

K973123

MAR 26 1998

Summary of Safety and Effectiveness Information  
EA-D IgG ELISA Test Kit

I. Immuno Probe Inc.  
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Frederick, Maryland 21701  
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Date of preparation: Jan 7, 1998

II. Description of Device

The Epstein-Barr Early Antigen Diffuse component (EA-D) IgG kit is an Enzyme-Linked Immunosorbent Assay (ELISA) for the qualitative determination of IgG antibodies in human serum to EA-D antigen. The Clark anti-EA-D IgG assay may be used in conjunction with other Epstein-Barr serologies (VCA IgG, VCA IgM, EBNA-1 IgG, EBNA-1 IgM and heterophile) as an aid in the diagnosis of infectious mononucleosis.

**For In Vitro Diagnostic Use Only.**

The EA-D IgG ELISA test is an enzyme linked immunosorbent assay to detect IgG antibodies to Epstein-Barr Early Antigen Diffuse component. Purified recombinant EA-D 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 EA-D IgG ELISA test is substantially equivalent to EBV serology. Equivalence is demonstrated by the following comparative results:

## Performance Characteristics

### 1. Sensitivity and Specificity Based on Serum Characterization

One hundred and ninety three selected serum were tested at a clinical lab. The serum from the study were characterized as seronegative ( no serological evidence of past or present EBV infection), early acute (VCA IgM and heterophile antibody present, EBNA IgG absent), late acute or transitional (VCA IgM, EBNA IgG and heterophile antibody present, approximately 4-12 weeks post infection), or seropositive (presence of VCA IgG antibodies and EBNA IgG, no evidence of VCA IgM or heterophile antibody, indicative of past infection). The sensitivity, specificity and agreement of the assay was determined based on this characterization. It was assumed that the EA-D IgG response should be negative for seronegative; early acute, and convalescent serum, and positive for late acute or transitional serum. The results are summarized in Table 1.

**Table 1**

		Early Acute VCA IgM+ EBNA IgG - Heterophile +	Late Acute VCA IgM+ EBNA IgG + Heterophile +	Seropositive VCA IgG+ EBNA IgG+ VCA IgM- Heterophile -	Seronegative VCA IgG- EBNA IgG - VCA IgM - Heterophile -
Clark EA-D IgG	Positive	1	9	26	0
	Equivocal	1	0	3	1
	Negative	32	0	106	14
	Total	34	9	135	15

Relative Sensitivity (Late Acute)	= 9/9	= 100%	95% Confidence Interval = 67.9%-100%*
Relative Specificity (Seronegative)	= 14/14	= 100%	95% Confidence Interval = 79.1%-100%*
Relative Specificity (Early Acute)	= 32/33	= 97.0%	95% Confidence Interval = 91.0%-100%
Relative Sensitivity (Seropositive)	= 26/132	= 19.7%	95% Confidence Interval = 12.8%-26.6%
Relative Specificity (Seropositive)	= 106/132	= 80.3%	95% Confidence Interval = 73.4%-87.2%
Relative Agreement	= 161/188	= 85.6%	95% Confidence Interval = 80.5%-90.8%

Equivocal results were not included in the calculations.

Equivocal results were not retested. They were reported as equivocal.

The 95% confidence intervals were calculated using the normal method.

\* The 95% confidence interval was calculated assuming one false result.

2. **Precision.** Seven different sera were assayed ten times each on three different assays at three different sites to determine the precision of the assay. The data from this study is presented in Table 2.

**Table 2**  
**EA-D IgG ELISA**  
**Inter-Site Precision Data**

<u>Serum #</u>	<u>X</u>	<u>S.D.</u>	<u>C.V.</u>
1	1.43	0.126	8.83%
2	1.29	0.100	7.73%
3	2.14	0.128	5.96%
4	2.12	0.124	5.85%
5	0.96	0.085	8.84%
6	0.31	0.035	11.35%
7	0.24	0.040	16.34%
HPC (n=9)	2.86	0.062	2.18%
CAL (n=27)	2.22	0.074	3.32%
LPC (n=9)	1.79	0.082	4.59%
NC (n=9)	0.01	0.012	154.52%

Serum #5 was the only serum to change status. It was equivocal 66 times, negative 21 times, and positive 3 times.

X = Mean ISR  
parameters.

SD = Standard Deviation

CV = Coefficient of Variation

The methods in NCCLS EP5 were utilized for precision

**3. Cross-Reactivity.** Serum containing IgG antibody detectable by ELISA to Herpes Simplex Virus I & II, Cytomegalovirus, and Varicella Zoster Virus were assayed. The data summarized in Table 3 indicates that antibodies to these Herpes Viruses do not cross-react with the EA-D IgG EIA kit.

**Table 3**  
**EA-D Cross-Reactive Sera**

<b>Serum</b>	<b>EA-D IgG</b>	<b>Alternate Assay</b>
1	0.26	3.59 (VZV IgG)
2	0.83	7.58 (VZV IgG)
3	0.45	2.17 (VZV IgG)
4	0.40	2.77 (VZV IgG)
5	0.74	3.95 (CMV IgG)
6	0.54	2.44 (CMV IgG)
7	0.31	1.57 (CMV IgG)
8	0.37	3.45 (HSV 1 IgG)
9	0.53	3.51 (HSV 1 IgG)
10	0.56	3.70 (HSV 1 IgG)
11	0.38	3.57 (HSV 2 IgG)
12	0.64	3.58 (HSV 2 IgG)

Sera  $\geq 1.10$  were considered positive.

Sera  $\leq 0.90$  were considered negative.



Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

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Clark Laboratories, Inc  
c/o Mr. William L. Boteler  
Immuno Probe, Inc.  
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Frederick, Maryland 21701

Re: K973123  
Trade Name: EA-D IgG ELISA  
Regulatory Class: I  
Product Code: LSE  
Dated: January 7, 1998  
Received: January 12, 1998

Dear Mr. Boteler:

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 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.

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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 I. Gutman, M.D., M.B.A.  
Director  
Division of Clinical Laboratory Devices  
Office of Device Evaluation  
Center for Devices and Radiological Health

Enclosure

