JUL 12 1999

K992191

510 (k) SUMMARY

SUBMITTED BY:

Judith J. Smith
DiaSorin, Inc.
9175 Guilford Rd. Suite 100
Columbia, MD 21046

NAME OF DEVICES:

Trade Name: DiaSorin ETI-EA-G
Epstein-Barr Viral Early Antigen Diffuse
EA (D) IgG ELISA

Common Names/Descriptions: Immunoassay for the detection of IgG antibodies to the Epstein-Barr Viral (EBV) Early Antigen Diffuse antigen

Classification Names: EBV Serology Test

PREDICATE DEVICES: DiaSorin EBV EA (D) IgG Clin-ELISA™
Gull Laboratories EBV EA IgG IFA

DEVICE DESCRIPTION:

INTENDED USE: The DiaSorin ETI-EA-G kit uses Enzyme Linked Immunosorbent Assay (ELISA) technology for the qualitative and/or semi-quantitative detection of IgG antibodies to the EBV Early Antigen Diffuse. The assay is designed for human serum. The presence of EA antibodies is used as an aid in the diagnosis of EBV associated infectious mononucleosis when used in conjunction with other EBV serologies in pediatric, adult, transplant donor and transplant recipient populations. When evaluating properly paired sera, the results of these assays are used to demonstrate seroconversion or significant change in antibody titer as evidence of recent infection. Both specimens should be tested simultaneously.

KIT DESCRIPTION: The method for the determination of specific anti-EA (D) IgG utilizes the enzyme-linked immunosorbent assay (ELISA) technique. Polystyrene microtiter wells are coated with recombinant EA (D) antigen. Diluted patient serum is incubated with the purified antigen bound to the solid surface of a microtiter well. The EA (D) IgG antibodies present in a patient's serum will be captured by the solid phase. After washing, affinity purified polyclonal goat anti-human IgG (Fc) antibodies conjugated to horseradish peroxidase are added to the well. After this incubation, chromogen containing tetramethylbenzidine is added. Enzyme action on the chromogen results in a color reaction. The color can be detected with a photometer at a wavelength of 450 nm. The measured enzyme activity is directly proportional to the concentration of specific anti-EA (D) IgG bound to the solid phase.

PERFORMANCE DATA:

Comparative Clinical Trial: Clinical trials were conducted at 1 clinical laboratory to evaluate the performance of ETI-EA-G in detecting IgG antibodies to EBV EA (D). Assay performance was compared to the Gull Laboratories, Inc. EA IgG IFA test. Patients from the disease states defined below were tested. The screening population is a group of samples from patients suspected of disease. The transplant recipients were patients who had received, or were awaiting, solid organ or bone marrow transplants. Patient samples excluded if they failed to fit a recognized EBV marker pattern determined by EBV VCA (IgG, IgM) and EBNA testing. Results are shown below.

Primary Disease State; Adult Population

Expected Pattern	+
Sensitivity (95% CI)	45/46 = 97.8% (88.5 – 99.9%)
Specificity (95% CI)	N/A
Agreement	45/46 = 97.8%
Prevalence ELISA	45/46 = 97.8%
Prevalence IFA	46/46 = 100%
Expected Prevalence	80-100%

Primary Disease State; Pediatric Population

Expected Pattern	+
Sensitivity (95% CI)	26/29 = 89.7% (72.6 – 97.8%)
Specificity (95% CI)	N/A
Agreement	26/29 = 89.7%
Prevalence ELISA	26/29 = 89.7%
Prevalence IFA	29/29 = 100%
Expected Prevalence	80-100%

Seronegative; Adult Population

Expected Pattern	-
Sensitivity (95% CI)	N/A
Specificity (95% CI)	7/7 = 100.0% (59.0 – 100.0%)
Agreement	7/7 = 100.0%
Prevalence ELISA	0/7 = 0.0%
Prevalence IFA	0/7 = 0.0%
Expected Prevalence	0%

Seronegative; Pediatric Population

Expected Pattern	-
Sensitivity (95% CI)	N/A
Specificity (95% CI)	48/50 = 96.0% (86.3 – 99.5%)
Agreement	48/50 = 96.0%
Prevalence ELISA	2/50 = 4.0%
Prevalence IFA	0/50 = 0.0%
Expected Prevalence	0%

Reactivated; Adult Population

Expected Pattern	+
Sensitivity (95% CI)	30/31 = 96.8% (83.3-99.9%)
Specificity (95% CI)	N/A
Agreement	30/31 = 96.8%
Prevalence ELISA	30/31 = 96.8%
Prevalence IFA	31/31 = 100%
Expected Prevalence	90-100%

Reactivated; Pediatric Population

Expected Pattern	**+**
Sensitivity (95% CI)	4/4 = 100.0% (39.8 – 100.0%)
Specificity (95% CI)	N/A
Agreement	4/4 = 100.0%
Prevalence ELISA	4/4 = 100.0%
Prevalence IFA	4/4 = 100.0%
Expected Prevalence	90-100%

Past Infection; Adult Population

Expected Pattern	**-/+**
Sensitivity (95% CI)	12/33 = 36.4% (20.4 – 54.9%)
Specificity (95% CI)	3/4= 75.0% (19.4-99.4)
Agreement	15/37 = 40.5%
Prevalence ELISA	13/37 = 32.4%
Prevalence IFA	33/37 = 89.2%
Expected Prevalence	10-40%

Past Infection; Pediatric Population

Expected Pattern	**-/+**
Sensitivity (95% CI)	2/3 = 66.7% (9.0 – 99.9)
Specificity (95% CI)	N/A
Agreement	2/3 = 66.7%
Prevalence ELISA	2/3 = 66.7%
Prevalence IFA	3/3 = 100.0%
Expected Prevalence	10-40%

Transplant Recipient patients; Adult Population

ELISA Result	EA (D) IgG
Sensitivity (95% CI)	10/21 = 47.6% (25.7 – 70.2%)
Specificity (95% CI)	1/3 = 33.3% (0.8% - 90.6%)
Agreement	11/24 = 45.8%
Prevalence ELISA	12/24 = 50.0%
Prevalence IFA	21/24 = 87.5%

Transplant Recipient patients; Pediatric Population

ELISA Result	EA (D) IgG
Sensitivity (95% CI)	N/A
Specificity (95% CI)	6/7 = 85.7% (42.1 – 99.6%)
Agreement	6/8 = 75.0%
Prevalence ELISA	1/8 = 12.5%
Prevalence IFA	1/8 = 12.5%

The ETI-EA-G ELISA demonstrates good sensitivity and specificity in Primary, Seronegative and Reactivated populations. The prevalence rates were within the expected range for each of these populations.

In the Past Infection population the prevalence rate for ETI-EA-G was consistent with published rates of 10-40%, while IFA rates were 90%. This appears to reflect the fact that the IFA detects both the Restricted and the Diffuse EA antigen, while ETI-EA-G detects only the Diffuse antigen. The Restricted antigen is only occasionally seen in acute IM cases, and then only late in the acute phase. Following IM, however, the Restricted antigen persists in a substantial number of patients for at least 10–104 months. In light of this, it is predictable that the Gull IFA would detect Early Antigen at a much higher rate in a Past Infection population than would the ETI-EA-G ELISA. The same situation appears to account for the results seen in the Transplant Recipients who included a high percentage of samples with EBV markers consistent with Past Infection. The results support the Transplant claim in the Intended Use.

Within each of the defined disease states, results were similar across the adult and pediatric populations, supporting the separate adult and pediatric claims in the Intended Use for ETI-EA-G.

Reproducibility: Reproducibility studies were performed at 3 sites using one lot of ETI-EA-G reagents. Assay reproducibility was determined using 6 samples that spanned

the range of the assay. Samples were tested in triplicate once a day for 3 days. Combined results are summarized below.

Reproducibility for ETI-EA-G based on Arbitrary Units (AU)

		Within-run	Between day	Between site	Total
Sample	Mean (AU)	%CV	%CV	%CV	%CV
Negative	7.6	12.14	22.02	14.77	21.63
Negative	9.2	14.24	24.19	20.01	19.61
low pos	29.4	7.57	4.97	11.37	8.18
low pos	26.0	13.47	12.32	9.59	15.88
mid pos	74.5	9.71	2.68	3.36	10.12
high pos	122.4	6.74	3.06	0.98	6.64

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 12 1999

DiaSorin, Inc.
c/o Ms. Carole Stamp
TÜV Product Service, Inc.
1775 Old Highway 8 NW
Suite 104
New Brighton, MN 55112-1891

Re: K992191
Trade Name: DiaSorin ETI-EA-G
Regulatory Class: I
Product Code: LSE
Dated: June 25, 1999
Received: June 28, 1999

Dear Ms. Stamp:

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

INDICATIONS FOR USE

510(k) Number (if known): Not known

Device Name: DiaSorin ETI-EA-G

Indications For Use:

The DiaSorin ETI-EA-G kit uses Enzyme Linked Immunosorbent Assay (ELISA) technology for the qualitative and/or semi-quantitative detection of IgG antibodies to the EBV Early Antigen Diffuse. The assay is designed for human serum. The presence of EA antibodies is used as an aid in the diagnosis of EBV associated infectious mononucleosis when used in conjunction with other EBV serologies in pediatric, adult, transplant donor and transplant recipient populations. When evaluating properly paired sera, the results of these assays are used to demonstrate seroconversion or significant change in antibody titer as evidence of recent infection. Both specimens should be tested simultaneously.

(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 K992191

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

(Optional Format 1-2-96)