K012450

OCT 2 6 2001

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: K012450

Applicant Information:

Date Prepared:	October 17, 2001
Name:	Diamedix Corporation
Address:	2140 N. Miami Avenue Miami, FL 33127
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Device Information:

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

Equivalent Device:
Orgentec Anti-cardiolipin IgA ELISA Assay

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

Intended Use: The assay is intended for the semi-quantitative measurement of IgA 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 disorders.

Principle of the Procedure:

The Is-anti-Cardiolipin IgA 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. Calibrators, controls and diluted patient samples are added to the wells. Any IgA antibodies in the patient sample bind to the well. Anti-human IgA 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 IgA antibodies in the patient sample.

SUMMARY OF SAFETY AND EFFECTIVENESS

Rev. 10/17/01

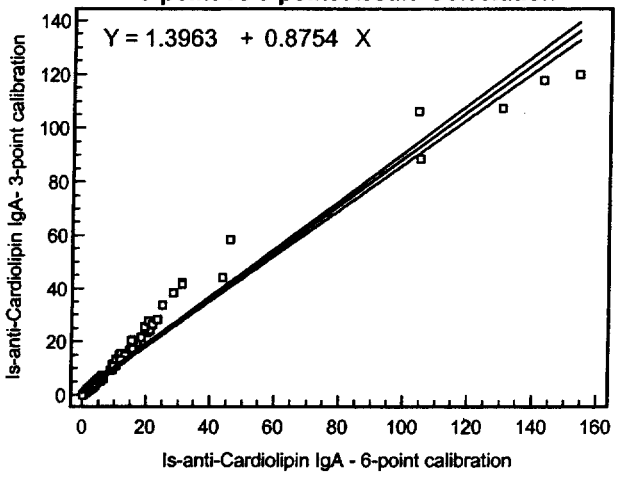
Performance Characteristics

All 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 190 samples tested using the Is-anti-Cardiolipin IgA Test Kit using either the 3-point or 6-point calibration systems were subjected to linear regression analysis. A scattergram and regression line of the results obtained with 95% confidence intervals is shown in FIGURE 1. Also included are the regression statistics.

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



Intercept	1.3963 (95% CI 0.8699 to 1.9226)
Slope	0.8754 (95% CI 0.8523 to 0.8985)
Sample Size	190
Coefficient of determination	= 0.9675
Correlation coefficient r	= 0.9836
95% CI for r = 0.9782 to 0.9877	

B. Relative Sensitivity and Specificity

Two hundred and thirty-seven frozen retrospective sera were tested for IgA antibodies using the Is-anti-Cardiolipin IgA Test Kit and a commercially available ELISA kit for detecting cardiolipin IgA antibodies. Based on the results of this testing the relative sensitivity, relative specificity and overall agreement were calculated. The results obtained are shown in TABLE 1. Further resolution of the discordant samples showed that of the ten samples that were negative in the Is anti-Cardiolipin IgA and positive by the other EIA, five were negative and five were positive by a referee EIA method. The sample that was positive in the Is-anti-Cardiolipin IgA and negative in the other EIA was positive by the referee method.

TABLE 1

Is-anti-Cardiolipin IgA

Other EIA	Positive	Negative	*Equivocal
Positive	60	10	6
Negative	1	142	3
*Equivocal	6	7	2

			**95% CI
Relative Sensitivity	60/70	= 85.7 %	75.3-92.9%
Relative Specificity	142/143	= 99.3%	96.2-100.0%
Overall Agreement	214/216	= 94.8%	90.9-97.4%

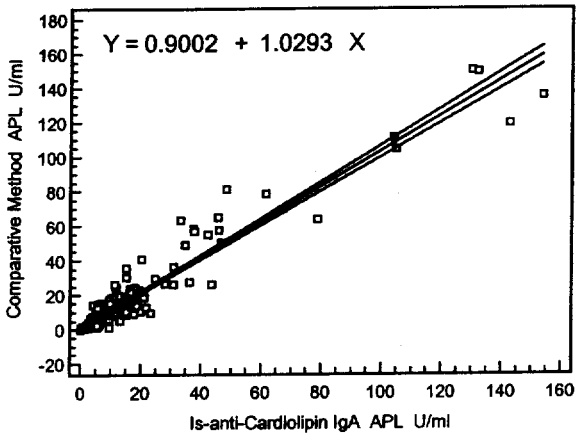
* Equivocal results were excluded from calculations.

** 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 analysis and a scattergram for the correlation study with the comparative method is shown in FIGURE 2.

FIGURE 2 : Is anti-Cardiolipin IgA Correlation with Comparative Method



Intercept	0.9002 (95% CI -0.0163 to 1.8167)
Slope	1.0293 (95% CI 0.9923 to 1.0662)
Sample Size	237
Coefficient of determination	= 0.9277
Correlation coefficient r	= 0.9632
95% CI for r = 0.9527 to 0.9714	

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 IgA 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 antiphospholipid 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 2.

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 0.2 APL U/ml.

TABLE 2

Patient Group	Total	Positive	Negative	Equivocal
Normals	214	3	210	1
APS	57	25	31	1
SLE	33	12	20	1
Other Autoimmune Diseases	35	3	32	0
RPR Positive	15	3	12	0

Clinical Specificity:	**# Neg/Total #**	
Normals	210/214	= 98.1%
RPR Positive	12/15	= 80.0%
Clinical Sensitivity :	**# Pos/Total #**	
APS	25/57	= 43.8%
SLE	12/33	= 36.4%
Other Autoimmune Diseases	3/35	= 8.6%

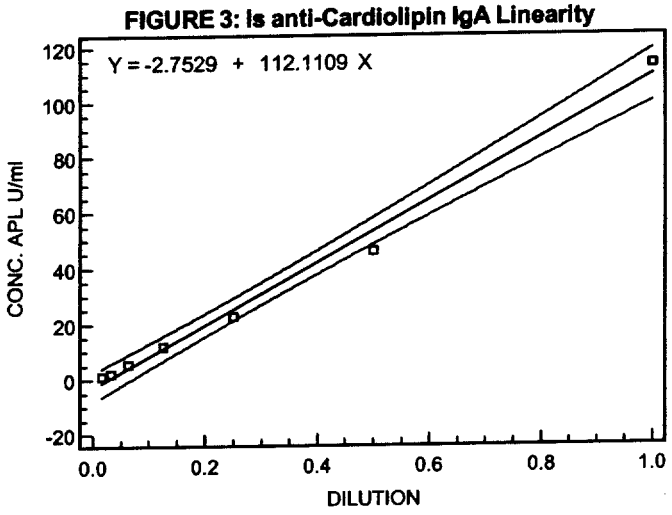
D. Cross Reactivity

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 IgA Test Kit. One sample positive for Jo-1 antibodies and one sample positive for dsDNA were positive in the Is-anti-Cardiolipin IgA test. The remaining 34 samples were negative.

E. Linearity

To assess the linearity of the Is-anti-Cardiolipin IgA Test Kit several highly positive samples were serially diluted using Sample Diluent and each dilution was tested. A representative linear regression graph and scattergram with 95% confidence intervals is presented in FIGURE 3.

FIGURE 3: Is anti-Cardiolipin IgA Linearity

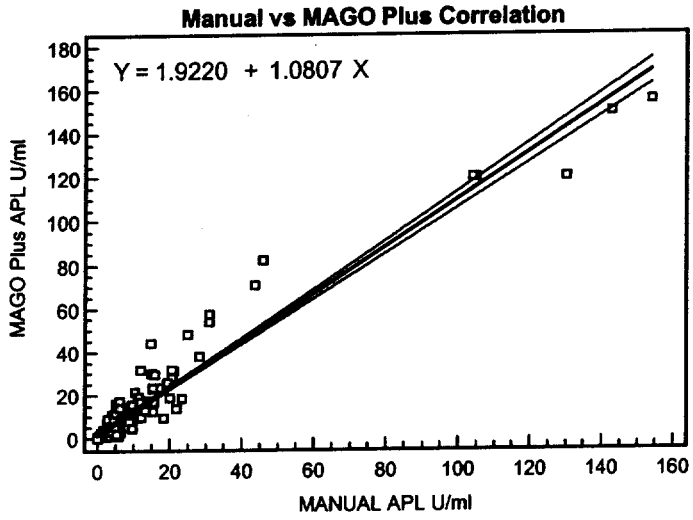


Intercept -2.75287 Slope 112.11092
Coefficient of determination = 0.9912
Correlation Coefficient r = 0.9956
95% CI for r = 0.9691 to 0.9994

F. Correlation of Manual and MAGO Plus results

The Is-anti-Cardiolipin IgA 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 190 serum samples tested for anti-Cardiolipin IgA antibodies by both the manual and automated methods were plotted. Scattergrams and regression lines of the results obtained with 95% confidence intervals are shown in FIGURE 4. The data indicate good correlation with a Correlation Coefficient (r) of 0.9688. Results obtained using either 3 Standards or 6 Standards were comparable.

FIGURE 4: Is anti-Cardiolipin IgA Manual vs MAGO Plus Correlation



Intercept 1.9220 (95% CI 1.0159 to 2.8280)
Slope 1.0807 (95% CI 1.0409 to 1.1204)
Sample Size: 190
Coefficient of determination = 0.9386
Correlation Coefficient r = 0.9688
95% CI for r = 0.9587 to 0.9765

With the 3-point calibration, linear regression showed (automated) = 1.2914 (manual) + 0.1773; r = 0.9794. 95% CI for slope and intercept are 1.2532 to 1.3297 and -0.6184 to 0.9730 respectively.

G. Precision

To assess the precision of the Is anti-Cardiolipin IgA 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. The results obtained using 6-point calibration are shown in TABLES 3 and 4.

TABLE 3 : Manual Intra-Assay and Interassay Precision for Is-anti-Cardiolipin IgA

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=9)		
	MEAN APL	SD	CV%	MEAN APL	SD	CV%	MEAN APL	SD	CV%	MEAN APL	SD	CV%
A	0.9	0.06	6.19	1.8	0.12	6.54	1.2	0.17	14.43	1.3	0.38	29.54
B	1.0	0.06	5.97	1.7	0.17	10.19	1.1	0.17	15.75	1.3	0.36	27.78
C	12.0	0.96	8.03	16.1	0.12	0.72	11.4	1.06	9.28	13.1	2.32	17.70
D	33.0	0.86	2.62	31.4	1.44	4.57	33.0	1.89	5.71	32.5	1.49	4.57
E	39.3	2.06	5.25	35.9	1.51	4.22	38.4	1.99	5.17	37.9	2.20	5.86
F	83.0	18.34	22.08	94.9	5.65	5.95	77.6	7.55	9.73	85.2	12.84	15.08

TABLE 4 : MAGO Plus Intra-Assay and Interassay Precision for Is-anti-Cardiolipin IgA

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=9)		
	MEAN APL	SD	CV%	MEAN APL	SD	CV%	MEAN APL	SD	CV%	MEAN APL	SD	CV%
A	1.6	0.17	10.83	2.2	0.25	11.27	2.0	0.49	24.26	2.0	0.40	20.63
B	1.5	0.06	3.94	1.8	0.06	3.27	1.8	0.12	6.54	1.7	0.17	9.95
C	15.1	0.51	3.41	16.5	0.93	5.64	18.1	1.88	10.39	16.5	1.69	10.22
D	43.6	1.50	3.45	41.1	2.54	6.18	50.9	2.75	5.41	45.2	4.86	10.75
E	38.3	4.37	11.41	46.1	3.12	6.77	54.2	3.10	5.71	46.2	7.58	16.40
F	89.8	22.48	25.04	82.9	12.78	15.42	103.8	8.90	8.58	92.2	16.50	17.91

Expected Values

The prevalence of anti-cardiolipin IgA 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 posiitve 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 IgA Test Kit. One hundred and forty-five sera (97.97%) were negative for IgA antibodies, two sera (1.35%) were positive and one serum (0.67%) were equivocal. The age distribution and antibody prevalence for this population are shown in TABLE 5.

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 IgA Test Kit. Twenty-five (43.9%) were positive, thirty (52.6%) were negative and two (3.5%) were equivocal for IgA antibodies.

Histograms showing the distribution of values for these normal and clinical populations are shown in FIGURES 5 and 6.

TABLE 5: Age Distribution and Prevalence of anti-Cardiolipin IgA in a Normal S. Florida Population

	Number of Donors	Prevalence
Total Number	148	
Geographic Location:	South Florida : 148	2.03%
Age		
10-19	7	0.0%
20-29	36	0.0%
30-39	73	2.7%
40-49	22	0.0%
50-59	8	0.0%
60-69	2	0.0%

FIGURE 5

Distribution of anti-Cardiolipin IgA in a Normal Population

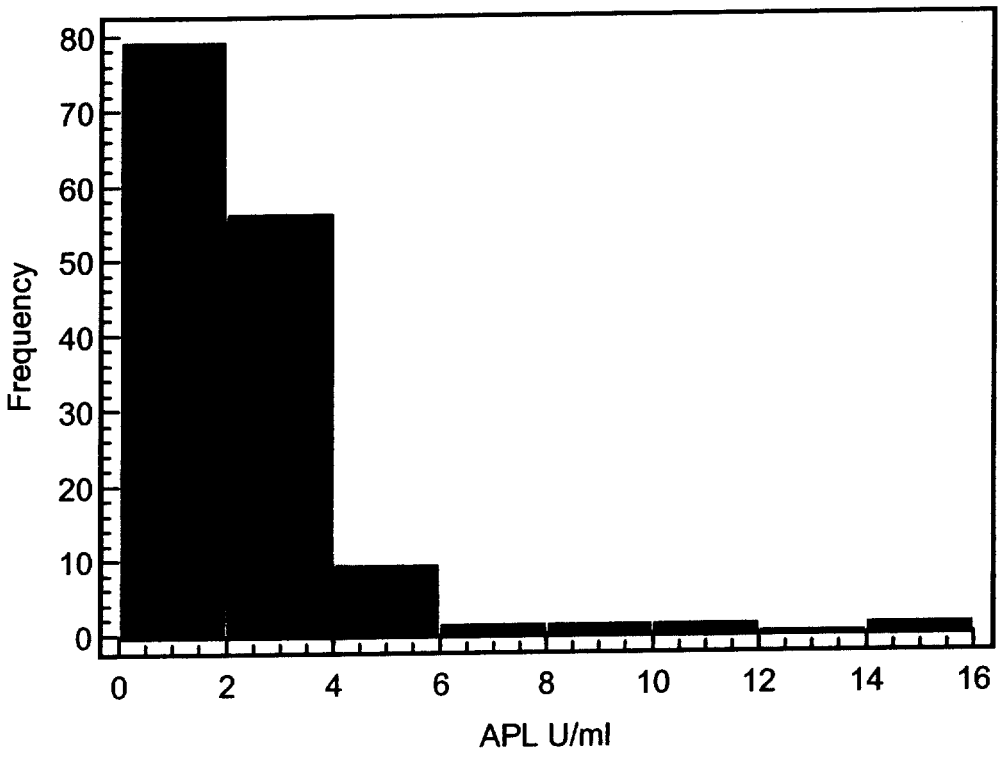
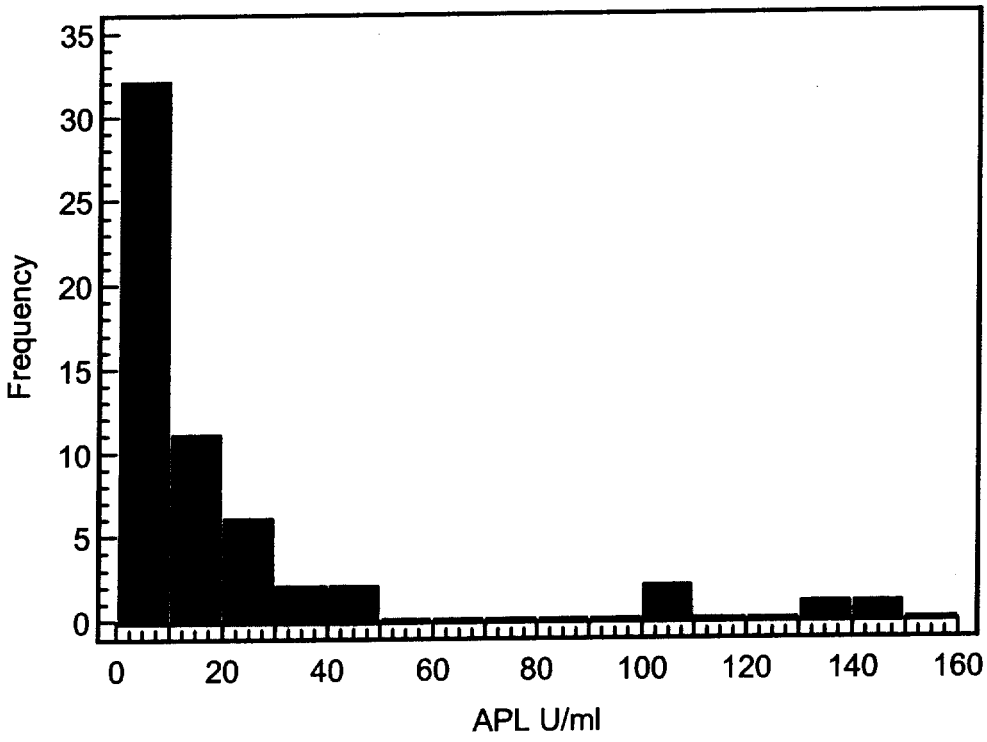


FIGURE 6

Distribution of anti-Cardiolipin IgA in a Clinical Population



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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

OCT 2 6 2001

Re: K012450
Trade/Device Name: Diamedix Is-anti-Cardiolipin IgA 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 : K012450

DEVICE NAME : Is anti-Cardiolipin IgA Test System

Indications for Use : The Diamedix Is anti-Cardiolipin IgA Test Kit is an indirect enzyme immunoassay (EIA) for the semi-quantitative measurement of IgA 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.

Sonsan S. Altaie

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K012450

For Prescription use ✓