K993294

OCT 25 1999

Appendix E. 510(k) Summary of Safety and Effectiveness

The following section is included as required by the Safe Medical Device Act (SMDA) of 1990.

Name:	Diamedix Corporation
Address:	2140 N. Miami Avenue Miami, FL 33127
Contact Person:	Dr. Lynne Stirling
Phone Number:	305-324-2354
Fax Number:	305-324-2388

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: K993294

Applicant Information:

Date Prepared:	September 29, 1999
Name:	Diamedix Corporation
Address:	2140 N. Miami Avenue Miami, FL 33127
Contact Person:	Dr. Lynne Stirling
Phone Number:	305-324-2354
Fax Number:	305-324-2388

Device Information:

Trade Name:	Is-ANA ELISA Screen Test System
Common Name:	ANA Screening Test
Classification Name:	Antinuclear Antibody Immunological Test System (866.5100), product code LLL

Equivalent Device:
Diamedix Immunosimplicity ANA (Is-ANA) Screen Test

Device Description: The Is-ANA ELISA ScreenTest System is an enzyme-linked immunosorbent assay (ELISA) for the detection of anti-nuclear antibodies (ANA) in human serum.

Intended Use: The assay is intended for use in detecting ANAs in human serum. The assay collectively detects in one well total ANAs against dsDNA, Histones, SSA, SSB, Sm, Sm/RNP, Scl-70, Jo-1 and centromeric antigens along with sera positive for IFA Hep-2 ANAs. The results of the assay can be used as an aid in the diagnosis of certain autoimmune disorders.

Principle of the Procedure:

The Is-ANA ELISA Screen Test System is an enzyme-linked immunosorbent assay to detect ANAs in human serum. Purified antigens and other antigens extracted from the HEp-2 nucleus are attached to a solid phase microtiter well. Diluted test sera are added to each well. If antibodies which recognize the antigens are present in the patient sample they will bind to the antigens in the well. After incubation, the wells are washed to remove unbound antibody. An enzyme labeled anti-human immunoglobulin (conjugate) is added to each test well. If antibody is present the enzyme-linked antibody will bind to it. After incubation, the wells are washed to remove unbound conjugate. A substrate solution is then added to each well. If enzyme is present from prior step, the reaction is stopped and the color intensity is measured photometrically producing an indirect measure of the specific antibodies present in the patient sample.

SUMMARY OF SAFETY AND EFFECTIVENESS

Performance Characteristics

A. Comparison Testing: Relative Sensitivity and Specificity

The Diamedix Is-ANA ELISA Screen Test Kit was evaluated relative to another commercially available ANA Screen test. One hundred and forty-six sera from normal blood donors and one hundred and eighty-five sera from clinical patients were tested by the Is-ANA Screen ELISA Test Kit and the comparative method. Testing by both methods was performed both manually and using the MAGO PLUS Automated EIA Processor. The results shown in Table 1 are the comparison of the Is-ANA ELISA Screen performed manually compared to the comparative method, both manual and automated. The results shown in Table 2 are the comparison of the Is-ANA ELISA Screen performed on the MAGO Plus compared to the comparative method, both manual and automated.

TABLE 1

Is-ANA ELISA Screen Manual	Other ELISA : Manual			Other ELISA : MAGO Plus		
	# of Sera	%	95%CI	# of Sera	%	95% CI
Relative Sensitivity	188/196	95.9	92.1-98.2	185/191	96.9	93.3-98.8
Relative Specificity	107/112	95.5	89.9-98.5	110/115	95.7	90.1-98.6
Overall Agreement	295/308*	95.8	92.7-97.7	295/306**	96.4	93.7-98.2

* Twenty-two samples equivocal in either or both methods were excluded from calculations; ** Twenty-one samples, equivocal in either or both methods were excluded from calculations.

TABLE 2

Is-ANA ELISA Screen MAGO Plus	Other ELISA : Manual			Other ELISA : MAGO Plus		
	# of Sera	%	95%CI	# of Sera	%	95% CI
Relative Sensitivity	183/188	97.3	93.9-99.1	183/187	97.9	94.6-99.4
Relative Specificity	105/112	93.8	87.5-97.5	109/116	94.0	88.0-97.5
Overall Agreement	288/300*	96.0	93.1-97.9	292/303**	96.4	93.6-98.2

* Twenty-two samples equivocal in either or both methods were excluded from calculations; ** Twenty-five samples, equivocal in either or both methods were excluded from calculations.

B. Clinical Sensitivity and Specificity using Characterized Sera

A total of three hundred and thirty-one characterized sera were assayed using the Is-ANA ELISA Screen test Kit. These consisted of a number of sera of known ANA reactivity and a number of samples with no known apparent ANA reactivity. Samples tested were as follows:

a. NORMAL BLOOD DONOR SERA
One hundred and forty-six samples from normal blood donors were tested in the Is-ANA ELISA Screen. Results are shown in Table 3.

b. MONOSPECIFIC SERA
Forty-five sera obtained from a variety of sources and shown to contain monospecific antibodies of clinical significance were tested in the Is-ANA ELISA Screeen Test Kit both manually and using the MAGO Plus Automated Processor. The results are summarized in Table 3.

b. IFA-ANA POSITIVE SERA

Seventy sera shown to be positive by the IFA- ANA method were tested in the Is-ANA ELISA Screen Test Kit. These seventy sera consisted of thirty-five sera with IFA-ANA titers between 1:40 and 1:320 and thirty-five sera with titers in excess of 1: 320. The results obtained are summarized in Table 3.

d. AUTOIMMUNE DISEASE STATE SERA

Seventy sera from a variety of sources from patients diagnosed with an autoimmune disorder were tested both manually and on the MAGO Plus using the Is-ANA ELISA Screen. Results are shown in Table 3.

TABLE 3

Patient group		Positive	Negative	Equivocal*	Total
a. *Normal Sera*	Manual	14	119	13	146
	MAGO Plus	14	116	16	146
b. *Monospecific Sera*	Manual & MAGO Plus	45	0	0	45
		44	0	0	44**
c. *IFA-ANA*					
Low Titer Sera	Manual	30	4	1	35
	MAGO Plus	34	0	1	35
High Titer Sera	Manual &	35	0	0	35
	MAGO Plus	35	0	0	35
d. *Autoimmune Disease Sera*	Manual &	70	0	0	70
	MAGO Plus	64	1	0	65***

* Equivocal results were excluded from calculations ** one sample QNS for MAGO Plus *** Five samples QNS for MAGO Plus

Clinical Specificity	Manual	95% CI	MAGO Plus	95% CI
Normals	119/133 = 89.5%	84.3-94.7	116/130 = 89.2%	83.9-94.6
Clinical Sensitivity				
Low Titer ANA+ Sera	30/34 = 88.2%	72.6-96.7	34/34 = 100.0%	89.7-100.0
High Titer ANA+ Sera	35/35 = 100.0%	90.0-100.0	35/35 = 100.0%	90.0-100.0
Monospecific Sera	45/45 = 100.0%	92.1-100.0	44/44 = 100.0%	92.0-100.0
Autoimmune Disease Sera	70/70 - 100.0%	94.9-100.0	64/65 = 98.5%	91.7-100.0

C. Precision

The precision of the Is-ANA ELISA Screen Test Kit was determined by testing six different sera (2 negative and 4 positive) plus the kit calibrator and controls in triplicate in two different runs on three different days. Precision was evaluated manually and using the MAGO PLUS Processor. The intra- and interassay precision for the manual procedure is shown in Table 4 and for the MAGO Plus Automated EIA Processor in Table 5.

TABLE 4: Manual Precision

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY		
	Mean Index	SD	CV%	Mean Index	SD	CV%	Mean Index	SD	CV%	Mean Index	SD	CV%
A (NEG)	0.262	0.007	2.7	0.223	0.024	10.8	0.280	0.019	6.8	0.255	0.030	11.6
B (NEG)	0.292	0.009	3.1	0.220	0.049	22.3	0.247	0.019	7.7	0.253	0.042	16.7
C (POS)	1.677	0.221	13.2	1.731	0.148	8.5	1.682	0.030	1.8	1.697	0.147	8.7
D (POS)	1.696	0.098	5.8	1.521	0.093	6.1	1.586	0.050	3.2	1.601	0.108	6.7
E (POS)	3.310	0.192	5.8	3.232	0.338	10.5	3.179	0.114	3.6	3.305	0.261	7.9
F (POS)	3.482	0.299	8.6	3.365	0.294	8.7	2.963	0.132	4.5	3.270	0.330	10.1
c/o CAL	1.022	0.068	6.7	0.992	0.110	11.1	0.999	0.121	12.1	1.004	0.097	9.6
POS	2.938	0.176	6.0	3.022	0.256	8.5	2.766	0.122	4.4	2.909	0.211	7.3
NEG	0.247	0.039	15.8	0.210	0.036	17.1	0.264	0.030	11.4	0.240	0.041	16.9

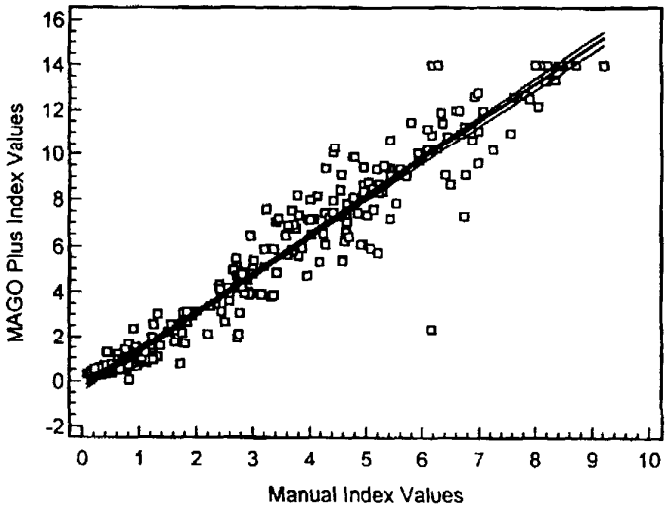
TABLE 5 : MAGO Plus Precision

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY		
	Mean Index	SD	CV%	Mean Index	SD	CV%	Mean Index	SD	CV%	Mean Index	SD	CV%
A (NEG)	0.377	0.028	7.4	0.407	0.052	12.8	0.395	0.068	17.2	0.39	0.051	12.9
B (NEG)	0.322	0.008	2.5	0.320	0.021	6.6	0.322	0.025	7.8	0.32	0.018	5.6
C (POS)	2.402	0.059	2.5	2.540	0.239	9.4	2.625	0.100	3.8	2.52	0.173	6.8
D (POS)	2.215	0.106	4.8	2.218	0.120	5.4	2.437	0.158	6.5	2.29	0.163	7.1
E (POS)	4.382	0.171	3.9	4.528	0.183	4.0	4.835	0.305	6.3	4.58	0.291	6.4
F (POS)	5.385	0.071	1.3	5.470	0.137	2.5	5.903	0.246	4.2	5.59	0.281	5.0
c/o CAL	0.968	0.053	5.5	1.025	0.078	7.6	1.113	0.055	4.9	1.04	0.085	8.2
POS	4.407	0.238	5.4	4.310	0.270	6.3	5.050	0.167	3.3	4.59	0.401	8.7
NEG	0.350	0.031	8.9	0.343	0.035	10.2	0.388	0.030	7.7	0.36	0.040	11.1

D. Correlation of Manual and MAGO PLUS Results

The Is-ANA ELISA Screen 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 three hundred and twenty-five serum samples tested by both methods were plotted. A scattergram and regression line of the results obtained with 95% confidence intervals is shown in FIGURE 1. The data indicate a good correlation with a correlation coefficient (r) of 0.9712.

FIGURE 1. Manual vs MAGO PLUS Correlation



Expected Values

The expected value for a normal patient is a negative result. However, positive ANA results may be found in apparently healthy individuals. In a recent study 12.4% of sera from normal healthy donors gave a detectable ANA result . Patient sera containing autoantibodies to those antigens represented in the Is-ANA ELISA Screen Test Kit will give positive results which can be further evaluated in specific tests. The number of positive samples detected is dependent upon the populations being tested.

The expected values in a normal S. Florida blood donor population were evaluated by assaying one hundred and forty-six sera both manually and using the MAGO Plus Automated EIA Processor. Figures 2 and 4 show the distribution of results in this normal population. For manual and MAGO PLUS testing 9.6% (14/146) gave positive results. Thirteen samples (8.9%) gave equivocal results manually and sixteen samples (11.4%) gave equivocal results on the MAGO Plus. The remainder of the samples gave negative results. Of the positive samples, three were found to contain specific autoantibodies and an additional two samples gave weakly positive IFA-ANA results.

In the present studies one-hundred and eighty-five clinical sera obtained from patients with an autoimmune disease or with a known autoantibody reactivity were also evaluated in the Is-ANA ELISA Screen Test Kit. (for MAGO Plus testing one hundred and seventy-nine were available, six being QNS). Figures 3 and 5 show the distribution of results for this positive population. For manual testing 97.2% (180/185) of samples were positive. For MAGO Plus testing 98.9% (177/179) were positive.

FIGURE 2. Expected Values Normal Samples - Manual

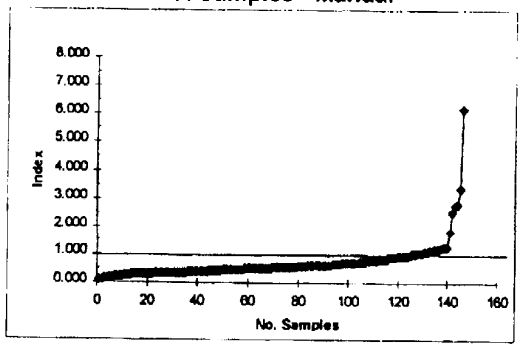


FIGURE 3. Expected Values Clinical Samples - Manual

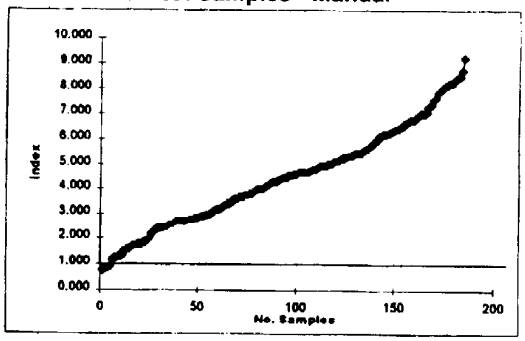


FIGURE 4. Expected Values Normal Samples - MAGO Plus

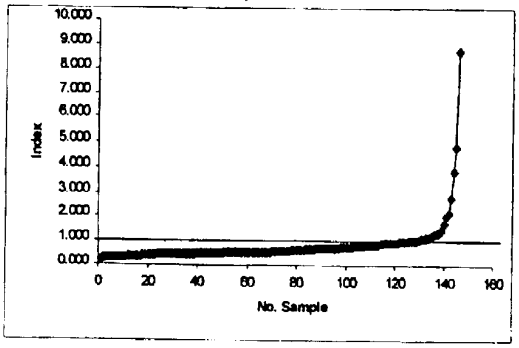
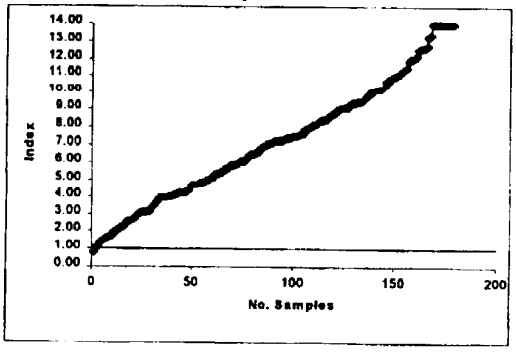


FIGURE 5. Expected Values Clinical Samples - MAGO Plus



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

OCT 25 1999

Dr. Lynne Stirling
Vice President, Regulatory Affairs
DiaMedix Corporation
2140 North Miami Avenue
Miami, Florida 33127

Re: K993294
Trade Name: Diamedix Is-ANA ELISA Screen Test System
Regulatory Class: II
Product Code: LKJ
Dated: September 29, 1999
Received: October 1, 1999

Dear Dr. Stirling:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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 (Premarket Approval), 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 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

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"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers 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

10(k) Number (if known): K993294

DEVICE NAME : Is-ANA ELISA Screen Test System

Indications for Use : The Diamedix Immunosimplicity (Is) ANA ELISA ScreenTest Kit is a qualitative enzyme immunoassay intended to screen for the presence of antinuclear antibodies (ANAs) in human serum as an aid in the diagnosis of certain systemic rheumatic diseases. This assay collectively detects in one well, total ANAs against double-stranded DNA (dsDNA and nDNA), Histones, SSA, SSB, Sm, Sm/RNP, Scl-70, Jo-1 and centromeric antigens along with sera positive for Immunofluorescent (IF) HEp-2 ANAs. These reagents can be used either manually or in conjunction with the MAGO Plus Automated EIA Processor.

(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 K993294

Prescription Use ✓ OR Over-The-Counter Use ___
(Per 21 CFR 801.109)

(Optional Format 1-2-96)