JUN 25 1999

K 984346

510(k) SUMMARY
FOR
PREMIER™ TYPE SPECIFIC
HSV-2 IgG ELISA TEST

SUBMITTER: Gull Laboratories, Inc.
1011 Murray Holladay Road
Salt Lake City, UT 84117
(801) 263-3524

CONTACT PERSON: Fred W. Rachford

DATE: June 22, 1999

DEVICE NAME:

Trade/Proprietary Name:	Premier™ Type Specific HSV-2 IgG ELISA Test
Common/Usual Name:	Anti-HSV-2 IgG Antibody Test
Classification Name:	Herpes Simplex Virus Type 2 Serological Reagent

PREDICATE DEVICE: HSV-2 IgG ELISA Test / Gull Laboratories, Inc.

DEVICE DESCRIPTION:

The Premier™ Type Specific HSV-2 IgG ELISA Test is an *in vitro* diagnostic medical device is intended for the qualitative detection of IgG antibody to the herpes simplex virus type 2 in human serum by the enzyme-linked immunosorbent assay (ELISA) method.

The Premier™ Type Specific HSV-2 IgG ELISA Test is comprised of the following items:

1. Antigen-Coated ELISA Plate: One 96-well plate comprised of twelve 8-well strips with breakaway wells, each well coated with affinity purified HSV-2 glycoprotein G (gG-2).

2. IgG Specimen Diluent: One bottle containing 30 ml of a lavender colored dilution buffer with sodium azide.

3. Conjugate: One bottle containing 15 ml of a pink colored solution of alkaline phosphatase-labeled antihuman IgG (Caprine) with sodium azide.

4. Substrate Buffer: One bottle containing 30 ml of a blue colored buffer solution with sodium azide.

5. p-NPP Tablets: One foil pack containing 6 tablets of p-nitrophenyl phosphate (p-NPP).

6. Stopping Reagent: One bottle containing 30 ml of a colorless solution of 1.5 N sodium hydroxide (NaOH).

7. Positive Control and Negative Control: One vial of each containing 200 µl of serum (human) with sodium azide.

8. Reference Serum: One vial containing 400 µl of serum (human) with sodium azide.

9. 20X Wash Solution: One bottle containing 60 ml of a green colored solution with detergent and sodium azide.

10. ELISA Plate Sealer: One acetate sheet with contact adhesive.

11. Resealable Storage Bag: One plastic sealable bag.

12. ELISA Worksheet: One worksheet for recording data.

When the Premier™ Type Specific HSV-2 IgG ELISA Test is employed, diluted patient serum is incubated with purified herpes simplex virus type 2 glycoprotein (gG2) bound to the ELISA plate wells. If antibodies to the herpes simplex virus type 2 are present, they bind to the antigen and do not rinse off. Subsequently when enzyme-labeled antihuman IgG is added to the reaction site it binds to the immobilized IgG antibodies. After washing and the addition of a chromogenic substrate and stopping reagent, specimens containing antibodies to the herpes simplex virus type 2 produce a color endpoint reaction which can be read with a standard ELISA plate reader.

INTENDED USE:

The Premier™ Type Specific HSV-2 IgG ELISA Test is intended for the qualitative detection of IgG antibody to herpes simplex virus type 2 in human serum by the enzyme-linked immunosorbent assay (ELISA) method. When performed according to instructions, the Premier™ Type Specific HSV-2 IgG ELISA Test is of value in the determination of immunological experience pertaining to infection with HSV-2 and as an aid in the diagnosis of herpes simplex virus-associated disease.

The Premier™ Type Specific HSV-2 IgG ELISA Test is not recommended for use in a pediatric population. The performance characteristics of this device have not been established for testing patients with other HSV associated disease, prenatal and neonatal screening, the testing of immunosuppressed patients, or the detection of early stages of HSV seroconversion.

TECHNOLOGICAL COMPARISON TO PREDICATE DEVICE:

The Premier™ Type Specific HSV-2 IgG ELISA Test and the HSV-2 IgG ELISA Test both are technologically based on the enzyme-linked immunosorbent assay (ELISA) method.

SUBSTANTIAL EQUIVALENCE PERFORMANCE DATA:

Seven hundred fifty six serum samples prospectively collected from unduplicated individuals attending two STD Clinics in the Pacific Northwest Region of the US were tested with the Premier™ Type Specific HSV-2 IgG ELISA Test and a Western Blot Method for type specific IgG antibody to HSV-2. Western Blot results were based on initial testing with the exception of specimens with initial atypical results which were reanalyzed. These repeat Western Blot results were used for patients returning for repeat analysis. Patients not returning for repeat testing were presumed to be negative. Specimens initially reported as equivocal with the Premier™ Type Specific HSV-2 IgG ELISA Test were retested with the second test result used. The relative agreement between the two methods was 93.1% (704/756). The relative sensitivity and relative specificity of the Premier™ Type Specific HSV-2 IgG ELISA Test were 80.5% (182/226) with a 95% confidence interval of 74.1%-85.7% and 98.5% (522/530) with a 95% confidence interval of 96.9%-99.3% respectively when compared with the Western Blot results. The predictive value positive and predictive value negative were 95.8% (182/190) with a 95% confidence interval of 91.6%-98.0% and 92.2% (522/566) and a 95% confidence interval of 89.6%-94.2% respectively.

Frozen samples of sequential sera from 193 patients were submitted to a clinical laboratory in the Pacific Northwest Region of the US for HSV antibody detection and typing. These specimens were tested for IgG antibodies to HSV-2 using the

Premier™ Type Specific HSV-2 IgG ELISA Test and a Western Blot Method for detection of HSV type specific antibody. The relative agreement between the two test systems was 97.2% (174/179) with a 95% confidence interval of 93.6%-99.1%. The relative sensitivity and relative specificity of the Premier™ Type Specific HSV-2 IgG ELISA Test were 98.0% (50/51) with a 95% confidence interval of 89.5%-99.9% and 96.9% (124/128) with a 95% confidence interval of 92.2%-99.1% respectively when compared with the Western Blot results. There were ten specimens which demonstrated either equivocal ELISA results or atypical Western Blot results and four specimens that could not be typed by Western Blot which were not included in the above calculations. The calculations for the 95% confidence interval were made by the Exact Method.

The following information is from a serum panel obtained from the Centers for Disease Control (CDC) and tested by Gull Laboratories, Inc. 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.

A serum panel comprised of one hundred clinical specimens (50 paired sera) was tested using the Premier™ Type Specific HSV-2 IgG ELISA Test. These specimens were characterized previously by CDC EIA and Western Blot testing. The panel of 100 samples contains more than 30% positive anti-HSV-2 samples. The Premier™ Type Specific HSV-2 IgG ELISA Test demonstrated 95.0% total agreement with the CDC results. Of the results obtained with the Premier™ Type Specific HSV-2 IgG ELISA Test there was 86.1% agreement with the anti-HSV-2 positive specimens and 100.0% agreement with the anti-HSV-2 negative specimens.

Three hundred thirty five archived serum samples from patients with culture documented HSV-2 infection were tested with the Premier™ Type Specific HSV-2 IgG ELISA Test. Based on repeat testing of equivocal samples 89.3% (299/335) of the serum samples from culture positive patients tested positive in the Premier™ Type Specific HSV-2 IgG ELISA Test. Since the above study was performed on pre-selected retrospective specimens, the assay's positive and negative predictive values could not be calculated or inferred.

The Premier™ Type Specific HSV-2 IgG ELISA Test also was used to test serum samples from individuals in low prevalence populations to determine the specificity of the assay. Serum samples from (a) one hundred ninety nine pediatric patients, one to twelve years of age, in the Northeast Region of the US, (b) two hundred nine individuals attending a University Student Health Clinic in the Pacific Northwest Region of the US, and (c) one hundred Blood Bank donors in the Northeast Region of the US were tested with the Premier™ Type Specific HSV-2 IgG ELISA Test and a Western Blot Method for type specific IgG antibody to HSV-2. Western Blot results were based on initial testing with the exception of specimens with initial atypical results which were reanalyzed. These repeat Western Blot results were used for analysis. Specimens initially reported as

equivocal with the Premier™ Type Specific HSV-2 IgG ELISA Test were retested with the second test result used.

For the pediatric patient specimens the relative agreement between the two methods was 78.9% (157/199). The relative sensitivity and relative specificity of the Premier™ Type Specific HSV-2 IgG ELISA Test were 100.0% (2/2) with a 95% confidence interval of 1.6%-100.0% and 78.7% (155/197) with a 95% confidence interval of 73.0%-84.4% respectively when compared to the Western Blot results. The predictive value positive and predictive value negative were 4.5% (2/44) with a 95% confidence interval of 0.6%-15.5% and 100.0% (155/155) and a 95% confidence interval of 97.6%-100.0% respectively.

For the University Student Health Clinic specimens the relative agreement between the two methods was 96.6% (198/205). The relative sensitivity and relative specificity of the Premier™ Type Specific HSV-2 IgG ELISA Test were 60.0% (3/5) with a 95% confidence interval of 14.7%-94.7% and 97.5% (195/200) with a 95% confidence interval of 94.3%-99.2% respectively when compared to the Western Blot results. The predictive value positive and predictive value negative were 37.5% (3/8) with a 95% confidence interval of 8.5%-75.5% and 99.0% (195/197) and a 95% confidence interval of 96.4%-99.9% respectively. There were four specimens which either demonstrated equivocal ELISA or atypical Western Blot results which were not included in the calculations.

For the Blood Bank specimens the relative agreement between the two methods was 91.0% (91/100). The relative sensitivity and relative specificity of the Premier™ Type Specific HSV-2 IgG ELISA Test were 76.5% (13/17) with a 95% confidence interval of 49.8.3%-92.2% and 94.0% (78/83) with a 95% confidence interval of 85.9%-97.8% respectively when compared with the Western Blot results. The predictive value positive and predictive value negative were 72.2% (13/18) with a 95% confidence interval of 46.9%-89.3% and 95.1% (78/82) with a 95% confidence interval of 87.3%-98.4% respectively.

CONCLUSIONS:

The Premier™ Type Specific HSV-2 IgG ELISA Test is believed to be substantially equivalent to the HSV-2 IgG ELISA Test. This assessment is based on (1) the two tests are technologically equivalent, both being based on the enzyme-linked immunosorbent assay methods, (2) the intended use of each test is comparable with both being used for the qualitative determination of antibody to HSV-2 with the Premier™ Type Specific HSV-2 IgG ELISA Test having improved specificity, and (3) the data from clinical studies conducted at Gull Laboratories, Inc. and two outside clinical institutions demonstrated acceptable agreement and the relative sensitivity and relative specificity when test results were compared with the expected specimen reactivity showed the Premier™ Type Specific HSV-2 IgG ELISA Test to demonstrate superior specificity for IgG antibody to HSV-2.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUN 25 1999

Alan Nickol, Ph.D.
Director of Clinical and Regulatory Affairs
Meridian Diagnostics, Inc.
3471 River Hills Drive
Cincinnati, OH 45244

Re: K984346
Trade Name: Premier™ Type Specific HSV-2 IgG ELISA Test
Regulatory Class: III
Product Code: LGC
Dated: April 4, 1999
Received: April 6, 1999

Dear Dr. Nickol:

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.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

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" (21 CFR 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 at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/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

EXHIBIT F - REVISED 06/22/99

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K984346

Device Name: PREMIER™ TYPE SPECIFIC HSV-2 IgG ELISA TEST

Product Number: H2S100

Indications For Use:

The PREMIER™ TYPE SPECIFIC HSV-2 IgG ELISA TEST is to be used in the testing of human serum specimens from individuals for whom the qualitative presence or absence of detectable IgG antibody to herpes simplex virus type 2 is warranted; specifically, when used in conjunction with the Premier™ Type Specific HSV-1 IgG ELISA in the screening of sexually active adults. This test is indicated for individuals at risk for a sexually transmitted HSV infection or disease (STD). For example, this test is to be used to screen samples from patients with or without clinical history of herpes and can clarify when an individual with symptoms suggestive of genital herpes has genital HSV-2 infection.

The PREMIER™ TYPE SPECIFIC HSV-2 IgG ELISA TEST is not recommended for use in a pediatric population. The performance characteristics of this device have not been established for prenatal and neonatal screening, the testing of patients with other HSV associated diseases and immunosuppressed patients, or the detection of early stages of HSV seroconversion.

(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 K984346