K131334

GOLD STANDARD DIAGNOSTICS

FEB 28 2014

510(k) Summary

1) **Submitter's Name:** Gold Standard Diagnostics
   Address: 2851 Spafford St. Davis, CA. 95618
   Phone Number: 530-759-8000
   Fax Number: 530-759-8012
   Contact Person: Napoleon Monce
   Date: February 11, 2014

2) **Product and Trade Name:**
   Herpes Simplex Virus Type 1 IgG ELISA Test

   Common Name:
   Herpes Simplex Virus, HSV-1

   Classification Name:
   Herpes simplex virus serological assays (Class 2, 21 CFR 866.3305)

   Product Code: MXJ

3) **Legally marketed device to which the submitter claims equivalence:**
   Focus Diagnostics HerpeSelect® 1 and 2 Immunoblot IgG for the qualitative detection of human IgG class antibody to HSV-1 and HSV-2. K000238.

4) **Description of the device:**
   The Gold Standard Diagnostics Herpes Simplex Virus (HSV) Type 1 IgG ELISA Test is an enzyme linked immunosorbent assay for the qualitative detection of IgG antibodies to HSV-1 in human serum. The assay requires a total of 90 minutes incubation time. The test uses microtiter wells coated with a recombinant gG1 protein of HSV-1. Serum is added to each well and incubated for 30 minutes at 37°C. If antibodies are present they will bind to the antigen in the well. Unbound antibodies are removed by washing the wells three times. A Horse Radish Peroxidase (HRP)-conjugated goat anti-human IgG (conjugate) is then added to each well and incubated for 30 minutes at 37°C. If antibodies are present in the patient's serum, the conjugate will bind to the antibody attached to the antigen on the well. The wells are again washed to remove any unbound conjugate. In order to detect the bound conjugate a substrate containing tetramethylbenzidine (TMB) is added to each well and incubated for 30 minutes at 37°C. If conjugate is present, the HRP will react with the substrate to generate a colored product. After the incubation period, the reaction is stopped with a Stop Solution and the color intensity is measured spectrophotometrically. The kit also includes a Wash Buffer, Diluent, a Negative Control, Positive Control, and a Cutoff Control. The cut-off control is used to determine the validity of the assay and subsequently to determine the result of the

sample. Positive and Negative controls are provided to determine if the assay is functioning properly. The kit contains 12 x 8well antigen coated microtiter strips in a frame. The reagents are sufficient for 96 determinations.

5) Intended Use / Indication for Use:

The Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test Kit is intended for the qualitative detection of IgG antibodies to Herpes Simplex Virus Type 1 (HSV-1) in human serum. The test is indicated for sexually active individuals and expectant mothers as an aid for the presumptive diagnosis of HSV-1 infection.

The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1. The test is not intended for screening of blood and plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates, or immunocompromised patients.

6) Comparison with the predicate device:

The Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test Kit was compared to a commercially manufactured by Focus Diagnostics, the HerpeSelect® 1 and 2 Immunoblot IgG test (K000238). Both kits have the same intended use. Below are tables comparing the reagents provided and the procedural steps performed by each device.

Table 1: Reagent Comparison

Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test Kit	Focus HerpeSelect® 1 and 2 Immunoblot IgG
Antigen coated Microtiter Plate – 96 wells	Antigen coated nitrocellulose strips
Wash Solution – 20x	Wash Buffer and Diluent – 10x
Diluent – Ready to Use	None
IgG Conjugate – Anti Human HRP	IgG Conjugate – Anti Human Peroxidase
Substrate – Tetramethylbenzidine (TMB)	Substrate – BCIP/NBT
Stop Solution – Acid mixture	Stop Solution – DI water
Positive Control	Positive Control
Cutoff Control	No Cutoff Control provided
Negative Control	Negative Control

Table 2: Procedure Comparison

Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test Kit	Focus HerpeSelect® 1 and 2 Immunoblot IgG
Intended Use: Qualitative detection of IgG antibodies to HSV-1 in human serum. The test is indicated for sexually active individuals and expectant mothers as an aid for the	Same

presumptive diagnosis of HSV-1 infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1. The test is not intended for screening of blood and plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates, or immunocompromised patients.	
Dilute Samples 1:101 in Diluent	Same
Add 100ul of Samples and Controls	Add 2ml of Samples and Controls
Incubate for 30 minutes at 37°C	Incubate for 60 minutes at RT while rocking
Wash four times with reconstituted Wash Solution	Wash three times with Wash Solution with 5 minute rocking incubation between washes
Add 100ul of Conjugate	Add 2ml of Conjugate
Incubate for 30 minutes at 37°C	Incubate for 60 minutes at RT while rocking
Wash four times with reconstituted Wash Solution	Wash three times with Wash Solution with 5 minute rocking incubation between washes
Add 100ul of Substrate	Add 2ml of Substrate
Incubate for 30 minutes at 37°C	Incubate for 5 to 30 minutes at RT while rocking
Add 50ul of Stop Solution	Rinse with DI water to stop the reaction
Read with Spectrophotometer at 450nm	Read visually

7) Analytical performance:

Precision:

A within-lab precision study was conducted for 12 days, two runs per day, two replicates per run and three lots. Every lot was tested for four days. The mean results are summarized in the table below:

Sample	N	Units		Within-Run	Between-Run	Between-Day	Total
High Positive	48	58.452	SD	1.544	1.261	5.644	7.652
			CV	2.6%	2.5%	9.7%	13.1%
Moderate Positive	48	24.955	SD	1.290	1.088	2.982	3.653
			CV	5.2%	5.0%	11.9%	14.6%
Low Positive	48	18.183	SD	0.664	0.601	1.856	2.732
			CV	3.7%	3.8%	10.2%	15.0%
Near	48	13.691	SD	0.601	0.501	1.388	1.871

Cutoff			CV	4.4%	4.2%	10.1%	13.7%
High Negative	48	6.565	SD	0.388	0.343	0.579	0.950
			CV	5.9%	6.1%	8.8%	14.5%
Negative	48	1.899	SD	0.153	0.133	0.256	0.342
			CV	8.0%	8.0%	13.5%	18.0%

Reproducibility:

The reproducibility of the assay was performed using six samples (a high positive, a low positive, a sample near the positive cutoff, a sample near the negative cutoff, a high negative and a negative sample). Each sample was tested for five days, twice a day, at three sites with two technicians per site, each performing one run per day. The mean results of the overall and per site reproducibility are summarized in the tables below:

Overall								
Sample	**N**	**Mean (Units)**		**Within-Run**	**Between-Run**	**Between-Day**	**Between-Site**	**Overall Total**
High Positive	60	60.909	SD	2.487	2.535	3.749	4.952	5.788
			CV	4.1%	4.2%	6.2%	8.1%	9.5%
Low Positive	60	14.754	SD	0.775	0.758	0.957	1.369	2.156
			CV	5.2%	5.1%	6.5%	9.3%	14.6%
Positive Cutoff	60	11.821	SD	0.235	0.235	0.379	0.615	0.617
			CV	2.0%	2.0%	3.2%	5.2%	5.2%
Negative Cutoff	60	9.585	SD	0.108	0.105	0.174	0.254	0.280
			CV	1.1%	1.1%	1.8%	2.7%	2.9%
High Negative	60	7.508	SD	0.194	0.195	0.447	0.760	0.821
			CV	2.6%	2.6%	6.0%	10.1%	10.9%
Negative	60	1.579	SD	0.093	0.094	0.160	0.213	0.231
			CV	5.9%	6.0%	10.1%	13.5%	14.6%

Site 1							
Sample	**N**	**Mean**		**Within-Run**	**Between-Run**	**Between-Day**	**Overall Total**
High Positive	20	59.224	SD	2.569	2.643	3.370	4.360
			CV	4.3%	4.5%	5.7%	7.4%
Low Positive	20	13.302	SD	0.868	0.845	0.942	1.303
			CV	6.5%	6.3%	7.1%	9.8%
Positive Cutoff	20	11.759	SD	0.133	0.138	0.291	0.585
			CV	1.1%	1.2%	2.5%	5.0%
Negative Cutoff	20	9.432	SD	0.131	0.121	0.192	0.239
			CV	1.4%	1.3%	2.0%	2.5%

High Negative	20	7.944	SD	0.205	0.199	0.451	0.752
			CV	2.6%	2.5%	5.7%	9.5%
Negative	20	1.693	SD	0.079	0.082	0.165	0.22
			CV	4.7%	4.8%	9.8%	12.9%

Site 2							
Sample	**N**	**Mean**		**Within-Run**	**Between-Run**	**Between-Day**	**Overall Total**
High Positive	20	58.440	SD	2.596	2.662	4.218	5.583
			CV	4.4%	4.6%	7.2%	9.6%
Low Positive	20	13.875	SD	0.787	0.767	0.990	1.462
			CV	5.7%	5.5%	7.1%	10.5%
Positive Cutoff	20	11.846	SD	0.213	0.210	0.285	0.671
			CV	1.8%	1.8%	2.4%	5.7%
Negative Cutoff	20	9.712	SD	0.102	0.104	0.193	0.249
			CV	1.1%	1.1%	2.0%	2.6%
High Negative	20	7.282	SD	0.223	0.230	0.324	0.760
			CV	3.1%	3.2%	4.5%	10.4%
Negative	20	1.473	SD	0.10	0.10	0.15	0.20
			CV	6.6%	6.6%	10.1%	13.7%

Site 3							
Sample	**N**	**Mean**		**Within-Run**	**Between-Run**	**Between-Day**	**Overall Total**
High Positive	20	65.062	SD	2.296	2.300	3.660	4.913
			CV	3.5%	3.5%	5.6%	7.6%
Low Positive	20	17.085	SD	0.669	0.663	0.939	1.341
			CV	3.9%	3.9%	5.5%	7.8%
Positive Cutoff	20	11.857	SD	0.359	0.356	0.561	0.588
			CV	3.0%	3.0%	4.7%	5.0%
Negative Cutoff	20	9.610	SD	0.090	0.091	0.138	0.275
			CV	0.9%	0.9%	1.4%	2.9%
High Negative	20	7.298	SD	0.153	0.155	0.565	0.770
			CV	2.1%	2.1%	7.7%	10.5%
Negative	20	1.571	SD	0.10	0.10	0.17	0.22
			CV	6.5%	6.6%	10.5%	13.9%

Cross Reactivity:

Potential cross reactivity was evaluated for infectious diseases and conditions. The samples were obtained from serum brokers who confirmed positivity for each respective disease and conditions using FDA cleared tests. Samples were tested on the Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test as well as on the predicate device. The results are summarized in the following table:

Positive For	Number Tested	Number Reactive
Cytomegalovirus (CMV)	10	0
Epstein-Barr Virus (EBV)	10	1*
Varicella-zoster Virus (VZV)	10	1*
Chlamydia trachomatis	10	0
Treponema pallidum	10	0
Human papilloma virus (HPV)	10	0
Rubella Virus	10	0
Toxoplasma gondii	10	3*
Candida albicans	10	2*
Neisseria gonorrhea	10	0
Rheumatoid Factor	10	0
ANA	10	0
Measles	10	0
HSV-2	10	0
HIV	10	4*
Bacteroides	1	0

*Samples were also reactive with the predicate device assay

Interfering Substances:

The effect of potential interfering substances on samples using the Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test was evaluated. High levels of hemoglobin, bilirubin, cholesterol, Triglycerides, and albumin in serum samples were tested at the assay cutoff in triplicate. The recommended concentrations from the guideline "Interference Testing In Clinical Chemistry" from the Clinical and Laboratory Standards Institute were used (CLSI EP7-A2). An acceptance criterion of ±20% was used. The tested substances did not affect the performance of the Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test if tested in the following concentration:

Substance	Concentration
Hemoglobin	2 g/L
Bilirubin	342 µmol/L
Cholesterol	13 mmol/L
Triglycerides	37 mmol/L
Albumin	60 g/L

Clinical performance:

Performance in the Intended Use Populations

The performance of the Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA assay was determined by conducting a correlation study tested at three different sites using a total of 703 samples representative of the intended use population, pregnant women and sexually active adults at risk. The samples were tested on both the Gold Standard Herpes Simplex Virus Type 1 IgG ELISA assay and a commercially available Herpes Simplex Virus Line Blot test being manufactured by

Focus Diagnostics. Samples from pregnant women and sexually active adult were prospectively collected, submitted for HSV testing. The combined results from all three sites are summarized in the following tables, sorted according to the intended use population tested. Equivocal results were treated as the worst case results (disagreement):

Pregnant Women		Focus Diagnostics HSV-1 Line Blot	
		Positive	Negative
Gold Standard Diagnostics HSV-1 IgG ELISA	Positive	96	1
	Equivocal	1	2
	Negative	3	82

Sensitivity = 96.0% (96/100) (95% C.I. = 90.1% - 98.9%)
Specificity = 96.5% (82/85) (95% C.I. = 90.0% - 99.3%)

Sexually Active Adults		Focus Diagnostics HSV-1 Line Blot	
		Positive	Negative
Gold Standard Diagnostics HSV-1 IgG ELISA	Positive	275	8
	Equivocal	3	2
	Negative	20	210

Sensitivity = 92.3% (275/298) (95% C.I. = 88.6% - 95.0%)
Specificity = 95.5% (210/220) (95% C.I. = 91.8% - 97.8%)

Performance in a Low Prevalence Population

The low prevalence samples were prospectively collected in a non-STD setting from sera ages 16-19 years old. They were only tested in-house. Equivocal results were treated as the worst case/disagreement results.

Low Prevalence		Focus Diagnostics HSV-1 Line Blot	
		Positive	Negative
Gold Standard Diagnostics HSV-1 IgG ELISA	Positive	15	3
	Equivocal	0	3
	Negative	1	78

Sensitivity = 93.8% (15/16) (95% C.I. = 69.7% - 99.8%)
Specificity = 92.9% (78/84) (95% C.I. = 85.1% - 97.3%)

Performance with a CDC Seroconversion Panel

A seroconversion panel consisting of well-characterized HSV 1 serum samples was obtained from the CDC and tested on the Gold Standard Herpes Simplex Virus Type 1 IgG ELISA test in an in-house study. The results are summarized in the table below. Equivocal results were treated as worst case/disagreement results.

[redacted]		CDC	
		Positive	Negative
Gold Standard Diagnostics HSV-1 IgG ELISA	Positive	45	3
	Equivocal	0	0
	Negative	1	51

Sensitivity = 97.8% (45/46) (95% C.I. = 88.5% - 99.9%)
Specificity = 94.4% (51/54) (95% C.I. = 84.6% - 98.8%)

Expected Values

To determine the prevalence of the test, a total of 703 sera consisting of pregnant women and sexually active adults were tested. The observed prevalence and the hypothetical prevalence for the two intended use populations are summarized below.

Observed Prevalence with Pregnant Women					
Age (years)	**Pos**	**Equ**	**Neg**	**Total**	**Prevalence**
16-19	7	0	11	18	**38.9%**
20-24	20	0	11	31	**64.5%**
25-29	23	0	18	41	**56.1%**
30-34	26	2	28	56	**46.4%**
35-39	16	1	14	31	**51.6%**
>40	5	0	3	8	**62.5%**
Totals	**97**	**3**	**85**	**185**	**53.5%**

Observed Prevalence with Sexually Active Adults					
Age (years)	**Pos**	**Equ**	**Neg**	**Total**	**Prevalence**
16-19	22	0	26	48	**45.8%**
20-24	27	1	50	78	**34.6%**
25-29	55	1	63	119	**46.2%**
30-34	58	1	30	89	**65.2%**
35-39	28	1	22	51	**54.9%**
>40	93	1	39	133	**69.9%**
Totals	**283**	**5**	**230**	**518**	**55.0%**

Hypothetical Predictive Values vs. Prevalence				
	Sexually Active Adults		Pregnant Women	
Prevalence	PPV	NPV	PPV	NPV
50%	95.4%	92.5%	96.5%	96.0%
40%	93.2%	94.9%	94.8%	97.3%
30%	89.8%	96.7%	92.2%	98.3%
25%	87.2%	97.4%	90.1%	98.6%
20%	83.7%	98.0%	87.3%	99.0%
15%	78.4%	98.6%	82.9%	99.3%
10%	69.5%	99.1%	75.3%	99.5%
5%	51.9%	99.6%	59.1%	99.8%

(Results are the worst case/disagreement results)

8) Conclusion:

From the data, we find that the Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA assay is substantially equivalent to the commercially available Herpes Simplex Virus Line Blot test being manufactured by Focus Diagnostics (K000238).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

GOLD STANDARD DIAGNOSTICS
NAPLEON MONCE
DIRECTOR OF PRODUCT DEVELOPMENT
2851 SPAFFORD ST
DAVIS CA 95618

February 28, 2014

Re: K131334
Trade/Device Name: Herpes Simplex Virus Type 1 IgG Elisa Test
Regulation Number: 21 CFR 866.3305
Regulation Name: Herpes simplex virus serological assays
Regulatory Class: II
Product Code: MXJ
Dated: January 29, 2014
Received: January 30, 2014

Dear Mr. Monce:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); 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.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Stephen J. Lovell -S for

Sally A. Hojvat, M.Sc., PhD.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K131334

Device Name
Herpes Simplex Virus Type 1 IgG ELISA Test

Indications for Use *(Describe)*
The Gold Standard Diagnostics Herpes Simplex Virus Type 1 IgG ELISA Test Kit is intended for the qualitative detection of IgG antibodies to Herpes Simplex Virus Type 1 (HSV-1) in human serum. The test is indicated for sexually active individuals and expectant mothers as an aid for the presumptive diagnosis of HSV-1 infection.

The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1. The test is not intended for screening of blood and plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates, or immunocompromised patients.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Stephen J. Lovell -S
2014.02.28 10:53:31 -05'00'

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