DEC 21 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: K013628

Applicant Information:

Date Prepared:	December 18, 2001
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Device Information:

Trade Name:	Is anti-β_2Glycoprotein I IgG/IgM Test System
Common Name:	Anti-β_2Glycoprotein I ELISA test
Classification Name:	Anti-β_2Glycoprotein I immunological test system

Equivalent Device:
QUANTA Lite β_2GPI IgG & QUANTA Lite β_2GPI IgM

Device Description: The Is anti-β_2Glycoprotein I IgG/IgM Test System is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative measurement of IgG or IgM antibodies to β_2 glycoprotein in human serum

Intended Use: The assay is intended for the semi-quantitative measurement of IgG or IgM anti-bodies to β_2 glycoprotein I in human serum. The results of the assay can be used as an aid in the diagnosis of certain autoimmune disease thrombotic disorders in patients with SLE or SLE-like dosorders.

Principle of the Procedure:

The Is-anti-β_2 Glycoprotein I IgG/IgM Test System is an indirect solid-phase enzyme immunoassay. Highly purified β2-Glycoprotein I is coated onto plastic microwells. 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 β2-glycoprotein I IgG or IgM antibodies in the sample.

SUMMARY OF SAFETY AND EFFECTIVENESS

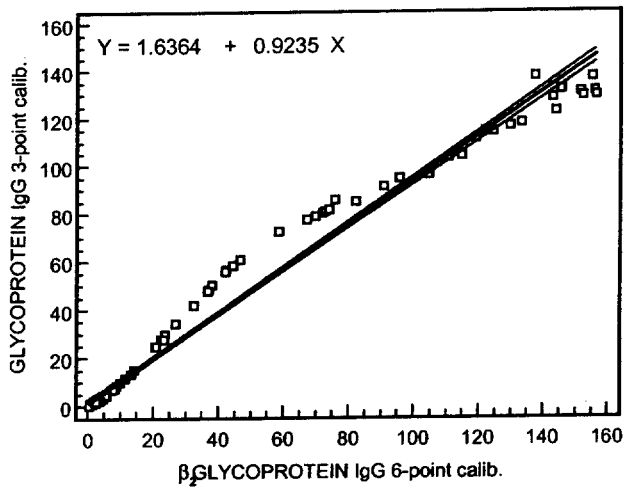
Performance Characteristics

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

A. 3-point vs 6-point calibration

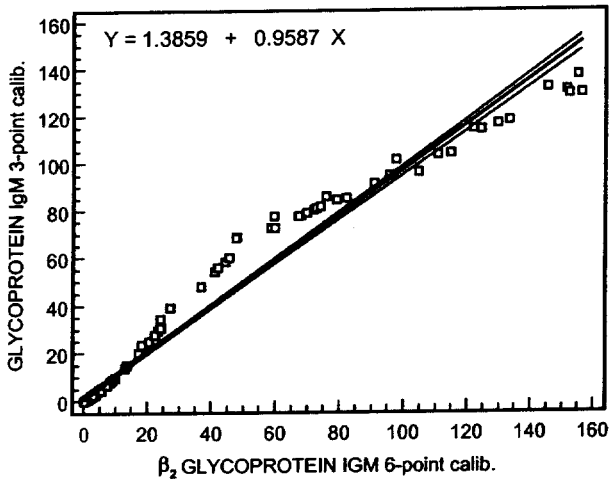
To demonstrate the equivalence of both calibration methods, the results of 178 samples tested using the Is-anti-β_2 Glycoprotein I IgG and 187 samples tested using the Is-anti-β_2Glycoprotein I IgM, calculated using either the 3-point or 6-point calibration systems, were subjected to linear regression 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-β_2-Glycoprotein IgG 3-point vs 6-point Result Correlation



Intercept 1.6364 (95% CI 0.6959 to 2.5771)
Slope 0.9235 (95% CI 0.9045 to 0.9426)
Coefficient of determination = 0.9812
Correlation coefficient r = 0.9905
95% CI for r = 0.9875 to 0.9931

FIGURE 2 : Is-anti-β_2-Glycoprotein IgM 3-point vs 6-point Result Correlation



Intercept 1.3859 (95% CI 0.4528 to 2.3189)
Slope 0.9587 (95% CI 0.9363 to 0.9811)
Coefficient of determination = 0.9747
Correlation coefficient r = 0.9872
95% CI for r = 0.9830 to 0.9904

B. Relative Sensitivity and Specificity

One hundred and seventy-two frozen retrospective sera were tested for IgG antibodies and one hundred and sixty-one frozen retrospective sera were tested for IgM antibodies using the Is-anti-β_2-Glycoprotein I IgG/IgM Test Kit and commercially available ELISA kits for detecting IgG and IgM β_2-glycoprotein I antibodies. Based on the results of this testing the relative sensitivity, relative specificity and overall agreement were calculated. The results obtained are shown in TABLES 1 and 2. For anti-β_2-Glycoprotein I IgG, further resolution of the discordant samples showed that the three samples that were negative in the Is anti-β_2-Glycoprotein I IgG and positive by the other EIA were also negative by a referee EIA method. Of the six samples positive in the Is anti-β_2-Glycoprotein I IgG and negative in the other EIA, one was positive and five were negative by a referee EIA method. For anti-β_2-Glycoprotein I IgM, further resolution of the discordant samples showed that of the four samples that were negative in the Is anti-β_2-Glycoprotein I IgM but positive in the other EIA, two were positive and two were negative by a referee EIA method.

TABLE 1

Is-anti-β_2Glycoprotein I IgG

Other EIAs	Positive	Negative	Equivocal
Positive	38	3	0
Negative	6	123	2
*Equivocal	0	0	0

			**95% CI
Relative Sensitivity	38/41	= 92.7%	80.1-98.5%
Relative Specificity	123/129	= 95.3%	90.2-98.3%
Overall Agreement	161/170	= 94.7%	90.2-97.6%

TABLE 2

Is-anti-β_2Glycoprotein I IgM

	Positive	Negative	Equivocal
Positive	31	4	2
Negative	0	124	0
*Equivocal	0	0	0

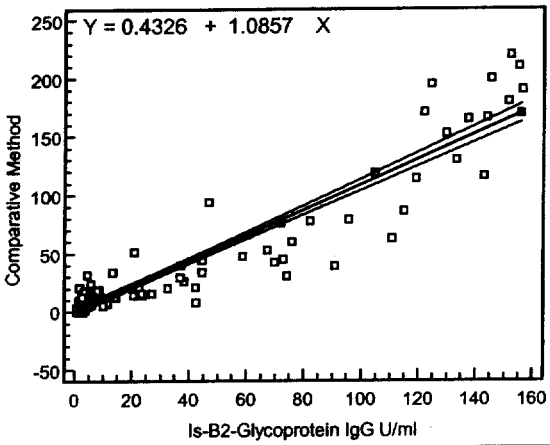
			**95% CI
Relative Sensitivity	31/35	= 88.6 %	73.3-96.8%
Relative Specificity	124/124	= 100.0%	97.1-100.0%
Overall Agreement	155/159	= 97.5%	93.7-99.3%

* 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.

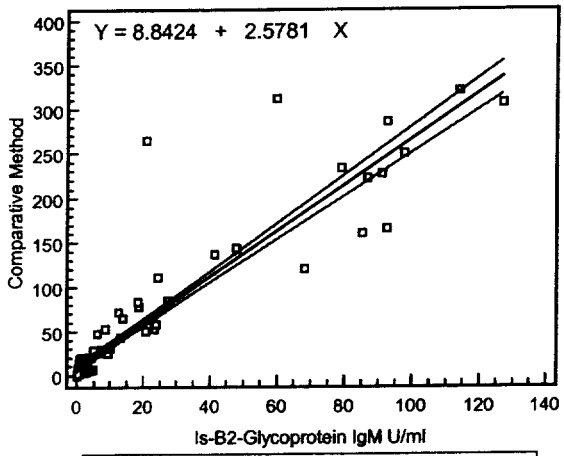
Linear regression analyses and scattergrams for the correlation studies with the comparative methods are shown in FIGURES 3 and 4.

FIGURE 3: Is anti-β_2-Glycoprotein I IgG Correlation with Comparative Method



Intercept 0.4326 (95% CI -2.1954 to 3.0605)
Slope 1.0857 (95% CI 1.0307 to 1.1407)
Coefficient of determination = 0.8994
Correlation coefficient r = 0.9484
95% CI for r = 0.9308 to 0.9616

FIGURE 4 : Is anti-β_2-Glycoprotein I IgM Correlation with Comparative Method



Intercept 8.8424 (95% CI 4.8121 to 12.8727)
Slope 2.5782 (95% CI 2.4199 to 2.7363)
Coefficient of determination = 0.8669
Correlation coefficient r = 0.9311
95% CI for r = 0.9070 to 0.9491

C. Clinical Sensitivity and Specificity

A total of three hundred and eighty-eight frozen retrospective, clinically characterized sera were assayed using the Is anti-β_2Glycoprotein I IgG/IgM Test Kit in order to assess both the clinical sensitivity and clinical specificity of the assay system. These samples consisted of 248 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.

TABLE 3

Patient Group	Total	*IgG*		*IgM*	
		Positive	Negative / Equiv.	Positive	Negative / Equiv.
Normals	248	3	245	3	245
APS	57	46	11	25	32
SLE	33	7	26	7	26
Other Autoimmune Diseases	35	3	32	2	33
RPR Positive	15	0	15	1	14

Clinical Specificity:	IgG	IgM
	# Neg or Equiv./Total #	*# Neg or Equiv./Total #*
Normals	245/248 = 98.8%	245/248 = 98.8%
RPR Positive	15/15 = 100.0%	14/15 = 93.3%
Other Autoimmune Diseases	32/35 = 91.4%	33/35 = 94.3%

Clinical Sensitivity :	IgG	IgM
	# Pos/Total #	*# Pos/Total #*
APS	46/57 = 80.7%	25/57 = 43.9%
SLE	7/33 = 21.2%	7/33 = 21.2%

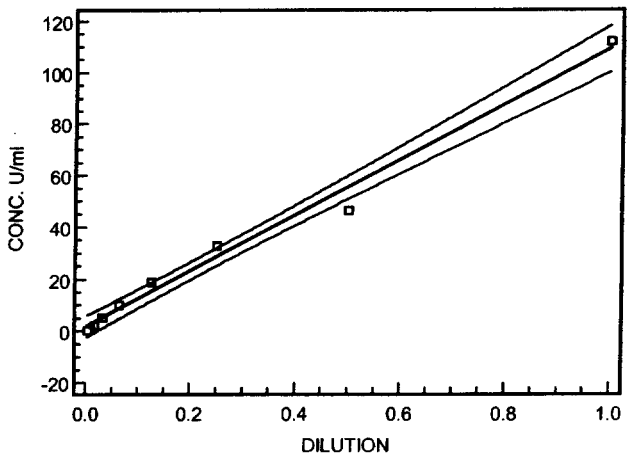
D. Cross-Reactivity

To assess the potential for positive results due to cross reactive antibodies, 50 samples which were reactive to various autoantibodies (SSA/SSB, Scl-70. Jo-1, dsDNA, RF and RPR positive) were tested using the Is anti-β_2Glycoprotein I IgG/IgM Test Kit. One sample positive for dsDNA was positive in both the Is anti-β_2Glycoprotein I IgG and IgM tests. One sample positive for Scl-70 antibodies was positive in the Is anti-β_2Glycoprotein I IgG test. One sample positive for Jo-1 antibodies was positive in both the Is anti-β_2Glycoprotein I IgG and IgM tests and one RPR positive sample was positive in the Is anti-β_2Glycoprotein I IgM test. The remaining samples were negative.

E. Linearity

To assess the linearity of the Is anti-β_2Glycoprotein I 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.

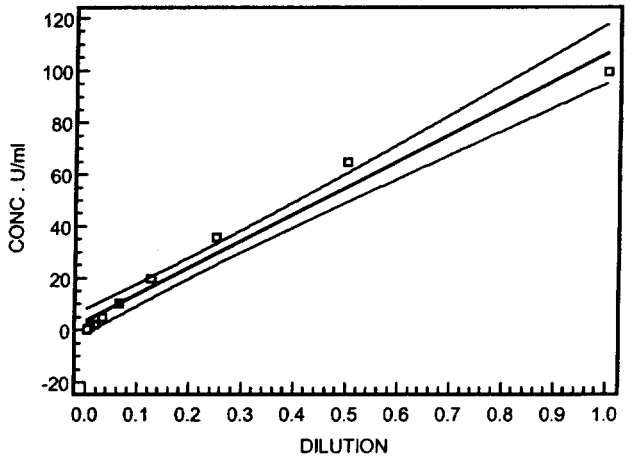
FIGURE 5: Is-anti-β_2-Glycoprotein IgG Linearity



Regression Equation
Y = 1.6732 + 107.5806

Intercept 1.67318 Slope 107.58059
Coefficient of Determination = 0.9876
Correlation Coefficient r = 0.9938
95% CI for r = 0.9695 to 0.9987

FIGURE 6: Is-anti-β_2-Glycoprotein IgM Linearity



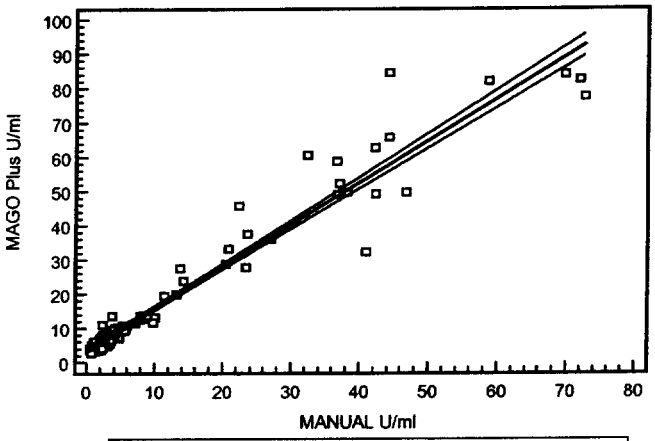
Regression Equation
Y = 3.3897 + 103.2019

Intercept 4.5071 Slope 118.93019
Coefficient of Determination = 0.9760
Correlation Coefficient r = 0.9879
95% CI for r = 0.9479 to 0.9972

F. Correlation of Manual and MAGO Plus results

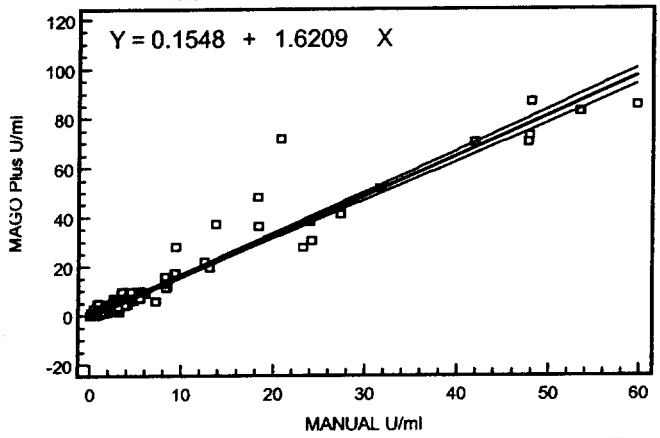
The Is anti-β_2Glycoprotein I IgG/IgM Test Kit has been developed for automated as well as manual use. To demonstrate the equivalence of the manual and MAGO Plus procedures, the results of 153 serum samples tested for anti-β_2-glycoprotein I IgG antibodies and 163 sera tested for anti-β_2-glycoprotein I IgM tested 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 Correlation Coefficients (r) of 0.9720 for anti-β_2-glycoprotein I IgG and 0.9513 for anti-β_2-glycoprotein I IgM.

FIGURE 7: Is anti-β_2-Glycoprotein I IgG Manual vs MAGO Plus Correlation



Intercept 3.6553 (95% CI 2.8680 to 4.4426)
Slope 1.2255 (95% CI 1.1778 to 1.2731)
Coefficient of determination = 0.9447
Correlation coefficient r = 0.9720
95% CI for r = 0.9616 to 0.9796

FIGURE 8: Is anti-β_2-Glycoprotein I IgM Manual vs MAGO Plus Correlation



Intercept 0.1548 (95% CI -0.4904 to 0.7800)
Slope 1.6209 (95% CI 1.5616 to 1.6802)
Coefficient of determination = 0.9418
Correlation coefficient r = 0.9704
95% CI for r = 0.9606 to 0.9779

With the 3-point calibration, linear regression of the IgG results showed (automated) = 1.1553 (manual) + 2.6132; r = 0.9766. 95% CI for the slope and intercept are 1.1144 to 1.1961 and 1.7875 to 3.4388 respectively. For IgM results (automated) = 1.2244 (manual) + 1.1552; r =9869. 95% CI for the slope and intercept 1.1956 to 1.2532 and 0.4133 to 1.8971 respectively.

G. Precision

To assess the precision of the Is anti-β_2Glycoprotein I 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-β_2-Glycoprotein I IgG

SERUM	INTRA-ASSAY RUN 1			INTRA-ASSAY RUN 2			INTRA-ASSAY RUN 3			INTERASSAY (n=9)		
	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%
A	1.8	0.208	11.35	1.7	0.153	8.81	2.0	0.153	7.77	1.8	0.181	9.82
B	3.0	0.208	7.02	3.1	0.300	9.68	3.3	0.173	5.25	3.1	0.249	7.97
C	25.9	0.252	0.97	25.7	0.058	0.22	26.8	0.557	2.08	26.1	0.589	2.26
D	33.6	0.850	2.53	32.0	1.193	3.73	31.7	1.662	5.25	32.4	1.439	4.44
E	46.7	0.700	1.50	44.6	0.608	1.36	45.5	0.643	1.41	45.6	1.074	2.36
F	57.4	8.088	14.09	59.1	1.332	2.25	59.4	3.675	6.19	58.6	4.587	7.82

TABLE 5 : MAGO Plus - Intra-Assay and Interassay Precision for Is-anti-β_2-Glycoprotein I IgG

SERUM	INTRA-ASSAY RUN 1			INTRA-ASSAY RUN 2			INTRA-ASSAY RUN 3			INTERASSAY (n=9)		
	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%
A	6.2	0.929	15.07	5.2	0.058	1.12	4.5	0.458	10.18	5.3	0.893	16.91
B	8.6	1.930	22.35	7.1	0.306	4.32	5.5	0.503	9.21	7.1	1.702	24.13
C	34.3	1.916	5.59	33.3	0.643	1.93	32.2	1.930	5.99	33.3	1.659	4.99
D	51.7	2.330	4.51	42.7	3.857	9.03	48.8	3.009	6.17	47.7	4.811	10.08
E	59.3	1.716	2.89	60.1	3.650	6.07	58.3	3.764	6.46	59.2	2.867	4.84
F	89.6	4.521	5.05	88.1	2.409	2.74	88.6	3.119	3.52	88.8	3.074	3.46

TABLE 6 : Manual Intra-Assay and Interassay Precision for Is-anti-β_2-Glycoprotein IgM

SERUM	INTRA-ASSAY RUN 1			INTRA-ASSAY RUN 2			INTRA-ASSAY RUN 3			INTERASSAY (n=9)		
	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%
A	1.2	0.208	17.84	1.1	0.208	19.52	0.9	0.058	6.19	1.1	0.181	17.15
B	4.8	0.208	4.37	4.9	0.000	0.00	4.6	0.208	4.49	4.8	0.187	3.92
C	13.2	1.940	14.73	12.9	1.375	10.66	12.2	0.100	0.82	12.8	1.266	9.93
D	19.3	1.790	9.26	18.3	2.003	10.97	15.2	1.480	9.74	17.6	2.409	13.69
E	37.8	3.499	9.26	39.4	4.451	11.30	36.7	0.153	0.42	38.0	3.062	8.06
F	51.7	2.330	4.51	54.2	3.318	6.12	55.5	0.781	1.41	53.8	2.657	4.94

TABLE 7 : MAGO Plus - Intra-Assay and Interassay Precision for Is-anti-β_2-Glycoprotein IgM

SERUM	INTRA-ASSAY RUN 1			INTRA-ASSAY RUN 2			INTRA-ASSAY RUN 3			INTERASSAY (n=9)		
	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%	MEAN U/ml	SD	CV%
A	2.1	0.361	17.17	1.6	0.173	10.83	2.0	0.265	13.23	1.9	0.332	17.46
B	6.2	0.306	4.90	6.5	0.529	8.14	7.3	0.709	9.76	6.7	0.660	9.89
C	16.8	2.454	14.64	19.2	3.453	18.02	22.0	4.466	20.33	19.3	3.815	19.77
D	21.5	2.369	11.00	26.4	1.823	6.90	25.8	1.069	4.15	24.6	2.796	11.38
E	43.4	2.754	6.35	48.9	2.646	5.41	53.0	3.958	7.46	48.4	5.020	10.37
F	65.3	9.794	15.01	77.6	1.501	1.93	75.7	4.130	5.45	72.9	7.878	10.81

Expected Values

The prevalence of anti-β_2-glycoprotein I 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–$\beta_2$glycoprotein I are generally absent, or have a very low incidence, in the normal healthy population. In a recently published study the distribution of anti-β_2-glycoprotein I antibodies in healthy controls was 3%. In patients with SLE the prevalence of $\beta_2$glycoprotein IgG & IgM antibodies has been found to range from 20-30%. The prevalence of these antibodies in anti-phospholipid syndrome (APS) patients has been found to range from 40 to 65%.

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-β_2Glycoprotein I IgG/IgM Test Kit for both IgG and IgM antibodies. Ninety-eight of these samples were from males and 50 were from females. For IgG antibodies, one hundred and forty-five sera (98.0%) were negative for antibodies, two sera (1.3%) were positive and one serum (0.7%) was equivocal. For IgM antibodies, one hundred and forty-three (96.6%) were negative, three sera (2.0%) were positive and two sera (1.4%) were equivocal. The gender, 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-β_2Glycoprotein I IgG/IgM test for both antibody types. Forty-six (80.7%) were positive, ten (17.5%) were negative and one (1.8%) was equivocal for IgG antibodies. Twenty-seven (43.8%) were positive, twenty-nine (52.6%) were negative, and two (3.6%) 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-β_2-Glycoprotein IgG and IgM Antibodies in a Normal S. Florida Population

	Number of Donors	Prevalence	
Total Number	148	**IgG**	**IgM**
Geographic Location:	South Florida : 148	1.3%	2.0%
Age			
10-19	7	14.3%	0.0%
20-29	36	0.0%	0.0%
30-39	73	1.4%	2.7%
40-49	22	0.0%	0.0%
50-59	8	0.0%	0.0%
60-69	2	0.0%	0.0%

FIGURE 9
Distribution of anti-β_2Glycoprotein I IgG in a Normal Population

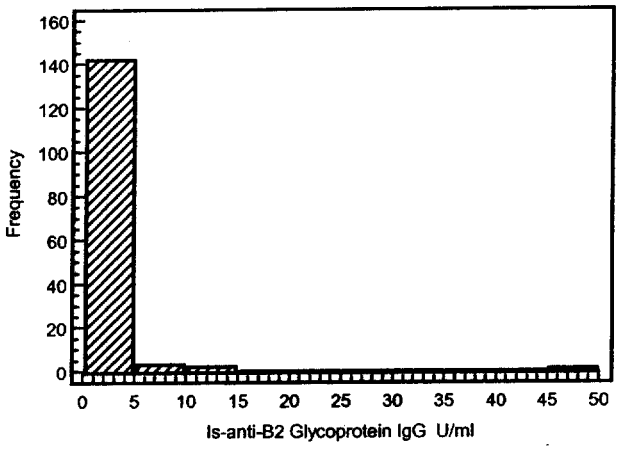


FIGURE 10
Distribution of anti-β_2Glycoprotein I IgM in a Normal Population

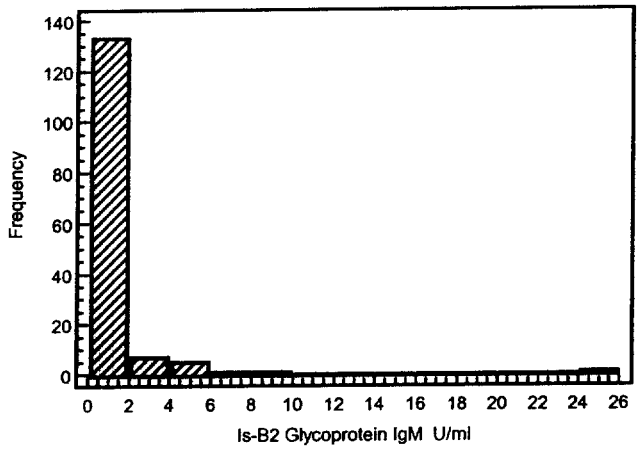


FIGURE 11
Distribution of anti-β_2Glycoprotein IgG I In a Clinical Population

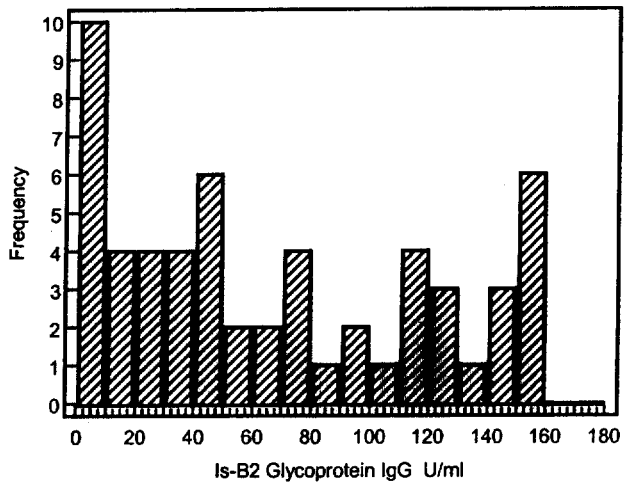
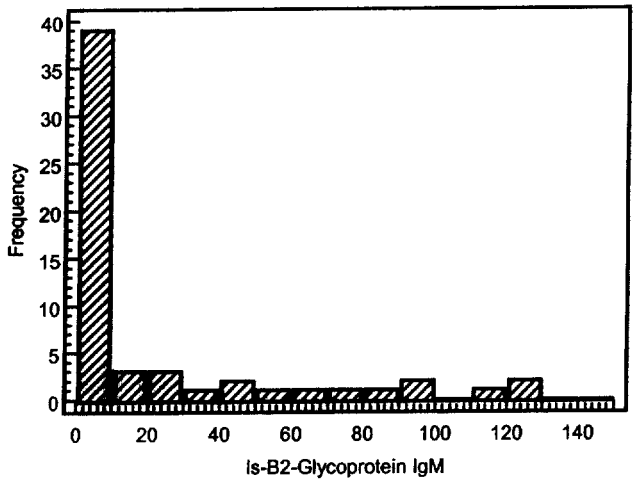


FIGURE 12
Distribution of anti-β_2Glycoprotein IgM I in a Clinical Population



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 21 2001

Dr. Lynne Stirling
VP Regulatory Affairs
Diamedix Corporation
2140 N. Miami Avenue
Miami, FL 33127

Re: k013628
Trade/Device Name: Is anti-β_2-Glycoprotein I IgG/IgM
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple autoantibodies immunological test system
Regulatory Class: Class II
Product Code: MSV
Dated: October 31, 2001
Received: November 5, 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

INDICATIONS FOR USE STATEMENT

510(K) NUMBER : K013628

DEVICE NAME : Is anti-β_2-Glycoprotein I IgG/IgM Test System

Indications for Use : The Diamedix Is anti-β_2Glycoprotein I IgG/IgM Test Kit is an Indirect enzyme Immunoassay (EIA) for the semi-quantitative measurement of IgG or IgM antibodies to $\beta_2$glycoprotein I in human serum as an aid in the diagnosis of certain autoimmune disease thrombotic disorders in patients with SLE or SLE-like disorders. These reagents can be used either manually or in conjunction with the MAGO® Plus Automated EIA Processor.

Prescription Use ✓

Rev.12/18

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K013628