by washing. Enzyme substrate and chromogen are added, and the color is allowed to develop. After adding the Stop Reagent, the resultant color change is quantified by a spectrophotometric reading of optical density (OD). Sample optical density readings are compared with reference cut-off OD readings to determine results.

Intended Use
Focus Technologies' HerpeSelect® 1 ELISA IgG test is intended for qualitatively detecting the presence or absence of human IgG class antibodies to HSV-1 in human sera. In conjunction with the Focus HerpeSelect® 2 ELISA IgG, the test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV infection. The assay can be used manually or in conjunction with an automated system as outlined in the package insert. **The user is responsible for assay performance characteristics when an automated system is used.** The performance of this assay has not been established for use in a pediatric population, for neonatal screening, or for testing of immunocompromised patients.

EXPECTED VALUES

An outside investigator assessed the device with masked, archived and unselected sera from 1) sexually active adults over the age of 14 (n = 246), and 2) from expectant mothers (n = 241). The reference method was a HSV-1 Western blot from a Pacific Northwest university. The observed prevalences and the hypothetical predictive values for the two populations are shown in the tables 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 ELISA IgG having

1) a hypothetical sensitivity of 91.2% & a hypothetical specificity of 92.3% (sexually active adults), and
2) a hypothetical sensitivity of 96.0% and a hypothetical specificity of 95.2% (expectant mothers).

Observed Prevalence with Sexually Active Adults & Expectant Mothers

Population	HSV-1 Serostatus	Observed Prevalence	
		WB	Focus ELISA
Sexually Active Adults *	neg	42.9%	41.2%
	+	55.9%	56.7%
Expectant Mothers †	neg	25.7%	22.4%
	+	73.9%	75.5%

* Excludes 3 atypical Western blots and 2 ELISA equivocals.
† Excludes 1 atypical Western blot and 1 ELISA equivocal.

Prevalence vs. Hypothetical Predictive Values

Prevalence	Sexually Active Adults		Expectant Mothers	
	PPV	NPV	PPV	NPV
50%	92.2%	92.3%	95.2%	95.2%
40%	88.8%	94.7%	93.0%	96.7%
30%	83.5%	96.5%	89.6%	97.9%
25%	79.8%	97.3%	87.0%	98.3%
20%	74.8%	98.0%	83.3%	98.8%
15%	67.6%	98.5%	77.9%	99.1%
10%	56.8%	99.1%	69.0%	99.4%
5%	38.4%	99.6%	51.3%	99.7%

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.

PERFORMANCE CHARACTERISTICS

Relative Sensitivity and Relative Specificity with Expectant Mothers †

An outside investigator assessed the device's relative sensitivity and relative specificity with sera from expectant mothers (n = 241). The sera were sequentially submitted to the laboratory, archived, and masked. The reference method was a HSV-1 Western blot (WB) from a Pacific Northwest university. Of 178 WB positives, HerpeSelect® 1 ELISA IgG (EL) was 170 positive, 7 negative and one equivocal. Of 62 Western blot negatives, HerpeSelect® 1 ELISA IgG was 59 negatives, and 3 positives. The one atypical Western blot was HerpeSelect® 1 ELISA IgG negative.

Relative Sensitivity and Relative Specificity with Expectant Mothers (n=241) †

Characteristic	% (EL/WB)*	95% CI
Sensitivity relative to Western blot	96.0% (170/177)	92.0-98.4%
Specificity relative to Western blot	95.2% (59/62)	86.5-99.0%

* Excludes one atypical Western blot and one ELISA equivocal.

† The word "relative" refers to comparing this assay's results with those of a similar assay. No attempt was made to correlate the assay results to disease presence or absence. No judgment can be made on the similar assay's accuracy in predicting disease. Assay performed by the manual method.

Relative Sensitivity and Relative Specificity with Sexually Active Adults †

An outside investigator assessed the device's relative sensitivity and relative specificity with sera from sexually active adults over the age of 14 (n = 246). The sera were sequentially submitted to the laboratory, archived, and masked. The reference method was a HSV-1 Western blot from a Pacific Northwest university. Of 138 Western blot positives, HerpeSelect® 1 ELISA IgG was 125 positive, 12 negatives, and one equivocal. Of 105 Western blot negatives, HerpeSelect® 1 ELISA IgG was 96 negative, eight positives, and one equivocal. Of three atypical Western blots, HerpeSelect® 1 ELISA IgG was one negative and two positives.

Relative Sensitivity and Relative Specificity with Sexually Active Adults (n = 246) †

Characteristic	% (EL/WB)*	95% CI
Sensitivity relative to Western blot	91.2% (125/137)	85.2-95.4%
Specificity relative to Western blot	92.3% (96/104)	85.4-96.6%

* Excludes three atypical Western blots and two ELISA equivocals.

† The word "relative" refers to comparing this assay's results with those of a similar assay. No attempt was made to correlate the assay results to disease presence or absence. No judgment can be made on the similar assay's accuracy in predicting disease. Assay performed by the manual method.

Relative Sensitivity with Culture Positives †

An outside investigator assessed the device's relative sensitivity using sera from culture positive patients (n = 38). Reference methods included culture (infection) and a HSV-1 Western blot (antibody) from a Pacific Northwest university. Of 38 culture positives: 1) Western blot was 37 positive and one negative; and 2) HerpeSelect® 1 ELISA IgG was 30 positive and eight negative. Of the 37 Western blot positives, HerpeSelect® 1 ELISA IgG was 30 positive and seven negatives.

Relative Sensitivity with Culture Positives (n = 38) †

Characteristic	% (EL/WB or Culture)	95% CI
Sensitivity relative to culture	78.9% (30/38)	62.7-90.4%
Sensitivity relative to Western Blot	81.1% (30/37)	64.8-92.0%

† The word "relative" refers to comparing this assay's results with those of a similar assay. No attempt was made to correlate the assay results to disease presence or absence. No judgment can be made on the similar assay's accuracy in predicting disease. Assay performed by the manual method.

Agreement with CDC Panel †

The following information is from a serum panel obtained from the CDC and tested by Focus Technologies. 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 panel consists of 59% positive and 41% negative samples. The Focus Technologies HerpeSelect® 1 ELISA IgG demonstrated 96.0% total agreement with the CDC results. Of the results obtained by Focus Technologies, there was 93.1% agreement with the positive specimens and 100% agreement with the negative specimens.

† Assay performed by the manual method.

Relative Specificity with a Low Prevalence Population †

An outside investigator assessed the device's relative specificity using sera from a population of college students claiming to lack sexual experience (n = 81), and having a published HSV-1 antibody prevalence of 26.9% (50/186).[13] The laboratory reference method was a HSV-1 Western blot from a Pacific Northwest university. Of 57 Western blot negatives, HerpeSelect® 1 ELISA IgG was 55 negatives, 1 positive and 1 equivocal. Of 24 Western blot positives, HerpeSelect® 1 ELISA IgG was 18 positive and 6 negatives.

Relative Specificity with a Low Prevalence Population (n = 81) †

Characteristic	% (EL/WB)*	95% CI
Specificity relative to Western blot	98.2% (55/56)	90.5-100%
Sensitivity relative to Western blot	75.0% (18/24)	53.3-90.2%

* Excludes one ELISA equivocal.

† The word "relative" refers to comparing this assay's results with those of a similar assay. No attempt was made to correlate the assay results to disease presence or absence. No judgment can be made on the similar assay's accuracy in predicting disease. Assay performed by the manual method.

Type Specificity with HSV-2 Western Blot Positives †

An outside investigator assessed the device's type specificity using HSV-2 Western blot positive and HSV-1 Western Blot negative sera from the above described populations (n = 90): expectant mothers, sexually active adults, low prevalence persons, and HSV-2 culture positives. Of 90 HSV-2 Western blot positive and HSV-1 Western blot negative samples, HerpeSelect® 1 ELISA IgG was 82 negatives, and eight positives.

Type Specificity with HSV-2 Western Blot Positives (n = 90)

Characteristic	% (EL/WB)	95% CI
Type-specificity relative to WB	91.1% (82/90)	83.2-96.1%
Type cross-reactivity relative to WB	8.9% (8/90)	3.9-16.8%

† The word "relative" refers to comparing this assay's results with those of a similar assay. No attempt was made to correlate the assay results to disease presence or absence. No judgment can be made on the similar assay's accuracy in predicting disease. Assay performed by the manual method.

Cross-reactivity with Taxonomically Related Viruses †

Focus assessed the device's cross-reactivity using sera (n = 26) that were 1) HSV sero-negative by another manufacturer's FDA cleared HSV ELISAs, and 2) IFA IgG positive for taxonomically similar viruses including CMV, EBV VCA, HHV6 and VZV. Discrepants between the FDA cleared HSV ELISAs and the HerpeSelect® 1 ELISA IgG were analyzed using a type specific Western blot from a major university located in the Northwestern United States. Excluding one HerpeSelect® 1 ELISA IgG equivocal that was not analyzed with the Western blot because of insufficient volume.

Cross-reactivity with Taxonomically Related Viruses

IFA IgG Pos	% Focus EL Neg	95% CI
CMV	100% (12/12)	73.5-100%
EBV VCA	100% (24/24)	85.5-100%
HHV6	100% (24/24)	85.5-100%
VZV	100% (23/23)	85.2-100%
Total	100% (83/83)	95.7-100%

† Assay performed by the manual method.

Intra-assay and Inter-assay Reproducibility †
An internal investigator assessed the device's intra-assay and inter-assay reproducibility by assaying seven samples in duplicate, twice a day, for twenty days, for a total of forty runs. Two sets of samples were masked duplicates.

Inter-lot Reproducibility †
An internal investigator assessed the device's inter-lot reproducibility. Seven samples were run on in duplicate and in parallel with three separate lots. Each of the three lots had at least a different lot of Antigen Wells.

Inter-laboratory Reproducibility †
An internal investigator and two off site laboratories assessed the device's inter-laboratory reproducibility. Each of the three laboratories ran seven samples in triplicate on three different days.

Reproducibility †

Sample	Inter- & Intra-assay			Inter-lot		Inter-Laboratory		
	Index Mean	Intra-assay %CV	Inter-assay %CV	Index Mean	Index %CV	Index Mean	Mean of Lab %CVs	%CV of Lab Means
11*	0.1	40.0	50.4	0.1	26.8	0.2	6.6	70.9
16*	0.1	0.0	11.6	0.1	20.2	0.2	23.6	63.1
12**	1.6	3.8	7.0	1.5	8.2	1.4	13.5	7.0
17**	1.6	40.0	5.4	1.4	2.9	1.5	13.0	4.3
13	2.7	3.6	4.9	2.5	11.1	2.4	10.8	5.7
14	3.1	3.9	6.5	2.6	9.4	2.7	10.7	7.5
15	12.0	2.2	5.6	10.9	25.1	14.2	24.3	64.6

* #11 & #16 are masked duplicates.

** #12 & #17 are masked duplicates.

† Assay performed by the manual method

% Agreement between the Manual and Automated Methods

An internal and an external investigator compared % agreement between the HerpeSelect automated method vs. the manual method as part of a CLIA validation for a major clinical laboratory located in Southern California. The external investigator sequentially selected and manually tested 248 samples. Each sample was from an adult, and was submitted for HSV testing. 246 samples were from the US, and two samples from outside the US. Of the 248 samples, the manual method detected 108 negatives, 3 equivocals, and 137 positives. Of the 108 negatives by the manual method, the automated method agreed with 98.1% (106/108). Of the 3 equivocals by the manual method, the automated method agreed with 66.7% (2/3). Of the 137 positives by the manual method, the automated method agreed with 97.8% (134/137). Overall, the two methods agreed 97.6% (242/248). Of the five discrepants, three resolved in favor of the automated method, and the other two did not resolve.

% Agreement between the Manual and Automated Methods

Interpretation*	% Agreement	95% CI
Negative	98.1% (106/108)	93.5-99.8%
Equivocal	66.7% (2/3)	9.4-99.2%
Positive	97.8% (134/137)	93.7-99.5%
Overall	97.6% (242/248)	94.8-99.1%

* Interpretation by manual method.

Reproducibility Using an Automated Instrument

An internal investigator assessed the device's inter-assay and intra-assay reproducibility with an automated instrument. Ten samples were tested in triplicate on three different days. The manual and automated methods agreed 98.9% (89/90). One point from Sample 3 was an outlier (162 standard deviations from the mean).

Reproducibility Using an Automated Instrument

Sample	Mean Index	Intra-assay %CV	Inter-assay %CV
2	0.2	7.8	17.5
7	0.3	9.8	3.1
8	0.4	6.7	6.1
10	1.2	4.4	6.2
9	2.0	7.6	7.0
4	3.0	15.7	3.9
5	3.9	6.8	6.1
3	5.3	14.0	2.2
1	5.6	13.5	1.4
6	7.6	5.0	8.0

Stability after Opening Reagents

An internal investigator assessed stability after the reagents had been opened. The kit was used in the inter-assay/intra-assay reproducibility study (above), re-closed, stored at 2-8C for at least 30 days, and then used again to re-test the same samples. The index values for when the reagents were opened and the two runs after at least 30 days are provided below. There was 96.7% agreement with the index when the reagents were opened.

Stability after Opening Reagents

Sample	Index when Opened	After at Least 30 Days (Run 1)	After at Least 30 Days (Run 2)
2	0.2	0.2	0.2
7	0.3	0.3	0.4
8	0.4	0.3	0.5
10	1.2	1.1	1.6
9	2.0	1.8	2.4
4	3.0	2.8	3.4
5	3.9	3.4	4.5
3	5.3	4.7	5.9
1	5.6	5.3	6.4
6	7.6	6.7	7.8

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 2 9 2002

Michael J. Wagner, Esq.
Senior Regulatory Affairs Specialist
Focus Technologies, Inc.
10703 Progress Way
Cypress, CA 90630

Re: K021429
Trade/Device Name: HerpeSelect ™ 1 ELISA IgG
Regulation Number: 21 CFR 866.3305
Regulation Name: Herpes Simplex Virus Serological Reagents
Regulatory Class: Class III Exempt
Product Code: MXJ
Dated: May 2, 2002
Received: May 3, 2002

Dear Mr. Wagner:

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 the Code of Federal Regulations, Title 21, Parts 800 to 898. 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 Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 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 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory-Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known):K021429

Device Name:

HerpeSelect® 1 ELISA IgG

Indications for Use:

Focus Technologies' HerpeSelect® 1 ELISA IgG test is intended for qualitatively detecting the presence or absence of human IgG class antibodies to HSV-1 in human sera. In conjunction with the Focus HerpeSelect® 2 ELISA IgG, the test is indicated for testing sexually active adults or expectant mothers for aiding in the presumptive diagnosis of HSV infection. The assay can be used manually or in conjunction with an automated system as outlined in the package insert. **The user is responsible for assay performance characteristics when an automated system is used.** The performance of this assay has not been established for use in a pediatric population, for neonatal screening, or for testing of immunocompromised patients.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woodly Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K021429

FOR PRESCRIPTION USE X

(Optional Format 3-10-98)