JUN 2 7 2003

PANBIO

K030863

1.10 10(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:

Applicant Information:

Date Prepared:	12th March, 2003
Name:	PANBIO Limited
Address:	116 Lutwyche Road, Windsor Queensland 4030 Australia
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Device Information:

Trade Name:	EBV VCA-p18 IgG ELISA
Common Name:	EBV VCA IgG EIA Test
Classification Name:	Epstein-Barr virus serological reagents.

Equivalent Device:

DiaSorin EBV VCA IgG ELISA

Device Description:

The EBV VCA-p18 IgG ELISA is an Enzyme Linked Immunosorbent Assay for the qualitative detection of IgG antibodies in human serum to EBV VCA antigen.

Intended Use:

The Epstein-Barr Virus Viral Capsid-p18 Antigen (EBV VCA-p18) IgG ELISA is for the qualitative detection of IgG antibodies to EBV VCA in serum as an aid in the clinical laboratory diagnosis of EBV infection in patients with clinical symptoms consistent with infectious mononucleosis (IM). The PANBIO EBV VCA-p18 IgG ELISA should be used in conjunction with other EBV serologies.

Principle of Procedure:

Serum containing antibodies to VCA antigen, when present, combine with EBV VCA-p18 antigen attached to the polystyrene surface of the microwells. The antigen is a synthetically produced peptide. 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 VCA IgG antibodies in the test sample.

PERFORMANCE CHARACTERISTICS

Study Site 1:

342 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: 45 seronegative, 41 with acute infectious mononucleosis and 256 with past exposure to EBV.

These sera were tested on the PANBIO EBV VCA-p18 IgG ELISA and the DiaSorin EBV VCA 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 DiaSorin results were compared to the EBV serological status (Table 2) and PANBIO results (Table 3), as summarised below.

TABLE 1
EBV STATUS VERSUS PANBIO ELISA

	PANBIO ELISA		
EBV Status	**Positive**	**Negative**	**Total**
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	0	45	45
Acute VCA IgM (+) EBNA IgG (-)	28	13	41
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	242	14	256
Total	270	72	342

			95% Confidence Interval
Relative Sensitivity (Acute)	= 28/41	= 68.3%	51.9 – 81.9%
Relative Sensitivity (Past)	= 242/256	= 94.5%	91.0 – 97.0%
Relative Specificity (Negative)	= 45/45	= 100.0%	92.1 – 100.0%
Relative Agreement	= 315/342	= 92.1%	88.7 – 94.7%

TABLE 2
EBV STATUS VERSUS DIASORIN ELISA

	PANBIO ELISA		
EBV Status	**Positive**	**Negative**	**Total**
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	0	45	45
Acute VCA IgM (+) EBNA IgG (-)	35	6	41
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	248	8	256
Total	283	59	342

			95% Confidence Interval
Relative Sensitivity (Acute)	= 35/41	= 85.4%	70.8 – 94.4%
Relative Sensitivity (Past)	= 248/256	= 96.9%	93.9 – 98.6%
Relative Specificity (Negative)	= 45/45	= 100.0%	92.1 – 100.0%
Relative Agreement	= 328/342	= 95.6%	93.2 – 97.7%

TABLE 3
PANBIO VERSUS DIASORIN ELISA

	PANBIO ELISA		
DiaSorin	**Positive**	**Negative**	**Total**
Positive	269	14	283
Negative	1	58	59
Total	270	72	342

			95% Confidence Interval
Relative Sensitivity	= 269/283	= 95.1%	91.8 – 97.3%
Relative Specificity	= 58/59	= 98.3%	90.9 – 100.0%
Relative Agreement	= 327/342	= 95.6%	92.9 – 97.5%

Study Site 3:

148 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: 25 seronegative samples, 23 samples from patients with acute Infectious Mononucleosis, and 100 samples from patients with past exposure to EBV.

These sera were tested on the PANBIO EBV VCA-p18 IgG ELISA and the DiaSorin EBV VCA 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 DiaSorin results were compared to the EBV serological status (Table 5) and PANBIO results (Table 6), as summarised below.

TABLE 4
EBV STATUS VERSUS PANBIO ELISA

PANBIO ELISA

EBV Status	Positive	Equivocal*	Negative	Total
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	0	1	24	25
Acute VCA IgM (+) EBNA IgG (-)	17	1	5	23
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	100	0	0	100
Total	117	2	29	148

			95% Confidence Interval
Relative Sensitivity (Acute)	= 17/23	= 73.9%	51.6 – 89.8%
Relative Sensitivity (Past)	= 100/100	= 100.0%	96.4 - 100%
Relative Specificity (Negative)	= 24/25	= 96.0%	79.6 – 99.9%
Relative Agreement	= 141/148	= 95.3%	90.5 – 98.1%

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

Note: "Serological" sensitivity and specificity refers to the comparison of the PANBIO assay results to that of other assays normally used to diagnose EBV associated IM. There was not an attempt to correlate the assay's results with disease presence or absence. No judgement can be made on the comparison's accuracy to predict disease. Since the above studies were performed on a pre-selected, retrospective, population, no calculations for the assay's positive and negative predictive value may be done or inferred.

TABLE 5
EBV STATUS VERSUS DIASORIN ELISA

	PANBIO ELISA		
EBV Status	**Positive**	**Negative**	**Total**
Seronegative VCA IgG (-) VCA IgM (-) EBNA IgG (-)	2	23	25
Acute VCA IgM (+) EBNA IgG (-)	23	0	23
Past Infection VCA IgG (+) VCA IgM (-) EBNA IgG (+)	100	0	100
Total	125	23	148

			95% Confidence Interval
Relative Sensitivity (Acute)	= 23/23	= 100.0%	85.2 – 100%
Relative Sensitivity (Past)	= 100/100	= 100.0%	96.4 – 100%
Relative Specificity (Negative)	= 23/25	= 92.0%	74.0 – 99.0%
Relative Agreement	= 146/148	= 98.6%	95.2 – 99.8%

TABLE 6
PANBIO VERSUS DIASORIN ELISA

	PANBIO ELISA			
DiaSorin	**Positive**	**Equivocal***	**Negative**	**Total**
Positive	117	1	7	125
Negative	0	1	22	23
Total	117	2	29	148

			95% Confidence Interval
Relative Sensitivity	= 117/125	= 93.6%	87.8 – 97.2%
Relative Specificity	= 22/23	= 95.7%	78.0 – 99.9%
Relative Agreement	= 139/148	= 93.9%	88.8 – 97.2%

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

REPRODUCIBILITY

Study Sites 1, 4 & 5:

The reproducibility of the PANBIO EBV VCA-p18 IgG ELISA 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 Limited. 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
PANBIO EBV VCA-p18 IgG Study
Precision Measures (Using Cut-Off Ratio*)

			Within		Between Day		Between Site		Total	
Sample	**n**	***Mean**	***S.D**	**CV**	***S.D**	**CV**	***S.D**	**CV**	***S.D**	**CV**
Positive	27	2.98	0.17	5.7%	0.06	2.0%	0.11	3.8%	0.20	6.7%
Cut-off	27	1.00	0.05	4.5%	0.00	0.0%	0.00	0.0%	0.04	4.1%
Negative	27	0.18	0.02	8.9%	0.00	2.4%	0.02	12.6%	0.02	13.9%
#1	27	5.11	0.37	7.2%	0.07	1.3%	0.00	0.0%	0.37	7.2%
#2	27	5.06	0.34	6.7%	0.14	2.8%	0.00	0.0%	0.35	7.0%
#3	27	5.35	0.32	6.0%	0.07	1.3%	0.50	9.4%	0.53	9.9%
#4	27	1.30	0.06	4.9%	0.00	0.0%	0.02	1.3%	0.06	4.8%
#5	27	1.93	0.11	5.6%	0.04	2.0%	0.05	2.8%	0.12	6.3%
#6	27	1.81	0.11	6.1%	0.03	1.6%	0.12	6.5%	0.15	8.3%
#7	27	0.97	0.05	5.0%	0.02	1.9%	0.04	4.4%	0.06	6.4%
#8	27	0.90	0.08	9.0%	0.00	0.0%	0.07	7.3%	0.10	10.8%

All values are calculated from Ratios (Cut-off using O.D)
SD = Standard Deviation; CV = Coefficient of Variation

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

*Cut-off Ratio is calculated as the Absorbance of the Sample divided by the Mean Absorbance of the Cut-off.

POTENTIAL CROSS-REACTIVITY

Study Site 5:

This study consisted of a panel of 30 specimens screened for IgG antibodies detectable by ELISA to disease types other than Epstein-Barr virus. The purpose of this study was to establish the analytical specificity of the EBV VCA-p18 IgG ELISA, 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 characterised with respect to disease diagnosis and analysed with the EBV VCA-p18 IgG ELISA. 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 data presented in Table 9 (see next page).

TABLE 8 – PANBIO EBV VCA-p18 IgG CROSS-REACTIVITY SPECIMEN PANEL SUMMARY

Disease (IgG Antibodies)	Total Specimens	Positive Result
Cytomegalovirus	5	(0/5)
Varicella zoster	10	(0/10)
Herpes simplex virus 1	8	(1/8)
Herpes simplex virus 2	1	(0/1)
Anti-Nuclear Antibody	3	(0/3)
Rheumatoid Factor	3	(0/3)
Total Antibody	**30**	**(1/30)**

Results indicate that one specimen (1/30) was positive when analysed with the EBV VCA-p18 IgG ELISA. The overall result of the above disease panel is consistent with good analytical specificity for the EBV VCA-p18 IgG ELISA.

TABLE 9 – PANBIO EBV VCA-p18 IgG CROSS-REACTIVITY SPECIMEN PANEL

	Gull IFA Merifluor EBV IgG Batch No. EB100.091	PANBIO EBV VCA-p18 IgG ELISA Batch No. 02282		Sample IgG Antibodies
	Result	Ratio	Result	
1	N	1.35	N	CMV IgG
2	N	1.82	N	CMV IgG
3	N	1.72	N	CMV IgG
4	N	3.56	N	CMV IgG
5	N	5.92	N	CMV IgG
6	N	3.56	N	VZV IgG
7	N	1.82	N	VZV IgG
8	N	1.18	N	VZV IgG
9	N	3.44	N	VZV IgG
10	N	1.35	N	VZV IgG
11	N	1.28	N	VZV IgG
12	N	5.92	N	VZV IgG
13	N	1.82	N	VZV IgG
14	N	1.60	N	VZV IgG
15	N	1.47	N	VZV IgG
16	N	3.56	N	HSV 1 IgG
17	N	1.97	N	HSV 1 IgG
18	N	5.92	N	HSV 1 IgG
19	N	1.47	N	HSV 1 IgG
20	N	1.28	N	HSV 1 IgG
21	N	1.60	N	HSV 1 IgG
22	N	2.04	N	HSV 1 IgG
23	N	13.73	P	HSV 1 IgG
24	N	5.70	N	HSV 2 IgG
25	N	0.75	N	ANA
26	N	0.73	N	ANA
27	N	0.84	N	ANA
28	N	0.58	N	RF
29	N	0.58	N	RF
30	N	0.67	N	RF

INTERPRETATION

ELISA	Positive = P	Equivocal	Negative = N
PANBIO	> 1.1	0.9 – 1.1	< 0.9

1.11 METHODS OF DATA ANALYSIS

Relative Sensitivity:

True Positives / (True Positives + False Negatives)

Relative Specificity:

True Negatives / (True Negatives + False Positives)

Relative Agreement:

(True Positives + True Negatives) / Total Samples

95% Confidence Interval:

CIA 'Confidence Interval Analysis' Software Program' from "Statistics with Confidence" by Prof. M. J. Gardner and British Medical Journal (1991). Version 1.1.

ANOVA Analysis of Variance Type II:

Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline. NCCLS (1999), EP5-A Vol. 19 No. 2.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 27 2003

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

Re: k030863
Trade/Device Name: EBV VCA-p18 IgG ELISA
Regulation Number: 21 CFR 866.3235
Regulation Name: Epstein-Barr Virus Serological Reagents
Regulatory Class: Class I
Product Code: LSE
Dated: May 13, 2003
Received: May 16, 2003

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 Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 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 information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 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
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

PANBIO

March 12, 2003

510(k) Number: K030863

Device Name: EBV VCA-p18 IgG ELISA

The Epstein Barr Virus Viral Capsid-p18 Antigen (EBV VCA-p18) IgG ELISA Test is for the qualitative detection of IgG antibodies to EBV VCA in serum as an aid in the clinical laboratory diagnosis of EBV infection in patients with clinical symptoms consistent with Infectious Mononucleosis (IM). The PANBIO EBV VCA-p18 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)

Prescription Use ✓ (Per 21 CFR 801.109) OR Over-the Counter Use ____ (Optional Format 1-2-96)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K030863