

Summary of Safety and Effectiveness Information
Herpes Group IgG ELISA Test Kit

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II. Description of Device

The Herpes Group IgG ELISA kit is an Enzyme-Linked Immunosorbent Assay (ELISA) for qualitative determination of IgG antibodies in human serum to *Herpes simplex* virus. The Herpes Group IgG ELISA kit may be used to evaluate paired sera for the presence seroconversions of IgG as an aid in the diagnosis of *Herpes simplex* virus infection.

The Herpes Group IgG ELISA test is an enzyme linked immunosorbent assay to detect IgG antibodies to *Herpes simplex* virus. Purified Herpes Group antigen is attached to a solid phase microtiter well. Diluted test sera is added to each well. If the antibodies are present that recognize the antigen, they will bind to the antigen in the well. After incubation the wells are washed to remove unbound antibody. An enzyme labeled anti-human IgG is added to each well. If antibody is present it will bind to the antibody attached to the antigen on the well. After incubation the wells are washed to remove unbound conjugate. A substrate solution is added to each well. If enzyme is present the substrate will undergo a color change. After an incubation period the reaction is stopped and the color intensity is measured photometrically, producing an indirect measurement of specific antibody in the patient specimen.

III. Predicate Device

The Herpes Group IgG ELISA test is substantially equivalent to Clarks HSV I and HSV II ELISA tests. Equivalence is demonstrated by the following comparative results:

Performance Characteristics

1. **Relative sensitivity and specificity.** Four different sites compared the Wampole Herpes Group IgG ELISA test relative to Clarks HSVI and HSVII ELISA assays. The first site was a R&D laboratory at a commercial company located in Maryland. The frozen sera were from normals with ages from 12-83, with various gender, and geographical areas. The results of the study are compiled and summarized in Table 1.

Note: Please be advised the "relative" refers to the comparison of this assay's results to that of a similar assay. There was not an attempt to correlate the assay's results with disease presence or absence. No judgment can be made on the comparison assay's accuracy to predict disease.

Table 1
Comparison of Herpes Group IgG ELISA and Clark HSV 1 and HSV 2
Study 1

		Wampole Herpes Group IgG ELISA			Total
		+	eq	-	
Clark HSV 1 & HSV 2	+*	104	1	1	106
	eq**	3	0	0	3
	-***	4	2	72	78
	Total	111	3	73	187

Relative Sensitivity = $104/105 = 99.1\%$ 95% Confidence interval = 97.2% - 100%
 Relative Specificity = $72/76 = 94.7\%$ 95% Confidence interval = 89.6% - 99.9%
 Relative Agreement = $176/181 = 97.2\%$ 95% Confidence interval = 94.8% - 99.7%

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.

- * Indicates positive on Clark HSV 1 and/or Clark HSV 2.
- ** Indicates equivocal on Clark HSV 1 and/or Clark HSV 2.
- *** Indicates negative on both Clark HSV 1 and Clark HSV 2.

The second site was a R&D laboratory at a commercial company located in New York. The frozen sera were from normals with ages from 17-59, with various gender, and geographical areas. The results of the study are compiled and summarized in Table 2.

Table 2
Comparison of Herpes Group IgG ELISA and Clark HSV 1 and Clark HSV 2
Study 2

		Wampole Herpes Group IgG ELISA			
		+	eq	-	Total
Clark HSV 1 and HSV 2	+*	92	6	2	100
	eq**	1	0	0	1
	-***	0	0	51	51
	Total	93	6	53	152

Relative Sensitivity = $92/94 = 97.9\%$ 95% Confidence interval = 94.9% - 100%
 Relative Specificity = $51/51 = 100\%$ 95% Confidence interval = 94.2% - 100%
 Relative Agreement = $143/145 = 98.6\%$ 95% Confidence interval = 96.7% - 100%

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.
 The 95% confidence interval for specificity was calculated assuming one false positive.

- * Indicates positive on Clark HSV 1 and/or Clark HSV 2.
- ** Indicates equivocal on Clark HSV 1 and/or Clark HSV 2.
- *** Indicates negative on both Clark HSV 1 and Clark HSV 2.

The third site was a clinical laboratory located in Pennsylvania. The sera were prospective samples sent in to the lab for Herpes antibody testing. The results of the studies are compiled and summarized in Table 3.

Table 3
Comparison of Herpes Group IgG ELISA and Clark HSV 1 and Clark HSV 2
Study 3

		Wampole Herpes Group IgG ELISA			
		+	eq	-	Total
Clark HSV 1 and HSV 2	+*	112	0	1	113
	eq**	1	0	1	2
	-***	3	4	54	61
	Total	116	4	56	176

Relative Sensitivity = $112/113 = 99.1\%$ 95% Confidence interval = 97.4% - 100%
 Relative Specificity = $54/57 = 94.7\%$ 95% Confidence interval = 88.8% - 100%
 Relative Agreement = $166/170 = 97.7\%$ 95% Confidence interval = 95.3% - 100%

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.

- * Indicates positive on Clark HSV 1 and/or Clark HSV 2.
- ** Indicates equivocal on Clark HSV 1 and/or Clark HSV 2.
- *** Indicates negative on both Clark HSV 1 and Clark HSV 2.

The fourth site was a clinical laboratory located in Wisconsin. The frozen sera were random normal samples. The results of the studies are compiled and summarized in Table 4.

Table 4
Comparison of Herpes Group IgG ELISA and Clark Herpes 1 & 2
Study 4

		Wampole Herpes Group IgG ELISA			Total
		+	eq	-	
Clark Herpes 1 & 2	+*	62	0	0	62
	eq**	0	0	0	0
	-***	1	0	25	26
	Total	63	0	25	88

Relative Sensitivity = $62/62 = 100.0\%$ 95% Confidence interval = 95.3% - 100%
 Relative Specificity = $25/26 = 96.2\%$ 95% Confidence interval = 96.2% - 100%
 Relative Agreement = $87/88 = 98.9\%$ 95% Confidence interval = 98.9% - 100%

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.
 The 95% confidence interval for sensitivity was calculated assuming one false negative.

- * Indicates positive on Clark HSV 1 and/or Clark HSV 2.
- ** Indicates equivocal on Clark HSV 1 and/or Clark HSV 2.
- *** Indicates negative on both Clark HSV 1 and Clark HSV 2.

The results of the four studies are compiled and summarized in Table 5.

Table 5
Comparison of Herpes Group IgG ELISA and Clark HSV 1 and HSV 2

		Wampole Herpes Group IgG ELISA			
		+	eq	-	Total
Clark HSV 1 & HSV 2	+*	370	7	4	381
	eq**	5	0	1	6
	-***	7	6	203	216
	Total	382	13	208	603

Relative Sensitivity = $370/374 = 98.9\%$ 95% Confidence interval = 97.9% - 100%
 Relative Specificity = $203/210 = 96.7\%$ 95% Confidence interval = 94.2% - 99.1%
 Relative Agreement = $573/584 = 98.1\%$ 95% Confidence interval = 97.0% - 99.2%

Equivocals were not included in the above calculations.
 The 95% confidence intervals were calculated using the normal method.

- * Indicates positive on Clark HSV 1 and/or Clark HSV 2.
- ** Indicates equivocal on Clark HSV 1 and/or Clark HSV 2.
- *** Indicates negative on both Clark HSV 1 and Clark HSV 2.

2. Precision. Seven sera were assayed ten times each on three different assays at three different sites. The intersite precision is shown in Table 6. With appropriate technique the user should obtain precision of <15% CV.

Table 6 Herpes Group IgG ELISA Inter Site Precision Study

Sera #	(n = 90)		
	X	SD	CV
1.	3.81	0.351	9.21%
2.	2.03	0.255	12.6%
3.	3.16	0.287	9.08%
4.	2.01	0.272	13.5%
5.	1.31	0.198	15.1%
6.	0.09	0.109	121%
7.	0.03	0.045	150%

3. CF Paired Serum Study. Twenty serum pairs tested by CF from patients suspected of having acute *Herpes simplex* infection were assayed on the Herpes Group IgG ELISA assay. Each serum pair was evaluated to determine a seroconversion. Six serum pairs could not be evaluated due to the acute being positive.

Three serum pairs could not be evaluated due to the convalescent being negative. The remaining eleven pairs all demonstrated a seroconversion thus giving a 100% sensitivity versus CF for showing a seroconversion in antibody for serum meeting the paired sera criteria.

4. Cross-Reactivity. Serum containing IgG antibody detectable by ELISA to Epstein Barr Virus, Cytomegalovirus, and Varicella Zoster Virus were assayed. The data summarized in Table 7 indicates that antibodies to these Herpes Viruses do not cross-react with the Herpes IgG ELISA kit.

Table 7 Cross-reactivity Study

SERUM	Herpes Group IgG	EBV VCA	CMV	VZV
1	0.17	2.6	Negative	2.7
2	0.05	2.3	Negative	1.6
3	0.00	Negative	Negative	2.2
4	0.00	1.8	Negative	2.0
5	0.14	6.3	1.2	2.1
6	0.08	2.4	Negative	3.3
7	0.09	1.1	Negative	2.1
8	0.12	7.2	1.1	3.2
9	0.18	Negative	2.9	3.0

Sera ≥ 1.10 were considered positive.

Sera ≤ 0.90 were considered negative.

The following information is from a serum panel obtained from the CDC and tested by Wampole Herpes Group IgG ELISA. 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 72% positive and 28% negative samples. Excluding two equivocal, the Wampole Herpes Group ELISA demonstrated 96.9% total agreement with the CDC results. Of the results obtained by the Wampole Herpes Group IgG ELISA, excluding two equivocal, there was 95.7% agreement with the positive specimens, and 100% agreement with the negative specimens.