OCT 2 6 2001

K012449

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: K012449

Applicant Information:

Date Prepared:	October 17, 2001
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Device Information:

Trade Name:	Is anti-Cardiolipin IgG/IgM Test System
Common Name:	Anti-Cardiolipin ELISA test
Classification Name:	Anticardiolipin immunological test system

Equivalent Device:
Orgentec Anti-cardiolipin ELISA Assay

Device Description: The Is anti-Cardiolipin IgG/IgM Test System is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative measurement of IgG or IgM antibodies to cardiolipin in human serum

Intended Use: The assay is intended for the semi-quantitative measurement of IgG or IgM antibodies to cardiolipin in human serum. The results of the assay can be used as an aid in the assessment of the risk of thrombosis in patients with SLE or SLE-like dosorders.

Principle of the Procedure:

The Is-anti-Cardiolipin IgG/IgM Test System is an indirect solid-phase enzyme immunoassay. Highly purified cardiolipin is coated onto plastic microwells and saturated with highly purified human β2-Glycoprotein I. Standards, controls and diluted patient samples are added to the wells. Any patient IgG or IgM antibodies in the sample bind to the well. Anti-human IgG or IgM horseradish peroxidase conjugate is then added After incubation and washing, a substrate solution is then added to each well. In the presence of bound enzyme, the substrate is converted to a blue colored product. After acid additon to stop the reaction, a yellow end product is formed that is read spectrophotometrically at 450 nm (reference 600-630 nm) and is directly proportional to the concentration of cardiolipin IgG or IgM antibodies in the sample.

SUMMARY OF SAFETY AND EFFECTIVENESS

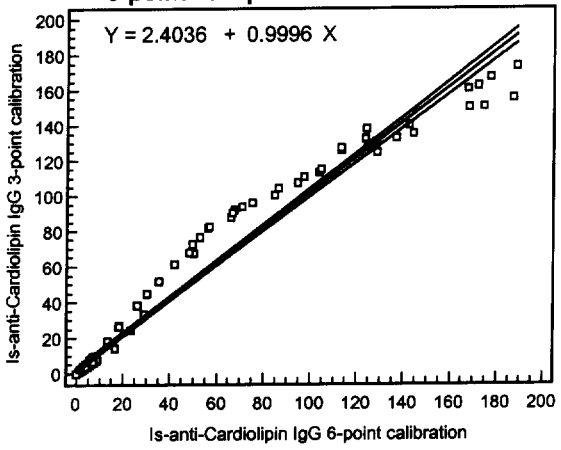
Performance Characteristics

Non-clinical studies were performed using the manual method and 6-point calibration unless otherwise indicated.

A. 3-point vs 6-point calibration

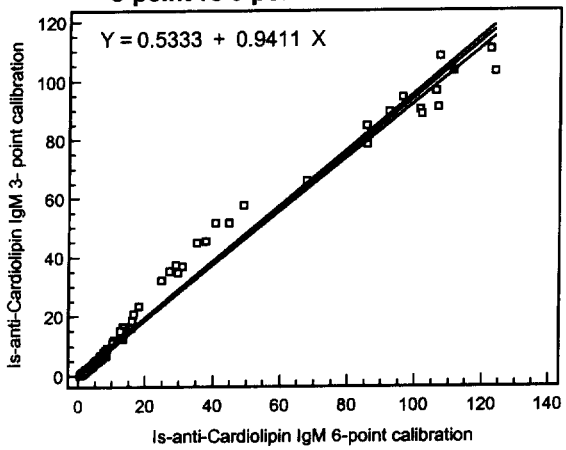
To demonstrate the equivalence of both calibration methods the results of 172 samples tested using the Is-anti-Cardiolipin IgG and 193 samples tested using the Is-anti-cardiolipin IgM calculated using either the 3-point or 6-point calibration systems were subjected to linear regression analysis. Scattergrams and regression lines of the results obtained with 95% confidence intervals are shown in FIGURES 1 and 2. Also included are the regression statistics.

FIGURE 1: Is anti-Cardiolipin IgG
3-point vs 6-point Result Correlation



Intercept	2.4036 (95% CI 1.0456 to 3.7616)
Slope	0.9996 (95% CI 0.9740 to 1.0251)
Sample Size	172
Coefficient of determination	= 0.9723
Correlation coefficient r	= 0.9861
95% CI for r = 0.9812 to 0.9897	

FIGURE 2: Is anti-Cardiolipin IgM
3-point vs 6-point Result Correlation



Intercept	0.5333 (95% CI -0.0325 to 1.0991)
Slope	0.9411 (95% CI 0.9230 to 0.9592)
Sample Size	162
Coefficient of determination	= 0.9850
Correlation coefficient r	= 0.9925
95% CI for r = 0.9898 to 0.9945	

B. Relative Sensitivity and Specificity

One hundred and seventy-two frozen retrospective sera were tested for IgG antibodies and one hundred and ninety--four frozen retrospective sera were tested for IgM antibodies using the Is-anti-Cardiolipin IgG/IgM Test Kit and a commercially available ELISA kit for detecting IgG and/or IgM cardiolipin antibodies. Based on the results of this testing the relative sensitivity, specificity and overall agreement were calculated. The resultsobtained are shown in TABLES 1 and 2. For anti-cardiolipin IgG, further resolution of the discordant samples showed that the four samples that were negative in the Is-anti-Cardiolipin IgG and positive by the other EIA were also negative by a referee EIA method. For anti-cardiolipin IgM, further resolution of the discordant samples showed that of the 16 samples negative in the Is-anti-Cardiolipin IgM and positive in the other EIA, thirteen were negative and three were positive by a referee method.

TABLE 1

Is-anti-Cardiolipin IgG

Other EIA	Positive	Negative	Equivocal
Positive	43	4	0
Negative	0	107	0
*Equivocal	3	15	0

			***95% CI*
Relative Sensitivity	43/47	= 91.5 %	79.6-97.6%
Relative Specificity	107/107	= 100.0%	96.6-100.0%
Overall Agreement	150/154	= 97.4%	93.5-99.3%

TABLE 2

Is-anti-Cardiolipin IgM

	Positive	Negative	Equivocal
Positive	58	16	6
Negative	0	87	0
*Equivocal	0	27	0

			***95% CI*
Relative Sensitivity	58/74	= 78.4 %	767.3-87.1%
Relative Specificity	87/87	= 100.0%	95.8-100.0%
Overall Agreement	145/161	= 90.1%	84.4-94.2%

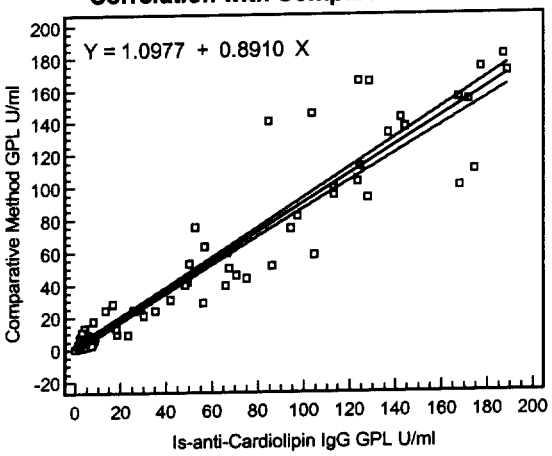
* Equivocal results were excluded from calculations.

** 95% Confidence Intervals (CI) calculated by the Exact Method .

NOTE : Please be advised that 'relative' refers to the comparison of the assay's results to that of a similar assay. 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.

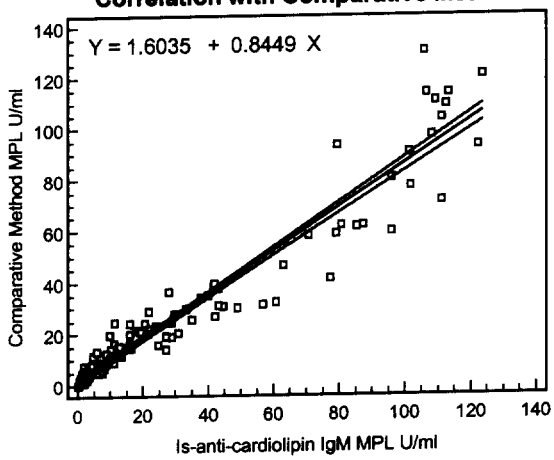
Linear regression analyses and scattergrams for the correlation studies with the comparative method are shown in FIGURES 3 and 4.

FIGURE 3: Is anti-Cardiolipin IgG Correlation with Comparative Method



Intercept	1.0977 (95% CI -0.9942 to 3.1896)
Slope	0.8910 (95% CI 0.8517 to 0.9304)
Coefficient of determination	= 0.9216
Correlation Coefficient r	= 0.9600
95% CI for r	= 0.9463 to 0.9703

FIGURE 4: Is anti-Cardiolipin IgM Correlation with Comparative Method



Intercept	1.6035 (95% CI 0.4892 to 2.7177)
Slope	0.8449 (95% CI 0.8141 to 0.8758)
Coefficient of determination	= 0.9383
Correlation Coefficient r	= 0.9687
95% CI for r	= 0.9586 to 0.9763

C. Clinical Sensitivity and Specificity

A total of three hundred and fifty-four frozen retrospective, clinically characterized sera were assayed using the Is anti-Cardiolipin IgG/IgM Test Kit in order to assess both the clinical sensitivity and clinical specificity of the assay system. These samples consisted of 214 normal sera, 57 sera from patients with diagnosed anti-phospholipid syndrome (APS), 33 sera from patients with systemic lupus erythematosus (SLE), 35 sera from patients with other autoimmune diseases such as Sjogren's Syndrome, scleroderma, polymyositis/dermatomyositis and rheumatoid arthritis and 15 samples from patients with positive RPR titers. Results are summarized in TABLE 3.

Note that the analytical sensitivity, or limit of detection, calculated by assaying Standard A 20 times and taking the mean of these values plus 2 Standard Deviations was determined as being 0.4 GPL or MPL U/ml.

TABLE 3

Patient Group	Total	*IgG*		*IgM*	
		Positive	Negative / Equiv.	Positive	Negative / Equiv.
Normals	214	1	213	3	211
APS	57	47	10	27	30
SLE	33	7	26	7	26
Other Autoimmune Diseases	35	3	32	5	30
RPR Positive	15	4	11	4	11

Clinical Specificity:	**IgG**	**IgM**
	# Neg or Equiv./Total #	***# Neg or Equiv./Total #***
Normals	213/214 = 99.5%	211/214 = 98.5%
RPR Positive	11/15 = 73.3%	11/15 = 73.3%

Clinical Sensitivity:	**IgG**	**IgM**
	# Pos/Total #	***# Pos/Total #***
APS	47/57 = 82.5%	27/57 = 47.4%
SLE	7/33 = 21.2%	7/33 = 21.2%
Other Autoimmune Diseases	3/35 = 8.6%	5/35 = 14.2%

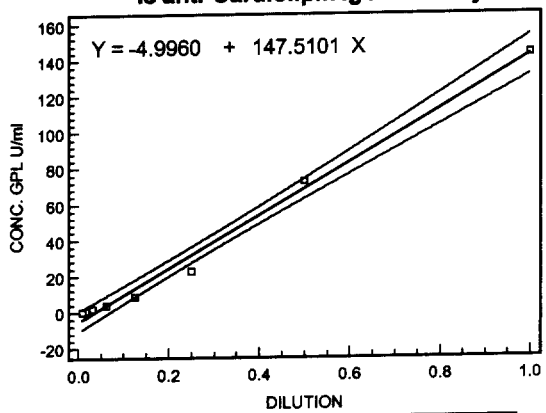
D. Cross Reactivity

To assess the potential for positive results due to cross reactive antibodies, 36 samples which were reactive to various autoantibodies (SSA/SSB, Scl-70, Jo-1, dsDNA and RF) were tested using the Is-anti-Cardiolipin IgG/IgM Test Kit. In all, 36 samples were tested. One sample positive for Jo-1 antibodies and one sample positive for dsDNA antibodies were positive in both the Is-anti-Cardiolipin IgG and IgM Tests. The remaining 34 samples were negative.

E. Linearity

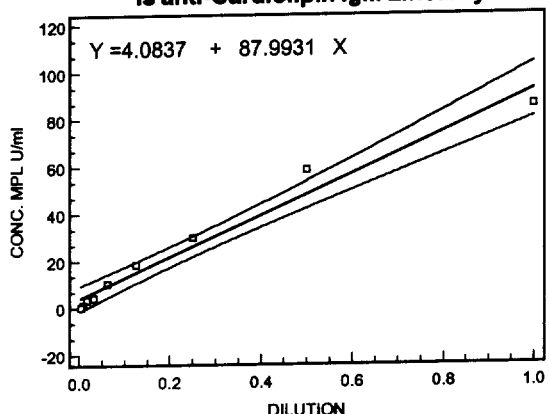
To assess the linearity of the Is-anti-Cardiolipin IgG/IgM Test Kit several highly positive samples were serially diluted using Sample Diluent and each dilution was then tested in the respective IgG or IgM assay systems. Representative linear regression graphs and scattergrams with 95% confidence intervals are presented in FIGURES 5 and 6.

FIGURE 5
Is anti-Cardiolipin IgG Linearity



Intercept -4.99597 Slope 147.51010
Coefficient of determination = 0.9915
Correlation Coefficient r = 0.9957
95% CI for r = 0.9756 to 0.9993

FIGURE 6
Is anti-Cardiolipin IgM Linearity

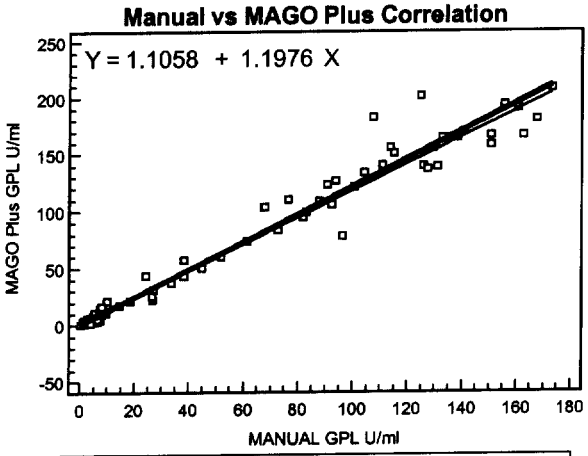


Intercept 4.08374 Slope 87.99309
Coefficient of determination = 0.9701
Correlation Coefficient r = 0.9849
95% CI for r = 0.9275 to 0.9969

F. Correlation of Manual and MAGO Plus results

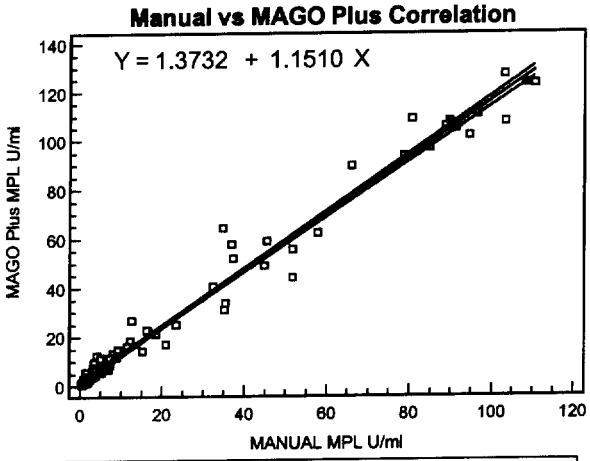
The Is-anti-Cardiolipin IgG/IgM Test Kit has been developed for automated as well as manual use. To demonstrate the equivalence of the manual and MAGO Plus procedures, the results of 172 serum samples tested for anti-cardiolipin IgG antibodies and 162 sera tested for anti-cardiolipin IgM by both the manual and automated methods were plotted. Scattergrams and regression lines of the results obtained with 95% confidence intervals are shown in FIGURES 7 and 8. The data indicate good correlation with a Correlation Coefficients (r) of 0.9883 for anti-cardiolipin IgG and 0.9917 for anti-cardiolipin IgM.

FIGURE 7: Is anti-Cardiolipin IgG
Manual vs MAGO Plus Correlation



Intercept	1.1058 (95% CI -0.4306 to 2.6422)
Slope	1.1976 (95% CI 1.1696 to 1.2256)
Sample Size:	172
Coefficient of determination	= 0.9768
Correlation Coefficient r	= 0.9883
95% CI for r = 0.9842 to 0.9913	

FIGURE 8: Is anti-Cardiolipin IgM
Manual vs MAGO Plus Correlation



Intercept	1.3732 (95% CI 0.6787 to 2.0676)
Slope	1.1510 (95% CI 1.1276 to 1.1743)
Sample Size:	162
Coefficient of determination	= 0.9835
Correlation Coefficient r	= 0.9917
95% CI for r = 0.9887 to 0.9939	

With the 6-point calibration, linear regression of the IgG results showed (automated) = 1.0696 (manual) + 4.0821; r =0.9517. 95% CI for the slope and intercept are 1.0174 to 1.1218 and 1.3042 to 6.8600 respectively. For IgM results (automated) = 1.0169 (manual) + 2.2121; r = 0.9772. 95% CI for the slope and the intercept are 0.9824 to 1.0514 and 1.1343 to 3.2899 respectively.

G. Precision

To assess the precision of the Is anti-Cardiolipin IgG/IgM Test Kit six serum samples of varying reactivity were tested in triplicate in three separate runs. Precision was assessed both manually and using the MAGO Plus Automated EIA Processor. Precision was assessed for both IgG and IgM antibody types. The results obtained using 6-point Calibration are shown in TABLES 4-7.

TABLE 4 : Manual Intra-Assay and Interassay Precision for Is-anti-Cardiolipin IgG

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=9)		
	MEAN GPL	SD	CV%	MEAN GPL	SD	CV%	MEAN GPL	SD	CV%	MEAN GPL	SD	CV%
A	1.6	0.00	0.00	1.6	0.06	3.69	1.6	0.12	7.07	1.6	0.07	4.42
B	1.1	0.06	5.41	1.1	0.06	5.41	1.1	0.06	5.09	1.1	0.06	5.52
C	17.4	0.45	2.59	17.6	1.69	9.63	18.6	1.53	8.23	17.9	1.28	7.17
D	25.4	2.11	8.30	24.8	1.39	5.60	27.2	1.21	4.46	25.8	1.78	6.89
E	35.3	0.72	2.05	29.0	0.58	1.99	31.2	1.59	5.10	31.8	2.92	9.17
F	58.1	2.19	3.77	74.6	2.00	2.68	73.5	10.15	13.82	68.7	9.57	13.93

TABLE 5 : MAGO Plus - Intra-Assay and Interassay Precision for Is-anti-Cardiolipin IgG

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=9)		
	MEAN GPL	SD	CV%	MEAN GPL	SD	CV%	MEAN GPL	SD	CV%	MEAN GPL	SD	CV%
A	2.5	0.47	18.90	3.2	0.58	17.86	3.9	1.23	31.51	3.2	0.95	29.69
B	1.3	0.15	11.75	2.0	0.12	5.87	1.9	0.10	5.26	1.7	0.35	20.59
C	29.1	1.15	3.96	31.8	1.06	3.33	40.0	6.32	15.79	33.6	5.90	17.56
D	39.7	7.45	18.76	42.9	1.18	2.76	49.2	4.51	9.16	44.0	6.07	13.80
E	41.5	0.90	2.16	45.2	2.68	5.92	51.5	1.76	3.41	46.1	4.69	10.17
F	95.3	2.30	2.42	81.1	5.00	6.16	71.3	7.04	9.87	82.6	11.34	13.73

TABLE 6 : Manual Intra-Assay and Interassay Precision for Is-anti-Cardiolipin IgM

SERUM	INTRA-ASSAY RUN 1			INTRA-ASSAY RUN 2			INTRA-ASSAY RUN 3			INTERASSAY (n=9)		
	MEAN MPL	SD	CV%	MEAN MPL	SD	CV%	MEAN MPL	SD	CV%	MEAN MPL	SD	CV%
A	0.8	0.15	18.33	1.1	0.00	0.00	0.8	0.12	15.06	0.9	0.18	20.03
B	1.1	0.12	10.19	1.4	0.00	0.00	0.9	0.06	6.19	1.2	0.21	18.41
C	26.0	0.35	1.35	26.2	0.61	2.32	21.2	2.18	10.29	24.5	2.73	11.15
D	35.3	0.53	1.50	36.1	1.50	4.17	31.5	0.85	2.70	34.3	2.29	6.67
E	61.4	2.60	4.23	65.6	1.86	2.83	55.5	0.35	0.62	60.8	4.67	7.67
F	63.3	3.87	6.11	65.3	3.23	4.96	62.6	2.60	4.16	63.7	3.08	4.84

TABLE 7 : MAGO Plus - Intra-Assay and Interassay Precision for Is-anti-Cardiolipin IgM

SERUM	INTRA-ASSAY RUN 1			INTRA-ASSAY RUN 2			INTRA-ASSAY RUN 3			INTERASSAY (n=9)		
	MEAN MPL	SD	CV%	MEAN MPL	SD	CV%	MEAN MPL	SD	CV%	MEAN MPL	SD	CV%
A	2.6	0.25	9.68	1.9	0.06	2.99	1.8	0.06	3.15	2.1	0.37	17.62
B	2.8	0.21	7.43	2.2	0.15	6.84	2.0	0.12	5.87	2.3	0.38	16.52
C	29.4	2.05	6.98	30.8	1.30	4.22	25.0	0.95	3.79	28.4	2.95	10.39
D	37.7	1.60	4.24	40.6	2.31	5.69	36.7	2.53	6.91	38.3	2.60	6.79
E	65.8	3.25	4.94	70.4	0.65	0.92	59.5	2.81	4.73	65.2	5.22	8.01
F	85.9	9.30	10.83	80.2	2.00	2.49	66.7	2.87	4.30	77.6	9.88	12.73

Expected Values

The prevalence of anti-cardiolipin IgG and/or IgM antibodies may vary depending on a number of factors such as age, gender, geographical location, race, type of test used and clinical history of individual patients. Antibodies to anti-cardiolipin are generally absent, or have a very low incidence, in the normal healthy population. Increased incidence can occur in the elderly population. A published study has shown a prevalence of 12% in the elderly population (mean age of 70 years) as opposed to 2% for a younger population. In addition, anti-cardiolipin antibodies were detected in 23% of elderly individuals who were also positive for anti-nuclear antibodies (13).

In the present study, the expected values for a normal, healthy population were assessed by testing sera from one hundred and forty-eight S. Florida blood donors in the Is-anti-Cardiolipin IgG/IgM Test Kit for both IgG and IgM antibodies. For IgG antibodies, one hundred and forty-seven sera (99.3%) were negative for antibodies, one serum (0.7%) was positive and none were equivocal. For IgM antibodies, one hundred and forty-six (98.6%) were negative, two sera (1.4%) were positive and none were equivocal. The age distribution and antibody prevalences for this population are shown in TABLE 8.

The expected values for a clinical population were assessed by testing fifty-seven sera from patients with a diagnosis of anti-phospholipid syndrome (APS) in the Is-anti-Cardiolipin IgG/IgM test for both antibody types. Forty-seven (82.5%) were positive, nine (15.8%) were negative and one (1.7%) was equivocal for IgG antibodies. Twenty-seven (47.3%) were positive, twenty-nine (50.9%) were negative, and one (1.7%) was equivocal for IgM antibodies.

Histograms showing the distribution of values for the normal and clinical populations for both IgG and IgM antibodies are shown in FIGURES 9-12.

TABLE 8: Age Distribution and Prevalence of anti-Cardiolipin IgG and IgM Antibodies in a Normal S. Florida Population

	Number of Donors	Prevalence	
Total Number	148	**IgG**	**IgM**
Geographic Location:	South Florida : 148	0.7%	1.4%
Age			
10-19	7	0.0%	0.0%
20-29	36	0.0%	0.0%
30-39	73	0.0%	2.7%
40-49	22	4.5%	0.0%
50-59	8	0.0%	0.0%
60-69	2	0.0%	0.0%

FIGURE 9
Distribution of anti-Cardiolipin IgG in a Normal Population

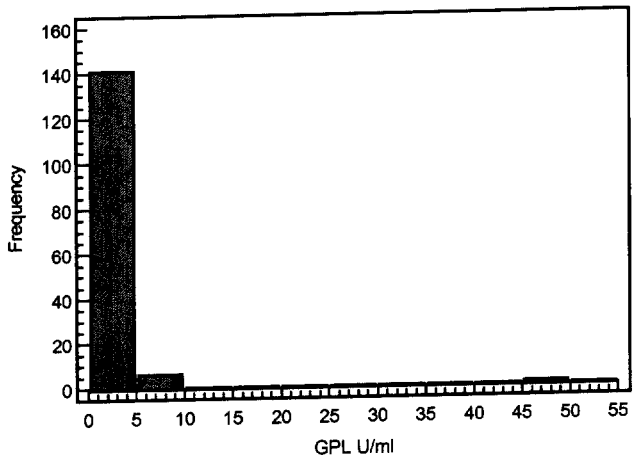


FIGURE 10
Distribution of anti-Cardiolipin IgM in a Normal Population

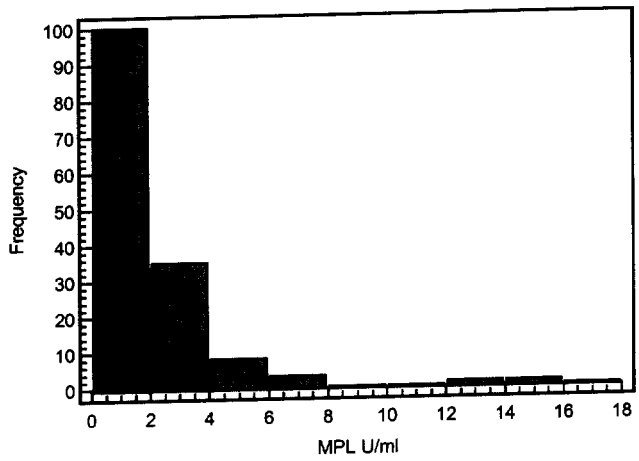


FIGURE 11
Distribution of anti-Cardiolipin IgG in a Clinical Population

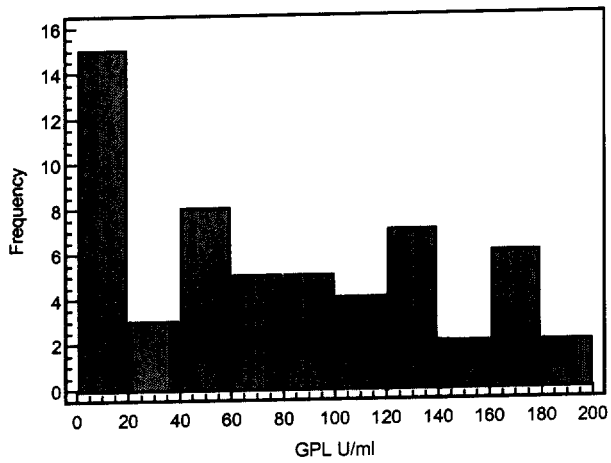
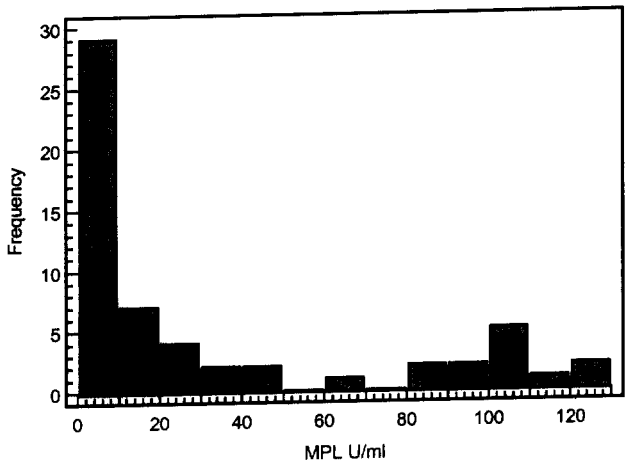


FIGURE 12
Distribution of anti-Cardiolipin IgM in a Clinical Population



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 2 6 2001

Lynne Stirling, Ph.D.
Vice President, Regulatory Affairs
Diamedix Corporation
2140 North Miami Avenue
Miami, Florida 33127

Re: K012449
Trade/Device Name: Diamedix Is-anti-Cardiolipin IgG/IgM Test System
Regulation Number: 21 CFR § 866.5660
Regulation Name: Multiple Autoantibodies Immunological Test System
Regulatory Class: Class II
Product Code: MID
Dated: September 28, 2001
Received: October 1, 2001

Dear Dr. Stirling:

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

Appendix G. Indications for Use Statement

INDICATIONS FOR USE STATEMENT

510(K) NUMBER : K012449

DEVICE NAME : Is anti-Cardiolipin IgG/IgMTest System

Indications for Use : The Diamedix Is anti-Cardiolipin IgG/IgM Test Kit is an indirect enzyme immunoassay (EIA) for the semi-quantitative measurement of IgG or IgM antibodies to cardiolipin in human serum as an aid in the assessment of the risk of thrombosis in patient with SLE or SLE-like disorders. These reagents can be used either manually or in conjunction with the MAGO® Plus Automated EIA Processor.

Susan St Hale

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K012449

For Prescription Use X