FEB 9 2000

K993754

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510(k) Summary of Safety and Effectiveness (Page 1 of 6)

Applicant:	**MRL Diagnostics** **a Focus/MRL Inc. Company** **10703 Progress Way** **Cypress, California 90630**
Establishment Registration No:	**2023365**
Contact Person:	**Michael J. Wagner, Esq.**
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E-mail:	**mwagner@mrlinfo.com**
Summary Date:	**October 31, 1999**
Device Name:	**HSV-1 ELISA IgG**
Classification:	**Herpes Simplex Virus Serological Reagents** **21 CFR §866.3305** **Class III**
Predicate Device:	**1) HSV-1 ELISA Test System, Zeus Scientific, Inc.** **2) HSV-1 Western Blot, University of Washington** **3) HSV-1 Culture, University of Washington**

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Device Description: In the MRL Diagnostics HSV-1 ELISA 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) which is directly proportional to the amount of antigen-specific IgG present in the sample. Sample optical density readings are compared with reference cut-off OD readings to determine results.

Intended Use: MRL Diagnostics' HSV-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 MRL HSV-2 ELISA IgG, the test is indicated for 1) testing sexually active adults, with or without a clinical history of herpes, for aiding in the presumptive diagnosis of HSV infection to identify persons who are at risk for transmitting or acquiring HSV so they may be counseled, and 2) testing expectant mothers for aiding in the presumptive assessment of the risk for acquiring and/or transmitting HSV to their child, so they may be counseled.

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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). Serological "truth" was defined using a type specific Western blot from a major university located in the Northwestern United States. Excluding four atypical Western blots and three ELISA equivocals, the observed vs expected prevalences and the positive predictive values (PPV) and negative predictive values (NPV) for the two populations are as follows:

Expected vs Observed Prevalence with Sexually Active Adults & Expectant Mothers

Population	HSV-1 Sero-status	Expected Prevalence		Observed Prevalence	
		%	95% CI	WB	MRL ELISA
Sexually Active Adults*	neg	59.0%	56.3-61.8%	55.7%	54.1%
	+	41.0%	38.2-43.7%	42.3%	43.9%
Expectant Mothers**	neg	65.2%	64.2-66.2%	71.0%	71.8%
	+	34.8%	33.8-35.8%	28.6%	24.5%

* Approximate prevalences for sexually active adult population estimated from unpublished values received from investigator at a major university in the Northwestern United States.

** Approximate prevalences for expected mother population estimated from published values.

Predictive Values vs Prevalence with Sexually Active Adults & Expectant Mothers

Pos Prev	Neg Prev	Sexually Active Adults*				Expectant Mothers**			
		PPV	PPV 95%CI	NPV	NPV 95%CI	PPV	PPV 95%CI	NPV	NPV 95%CI
90%	10%	99.1%	98.1-99.6%	57.1%	39.4-75.9%	99.4%	98.4-99.9%	68.8%	41.6-91.7%
80%	20%	97.9%	95.9-99.1%	75.0%	59.4-87.7%	98.8%	96.5-99.7%	83.2%	61.6-96.1%
70%	30%	96.5%	93.2-98.5%	83.7%	71.5-92.4%	97.9%	94.1-99.6%	89.5%	73.3-97.7%
60%	40%	94.7%	89.7-97.7%	88.9%	79.6-95.0%	96.8%	91.1-99.3%	93.0%	81.0-98.5%
50%	50%	92.2%	85.4-96.6%	92.3%	85.4-96.6%	95.2%	87.2-99.0%	95.2%	86.5-99.0%
40%	60%	88.8%	79.6-94.9%	94.7%	89.8-97.7%	93.0%	82.0-98.5%	96.7%	90.6-99.3%
30%	70%	83.5%	71.4-92.3%	96.5%	93.2-98.5%	89.6%	74.5-97.7%	97.9%	93.7-99.6%
20%	80%	74.8%	59.3-87.5%	98.0%	95.9-99.1%	83.3%	63.0-96.1%	98.8%	96.2-99.7%
10%	90%	56.8%	39.3-75.7%	99.1%	98.1-99.6%	69.0%	43.1-91.6%	99.4%	98.3-99.9%

* MRL HSV-1 ELISA IgG having 91.2% sensitivity & 92.3% specificity with sexually active adults.

** MRL HSV-1 ELISA IgG having 96.0% sensitivity & 95.2% specificity with expectant mothers.

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Sensitivity and Specificity with Expectant Mothers

An outside investigator assessed the device's sensitivity and specificity with masked, archived and unselected sera from expectant mothers (n = 241). Serological "truth" was defined using a type specific Western blot from a major university located in the Northwestern United States. Excluding one atypical Western blots and one ELISA equivocal, the results are:

Sensitivity, Specificity & Predictive Values with Expectant Mothers

Attribute	%	Ratio (n/N)	95% CI
Sensitivity	96.0%	170/177	92.0-98.4%
Specificity	95.2%	59/62	86.5-99.0%
Pos Predictive Value	98.3%	170/173	95.0-99.6%
Neg Predictive Value	88.9%	59/69	75.0-92.8%

Sensitivity, Specificity & Predictive Values with Sexually Active Adults

An outside investigator assessed the device's sensitivity and specificity with masked, archived and unselected sera from sexually active adults over the age of 14 (n = 246). Serological "truth" was defined using a type specific Western blot from a major university located in the Northwestern United States. Excluding three atypical Western blots and two ELISA equivocal, the results are:

Sensitivity, Specificity & Predictive Values with Sexually Active Adults

Attribute	%	Ratio (n/N)	95% CI
Sensitivity	91.2%	125/137	85.2-95.4%
Specificity	92.3%	96/104	85.4-96.6%
Pos Predictive Value	94.0%	125/133	88.5-97.4%
Neg Predictive Value	88.9%	96/108	81.4-94.1%

Sensitivity with Culture Positives

An outside investigator assessed the device's sensitivity using sera from culture positive patients (n = 38). Disease state was defined using culture positivity and a type specific Western blot from a major university located in the Northwestern United States. The results are:

Sensitivity with Culture Positives

Comparison	%	Ratio (n/N)	95% CI
MRL EL vs. Culture	78.9%	30/38	62.7-90.4%
MRL EL vs. WB	81.1%	30/37	64.8-92.0%

Evaluation of CDC's HSV/CMV Panel

An internal investigator evaluated the CDC's HSV/CMV serum panel (n = 99). The CDC panel 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 results of the CDC panel evaluation were:

Evaluation of CDC's HSV/CMV Panel

Interpretation			%	Ratio (n/N)	95% CI
CDC HSV-1	CDC HSV-1	MRL ELISA			
+	+ or neg	+	93.1%	54/58	83.3-98.1%
+	neg	neg	100%	13/13	75.3-100%
neg	neg	neg	100%	28/28	87.7-100%

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Specificity with a Low Prevalence Population

An outside investigator assessed the device's specificity using sera from a low prevalence population of college students. Serological "truth" was defined using a type specific Western blot from a major university located in the Northwestern United States. Excluding one ELISA equivocal, the results are:

Specificity with a Low Prevalence Population

Interpretation		%	Ratio (n/N)	95% CI
WB-1	MRL ELISA			
neg	neg	98.2%	55/56	90.5-100%
+	+	75.0%	18/24	53.3-90.2%

Type Specificity with HSV-2 Western Blot Positives

An outside investigator assessed the device's type specificity using HSV-1 Western blot negative and HSV-2 Western blot positive sera from the above described populations (n = 90): expectant mothers, sexually active adults, low prevalence persons, and HSV-1 culture positives. Serological "truth" was defined using a type specific Western blot from a major university located in the Northwestern United States. The results are:

Type Specificity with HSV-2 Western Blot Positives

Group			%	Ratio (n/N)	95% CI
WB-1	WB-2	MRL EL			
neg	+	neg	91.1%	82/90	83.2-96.1%
neg	+	+	8.9%	8/90	3.9-16.8%

Cross-reactivity with Taxonomically Related Viruses

MRL assessed the device's cross-reactivity using sera (n=26) from 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 MRL device were analyzed using a type specific Western blot from a major university located in the Northwestern United States. Excluding one ELISA equivocal that was not analyzed with the Western blot because of insufficient volume, the results are:

Cross-reactivity with Taxonomically Related Viruses

IFA IgG Pos	% MRL EL Neg	Ratio (n/N)	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%

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Intra-assay and Inter-assay Reproducibility Study

MRL assessed the device's intra-assay and inter-assay reproducibility using a slightly modified version of "Evaluation of Precision Performance of Clinical Chemistry Devices", NCCLS Document EP5-T2 (March 1992). Briefly, seven samples were run in duplicate, twice a day, for twenty days, for a total of forty runs, for a total of forty data points for each sample. Two sets of samples were masked duplicates.

Intra-assay & Inter-assay Reproducibility

Sample	Index Mean	Intra-assay % CV	Inter-assay % CV
11*	0.10	40.0%	50.4%
16*	0.10	0.0%	11.6%
12**	1.58	3.8%	7.0%
17**	1.55	40.0%	5.4%
13	2.67	3.6%	4.9%
14	3.08	3.9%	6.5%
15	11.96	2.2%	5.6%

* #11 & #16 are masked duplicates. ** #12 & #17 are masked duplicates.

Inter-lot Reproducibility

An internal investigator assessed the device's inter-lot reproducibility. Five samples were run on three separate days with three separate lots. For one lot, the samples were run in triplicate, and run in duplicate with the other two lots. Each of the three lots had at least a different lot of Antigen Wells. The results are:

Inter-lot Reproducibility

Sample	Index Mean	% CV
11*	0.09	26.8%
16*	0.09	20.2%
12**	1.47	8.2%
17**	1.41	2.9%
13	2.48	11.1%
14	2.64	9.4%
15	10.85	25.1%

* #11 & #16 are masked duplicates. ** #12 & #17 are masked duplicates.

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.

Inter-lab Reproducibility

Sample	Mean Index	%CV of Lab Means	Mean of Lab %CVs
11*	0.15	6.6%	70.9%
16*	0.15	23.6%	63.1%
12**	1.44	13.5%	7.0%
17**	1.48	13.0%	4.3%
13	2.37	10.8%	5.7%
14	2.72	10.7%	7.5%
15	14.24	24.3%	64.6%

* #11 & #16 are masked duplicates. ** #12 & #17 are masked duplicates.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 9 2000

Mr. Michael J. Wagner, Esq.
Senior Regulatory Affairs Specialist
MRL Diagnostics
10703 Progress Way
Cypress, California 90630

Re: K993754
Trade Name: HSV-1 ELISA IgG Test
Regulatory Class: III
Product Code: MXJ
Dated: January 31, 2000
Received: February 2, 2000

Dear Mr. Wagner:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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 (Premarket Approval), 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 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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 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): K993754

Device Name:

HSV-1 ELISA IgG

Indications for Use:

MRL Diagnostics' HSV-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 MRL HSV-2 ELISA IgG, the test is indicated for 1) testing sexually active adults, with or without a clinical history of herpes, for aiding in the presumptive diagnosis of HSV infection to identify persons who are at risk for transmitting or acquiring HSV so they may be counseled, and 2) testing expectant mothers for aiding in the presumptive assessment of the risk for acquiring and/or transmitting HSV to their child, so they may be counseled.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K993754

Prescription Use X OR Over-The Counter Use ____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)