SEP 27 2002

1.10 510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K021793

Applicant Information:

Date Prepared:	September 26, 2002
Name:	PANBIO Limited
Address:	116 Lutwyche Road Windsor 4030 Australia
Contact Person:	Helen Jennings
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Device Information:

Trade Name:	EBV EA-D IgG ELISA Kit
Common Name:	EBV EA-D IgG EIA Test
Classification Name:	EBV EA-D IgG Serological Reagent

Equivalent Device:
Trinity Biotech Captia™ EBV EA-D IgG ELISA

Device Description: The EBV EA-D IgG ELISA Kit is an enzyme-linked immunosorbent assay (ELISA) for the detection of IgG antibodies to EBV EA-D antigen in human serum.

Intended Use: The Epstein Barr Virus Early Diffuse Antigen (EBV EA-D) IgG ELISA Test is for the qualitative detection of IgG antibodies to EBV EA-D as an aid in the diagnosis of EBV infection in patients with clinical symptoms of Infectious Mononucleosis (IM). The PANBIO EBV EA-D IgG ELISA should be used in conjunction with other EBV serologies.

Principle of Procedure:

Serum antibodies of the IgG class, when present, combine with EBV Early Antigen, which is purified by immunoaffinity chromatography, and attached to the polystyrene surface of the microwells. Residual serum is removed by washing and peroxidase conjugated anti-human IgG is added. The microwells are washed and a colourless substrate system, tetramethylbenzidine/ hydrogen peroxide (TMB/H_2O_2) is added. The substrate is hydrolysed by the enzyme and the chromogen changes to a blue colour. After stopping the reaction with acid, the TMB becomes yellow. Colour development is indicative of the presence of EBV EA-D IgG antibodies in the test sample.

PERFORMANCE CHARACTERISTICS

Study Site 2:

346 frozen retrospective sera of various ages and genders were submitted to a state health laboratory in Maryland USA for EBV testing. The sera include samples from the following groups: 52 seronegative samples, 51 samples from patients with acute Infectious Mononucleosis, and 243 samples from patients with past exposure to EBV.

These sera were tested on the PANBIO EBV EA-D IgG ELISA and the Trinity Biotech EBV EA-D IgG ELISA. The PANBIO results were compared to the EBV status of the sera to determine the sensitivity, specificity, and agreement of the assay relative to the EBV serological status (table 1). Additionally, the Trinity Biotech results were compared to the EBV serological status (table 2), and the PANBIO versus the Trinity Biotech results (table 3) and are summarised below.

TABLE 1
EBV STATUS VERSUS PANBIO ELISA

	PANBIO ELISA			
EBV Status	Positive	Equivocal	Negative	Total
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	0	1	51	52
Acute VCA IgM (+) EBNA IgG (-)	16	6	29	51
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	60	22	161	243
Total	76	29	241	346

			95% Confidence Interval
Relative Sensitivity (Acute)	= 16/51	= 31.4 %	19.1 – 45.9 %
Relative Sensitivity (Past)	= 60/243	= 24.7%	19.3 – 30.1%
Relative Specificity (Past)	= 161/243	= 66.3 %	60.3 – 72.2 %
Relative Specificity (Negative)	= 51/52	= 98.1 %	89.7 – 100.0 %
Relative Agreement	= 228/346	= 65.9 %	60.9 – 70.9 %

*Retesting of equivocal samples was not conducted, as the samples were unavailable.

TABLE 2
EBV STATUS VERSUS TRINITY BIOTECH ELISA

PANBIO ELISA

EBV Status	Positive	Equivocal	Negative	Total
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	4	2	46	52
Acute VCA IgM (+) EBNA IgG (-)	29	6	16	51
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	92	21	130	243
Total	125	29	192	346

			95% Confidence Interval
Relative Sensitivity (Acute)	= 29/51	= 56.9%	42.2 – 70.7%
Relative Sensitivity (Past)	= 92/243	= 37.9%	31.8 – 44.0%
Relative Specificity (Past)	= 130/243	= 53.5%	47.2 – 59.8%
Relative Specificity (Negative)	= 46/52	= 88.5%	76.6 – 95.6%
Relative Agreement	= 205/346	= 59.2%	54.1 – 64.4%

*Retesting of equivocal samples was not conducted, as the samples were unavailable.

TABLE 3
TRINITY BIOTECH VERSUS PANBIO ELISA

PANBIO ELISA

Trinity Result	Positive	Equivocal	Negative	Total
Positive	72	16	37	125
Equivocal	2	4	23	29
Negative	2	9	181	192
Total	76	29	241	346

			95% Confidence Interval
Relative Sensitivity	= 72/125	= 57.6%	48.9 – 66.3%
Relative Specificity	= 181/192	= 94.3 %	90.0 – 97.1%
Relative Agreement	= 253/346	= 73.1%	68.5 – 77.8%

*Retesting of equivocal samples was not conducted, as the samples were unavailable.

Study Site 3:

330 prospective sera of various ages and genders were tested at a private pathology laboratory in Queensland Australia for EBV testing. The sera include the following groups: 47 seronegative, 35 with acute infectious mononucleosis and 248 with past exposure to EBV.

These sera were tested on the PANBIO EBV EA-D IgG ELISA and the Trinity Biotech EBV EA-D IgG ELISA. The PANBIO results were compared to the EBV status of the sera to determine the sensitivity, specificity, and agreement of the assay relative to the EBV serological status (table 4). Additionally, the Trinity Biotech results were compared to the EBV serological status (table 5), and the PANBIO versus the Trinity Biotech results (table 6) and are summarised below.

TABLE 4
EBV STATUS VERSUS PANBIO ELISA

	PANBIO ELISA			
EBV Status	**Positive**	**Equivocal**	**Negative**	**Total**
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	2	0	45	47
Acute VCA IgM (+) EBNA IgG (-)	13	0	22	35
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	33	1*	214	248
Total	48	1	281	330

			95% Confidence Interval
Relative Sensitivity (Acute)	= 13/35	= 37.1%	21.5 – 55.1%
Relative Sensitivity (Past)	= 33/248	= 13.3%	9.1 – 17.5%
Relative Specificity (Past)	= 214/248	= 86.3%	82.0 – 90.6%
Relative Specificity (Negative)	= 45/47	= 95.7%	85.5 – 99.5%
Relative Agreement	= 272/330	= 82.4%	78.3 – 86.5%

*Equivocal samples were inconclusive following repeat testing on the alternative method (IFA).

TABLE 5
EBV STATUS VERSUS TRINITY BIOTECH ELISA

PANBIO ELISA

EBV Status	Positive	Equivocal	Negative	Total
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	1	0	46	47
Acute VCA IgM (+) EBNA IgG (-)	21	0	14	35
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	38	1*	209	248
Total	60	1	269	330

			95% Confidence Interval
Relative Sensitivity (Acute)	= 21/35	= 60.0%	42.1 – 76.1%
Relative Sensitivity (Past)	= 38/248	= 15.3%	10.8 – 19.8%
Relative Specificity (Past)	= 209/248	= 84.3%	79.7 – 88.8%
Relative Specificity (Negative)	= 46/47	= 97.9%	88.7 – 99.9%
Relative Agreement	= 276/330	= 83.7%	79.8 – 87.7%

*Equivocal samples were inconclusive following repeat testing on the alternative method (IFA).

TABLE 6
TRINITY BIOTECH VERSUS PANBIO ELISA

PANBIO ELISA

Trinity Biotech	Positive	Equivocal	Negative	Total
Positive	35	1	24	60
Equivocal	0	0	1	1
Negative	13	0	256	269
Total	48	1	281	330

			95% Confidence Interval
Relative Sensitivity	= 35/60	= 58.3%	44.9 – 70.9%
Relative Specificity	= 256/269	= 95.2%	91.9 – 97.4%
Relative Agreement	= 291/330	= 88.2%	84.7 – 91.7%

*Equivocal samples were inconclusive following repeat testing on the alternative method (IFA).

REPRODUCIBILITY

Study Sites 3, 4 & 5:

The reproducibility of the PANBIO EBV EA-D IgG ELISA kit was determined by testing 8 sera 3 times each on three different days at three Australian study sites. Two sites were private pathology laboratories and the third site was PANBIO. Within-run, between day, between site and total precision were estimated by analysis of variance (ANOVA Type II). The results are presented in table 7 below.

TABLE 7 – Reproducibility Data
PANBIO EBV EA-D IgG Study Sites 1, 2 & 3

Precision Measures (Using Ratio)

			Within		Between Day		Between Site		Total	
Sample	**n**	***Mean**	***S.D**	**CV**	***S.D**	**CV**	***S.D**	**CV**	***S.D**	**CV**
Positive	27	1.94	0.39	20.3%	0.00	0.0%	0.08	4.3%	0.39	20.1%
Cut-off	27	1.00	0.11	10.9%	0.00	0.0%	0.00	0.0%	0.10	10.1%
Negative	27	0.11	0.02	18.9%	0.00	0.0%	0.01	5.8%	0.02	19.4%
1	27	3.78	0.34	9.0%	0.00	0.0%	0.16	4.1%	0.36	9.4%
2	27	0.94	0.11	11.7%	0.02	2.4%	0.04	4.7%	0.12	12.5%
3	27	1.61	0.17	10.8%	0.00	0.0%	0.00	0.0%	0.17	10.4%
4	27	0.87	0.09	10.9%	0.00	0.0%	0.00	0.0%	0.09	10.2%
5	27	1.26	0.18	14.0%	0.00	0.0%	0.04	3.3%	0.17	13.9%
6	27	2.51	0.30	12.2%	0.07	2.7%	0.00	0.0%	0.31	12.2%
7	27	1.16	0.11	9.5%	0.11	9.1%	0.06	5.5%	0.15	13.0%
8	27	1.12	0.16	14.0%	0.11	9.9%	0.04	3.7%	0.19	16.5%

SD = Standard Deviation
CV = Coefficient of Variation (%)
* Values calculated from ratios

Site 1: Three days of triplicates
Site 2: Three days of triplicates
Site 3: Three days of triplicates

Note:
Standard Deviation results have been rounded to two decimal places for tabulation purposes.

POTENTIAL CROSS-REACTIVITY

Study Site 5:

This study consisted of a panel of 50 specimens screened for IgG antibodies detectable by ELISA to disease types other than Epstein Barr Virus. The purpose of this study is to establish the analytical specificity of the EBV EA-D IgG ELISA Test, through the analysis of specimens from patients with diseases that have the potential for cross-reactivity. Each of the specimens included in the study was characterized with respect to disease diagnosis prior to analysis of the specimens with the EBV EA-D IgG ELISA Test. Table 9 on the following page lists the cross-reactivity results for each type of specimen included in the disease panel. Table 8 below provides a summary of the cross-reactivity data.

TABLE 8 – PANBIO EBV EA-D IgG

CROSS-REACTIVITY SPECIMEN PANEL SUMMARY

Disease (IgG Antibodies)	Total Specimens	Positive Result
Cytomegalovirus	10	(0/10)
Varicella zoster	13	(0/13)
Herpes simplex virus 1	8	(0/8)
Herpes simplex virus 2	2	(0/2)
Anti-Nuclear Antibody	8	(0/8)
Rheumatoid Factor	9	(0/9)
Total Antibody	**50**	**(0/50)**

Results indicate that no specimens (0/50) were positive when analysed with the EBV EA-D IgG ELISA Kit.

The true negative result of 100% for the above disease panel is consistent with good analytical specificity for the EBV EA-D IgG ELISA Test.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 27 2002

Ms. Kate Wersin
Regulatory Affairs Officer
PANBIO Limited
116 Lutwyche Road
Windsor
Brisbane, Queensland
Australia 4030

Re: k021793
Trade/Device Name: EBV-EA-D IgG ELISA
Regulation Number: 21 CFR 866.3235
Regulation Name: Epstein-Barr Virus Serological Reagents
Regulatory Class: Class I
Product Code: LSE
Dated: August 12, 2002
Received: August 15, 2002

Dear Ms. Wersin:

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), 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 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 Part 801); 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.

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" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/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

510(k) Number (if known): K021793

Device Name: EBV-EA-D IgG ELISA

Indications For Use:

The Epstein Barr Virus Early Diffuse Antigen (EBV EA-D) IgG ELISA Test is for the qualitative detection of IgG antibodies to EBV EA-D as an aid in the diagnosis of EBV infection in patients with clinical symptoms of Infectious Mononucleosis (IM). The PANBIO EBV EA-D IgG ELISA should be used in conjunction with other EBV serologies.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K021793

(Optional Format 3-10-98)