

K974889

MAR - 6 1998

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.**

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Address: 2140 N. Miami Avenue
Miami, FL 33127

Contact Person: Dr. Lynne Stirling
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000241

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: K974889

Applicant Information:

Date Prepared: December 29, 1997
Name: Diamedix Corporation
Address: 2140 N. Miami Avenue
Miami, FL 33127

Contact Person: Dr. Lynne Stirling
Phone Number: 305-324-2354
Fax Number: 305-324-2585

Device Information:

Trade Name: Is-RF Test System
Common Name: RF EIA Test
Classification Name: RF Immunological Reagents

Equivalent Device:

RF Microassay

Device Description: The Is-RF Test Kit System is an enzyme-linked immunosorbent assay (ELISA) for the detection and quantitation of RF IgM-class in human serum.

Intended Use: The assay is intended for use in detecting RF IgM antibodies in a single human serum sample. The results of the assay are to be used as an aid in the diagnosis of RA.

Principle of the Procedure:

The Is-RF Test System is an enzyme-linked immunosorbent assay to detect RF-IgM in human serum. Purified human IgG is attached to a solid phase microtiter well. Diluted test sera are added to each well. If RF-IgM antibodies are present in the patient sample they will bind to the human IgG on 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 antibody present in the patient sample.

SUMMARY OF SAFETY AND EFFECTIVENESS

Performance Characteristics

A. Comparison Testing

The Diamedix Is-RF Test Kit was evaluated relative to another commercially available RF EIA test kit that is also standardized against the WHO RF Reference preparation. Two hundred sera from normal blood donors and 49 sera from clinical patients were tested by the Is-RF test kit and the comparative method. Testing was performed both manually and using the MAGO Automated Processor. Results are shown in Table 1.

TABLE 1

	Manual			MAGO		
	# of Sera	%	95% CI	# of Sera	%	95% CI
Relative Sensitivity	65/66	98.5	91.8-100.0	64/65	98.5	91.7-100.0
Relative Specificity	173/174	99.4	96.8-100.0	176/179	98.3	95.2-99.7
Overall Agreement	238/240*	99.2	97.9-99.9	240/244**	98.4	95.2-99.7

* 9 equivocal results excluded from calculations

** 5 equivocal results excluded from calculations

For manual testing one sample was positive by the Is-RF and negative by the comparative method and one sample was negative in the Is-RF and positive by the comparative method. Both samples were negative by a referee method. For MAGO testing there were three samples that were positive in the Is-RF and negative in the comparative method and one sample that was negative in the Is-RF and positive by the comparative method. When the three samples that were positive by the Is-RF were tested by a referee method one was positive and two were negative. The sample that was negative in the Is-RF but positive by the comparative method was also negative in the referee method.

B. Linearity

Figures 1 and 2 show typical examples of the Is-RF linearity. These figures depict the results of the in-house reference standard (which has been standardized against the WHO Reference) tested by the Is-RF after serial two-fold manual dilution in Sample Diluent. Separate dilutions were tested both manually and with MAGO. The results demonstrate a high degree of linearity for the Is-RF Test Kit throughout the reportable range of the assay.

FIGURE 1 - MANUAL LINEARITY

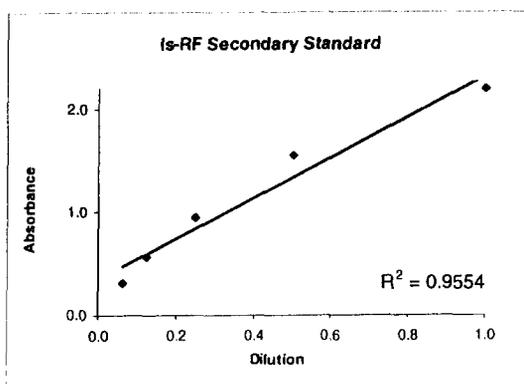
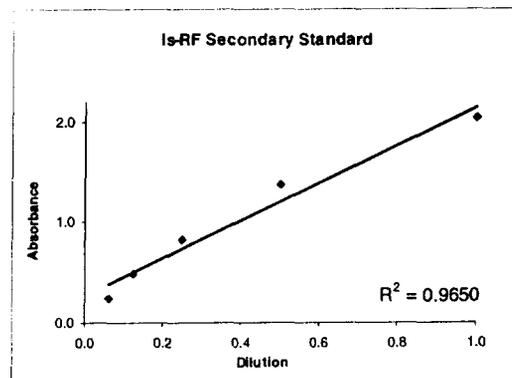


FIGURE 2 - MAGO LINEARITY



C. Precision

The precision of the Is-RF test kit was determined by testing six different sera and the kit calibrator and controls in triplicate in two runs on three different days. Precision was evaluated both manually and using the MAGO. The intra- and interassay precision is shown in Tables 2 and 3.

Is-RF Precision (Manual)

TABLE 2

SERUM	Intra-assay (n=6)									Interassay (n=18)		
	Day 1			Day 2			Day 3			Mean	SD	%CV
	Mean	SD	%CV	Mean	SD	%CV	Mean	SD	%CV			
A (Neg)	1.4	0.4	N/A	1.2	0.3	N/A	1.4	0.1	N/A	1.4	0.3	N/A
B (Neg)	0.4	0.1	N/A	0.4	0.1	N/A	0.6	0.1	N/A	0.5	0.1	N/A
C (Pos)	37.7	2.8	7.4	39.7	2.9	7.2	41.9	4.0	9.6	39.8	3.6	9.0
D (Pos)	54.5	2.8	5.2	56.7	2.8	5.0	60.6	3.4	5.6	57.3	3.9	6.7
E (Pos)	80.4	2.4	3.0	82.7	4.1	4.9	87.8	1.5	1.7	83.6	4.2	5.0
F (Pos)	113.3	4.7	4.1	113.8	7.1	6.2	113.4	3.9	3.4	113.5	5.1	4.5
Cal.	110.4	5.5	5.0	114.2	6.1	5.4	107.5	4.4	4.1	110.7	5.8	5.2
Pos.	46.7	2.6	5.7	48.9	3.5	7.2	47.7	3.8	7.9	47.7	3.3	6.9
Neg.	0.7	0.2	N/A	0.6	0.1	N/A	0.8	0.2	N/A	0.7	0.2	N/A

Is-RF Precision (MAGO)

TABLE 3

SERUM	Intra-assay (n=6)									Interassay (n=18)		
	Day 1			Day 2			Day 3			Mean	SD	%CV
	Mean	SD	%CV	Mean	SD	%CV	Mean	SD	%CV			
A (Neg)	1.7	0.3	N/A	1.4	0.4	N/A	1.3	0.4	N/A	1.4	0.4	N/A
B (Neg)	0.8	0.3	N/A	0.6	0.6	N/A	0.5	0.4	N/A	0.6	0.4	N/A
C (Pos)	37.7	1.1	2.9	39.2	1.3	3.3	40.8	3.2	7.8	39.2	2.4	6.0
D (Pos)	56.9	2.1	3.6	59.3	1.9	3.2	63.4	2.6	4.1	59.8	3.5	5.8
E (Pos)	87.7	1.8	2.1	88.1	4.5	5.1	90.7	5.1	5.6	88.8	4.0	4.5
F (Pos)	115.9	3.5	3.0	113.5	3.5	3.1	116.1	3.6	3.1	115.1	3.5	3.1
Cal.	111.9	3.5	3.1	111.9	4.0	3.6	113.4	2.6	2.3	112.4	3.3	2.9
Pos.	49.2	1.8	3.7	48.6	2.2	4.5	49.6	2.3	4.6	49.2	2.0	4.2
Neg.	1.4	0.4	N/A	1.2	1.0	N/A	0.6	0.6	N/A	1.1	0.7	N/A

D. Crossreactivity/Interference

Antinuclear antibodies (ANA) have been found in 14 to 28% of patients with RA and are usually found in patient with more advanced disease (1). Several RF-negative samples containing various ANA were evaluated to ensure lack of interference from these antibodies in RF-negative sera. These results are shown in Table 4. In addition, no prozone interference was encountered when testing high titered sera.

TABLE 4

Sample #	Is-RF IU/ml	Interp	ANA Specificity
1	1.6	NEG	Scl-70, SSA
2	1.4	NEG	Scl-70, SSA
3	2.0	NEG	Jo-1, SSA, Sm/RNP
4	11.6	NEG	Jo-1, Sm/RNP
5	3.6	NEG	SSA, SSB
6	10.6	NEG	SSA, SSB
7	4.2	NEG	SSA, Sm/RNP
8	2.4	NEG	SSA, Sm/RNP
9	0.6	NEG	SSA
10	0.6	NEG	SSA
11	1.8	NEG	Sm/RNP
12	1.4	NEG	Sm/RNP
13	1.0	NEG	SSA, SSB, dsDNA
14	5.6	NEG	SSA, dsDNA

E. Expected Values

The expected value in the normal population is negative. However, apparently healthy asymptomatic individuals may have RF. These individuals usually have low titers. The incidence of false positives increases with age and is similar in males and females. Figures 3 and 5 show the distribution of RF results in the normal S. Florida donor population performed manually and on MAGO respectively. For manual testing 8.5% of the normals gave positive values; for MAGO testing the positive frequency was 9.0%.

The distribution of IU/ml values for 49 sera from clinical patients is shown in Figures 4 and 6 performed manually and on MAGO respectively. All clinical sera were positive for RF using either testing method.

FIGURE 3 - MANUAL

Normals

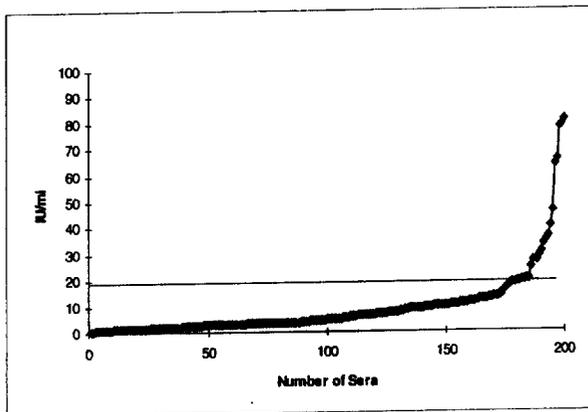


FIGURE 4 - MANUAL

Clinical patients

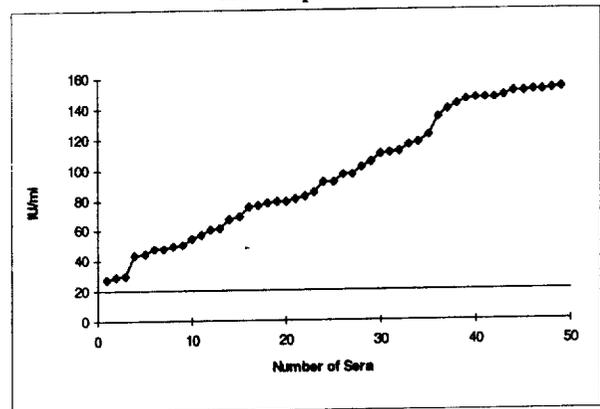


FIGURE 5 - MAGO

Normals

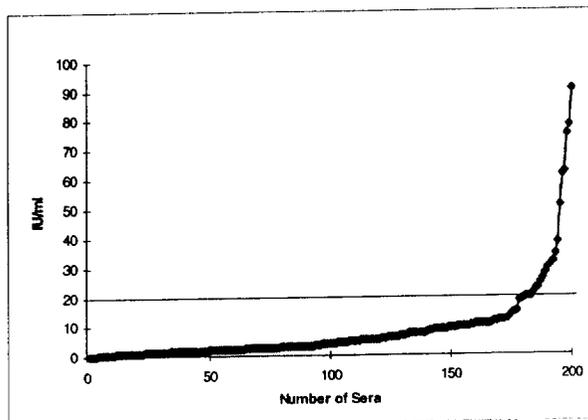
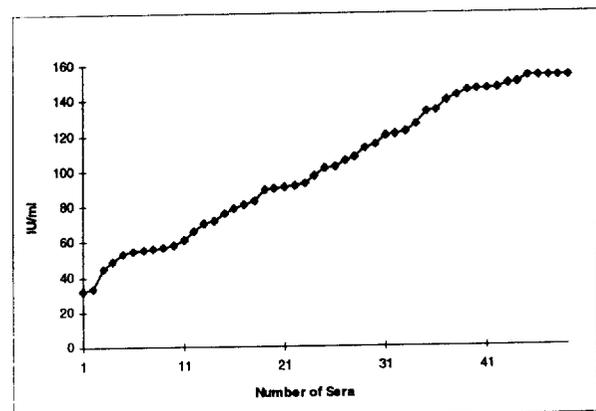


FIGURE 6 - MAGO

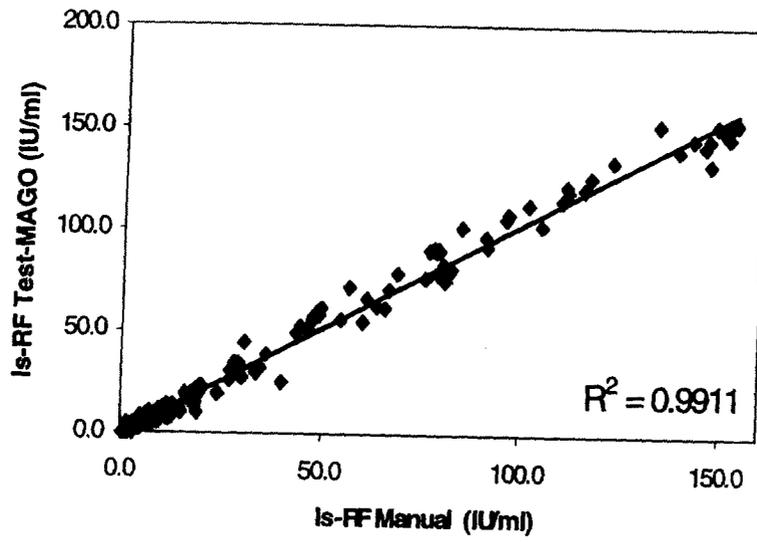
Clinical patients



F. Correlation of Manual and Mago Results

Correlation of manual and MAGO IU/ml values for 249 samples tested in the Is-RF Test Kit yielded an R^2 value of 0.9911 as shown in Figure 7.

FIGURE 7



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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Lynne Stirling, Ph.D.
Diamedix® Corporation
2140 North Miami Avenue
Miami, Florida 33127

MAR - 6 1998

Re: K974889
Trade Name: Diamedix Is-RF Test System
Regulatory Class: II
Product Code: DHR
Dated: December 29, 1997
Received: December 30, 1997

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 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 (Pre-market 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 requirement, 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 pre-market 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.

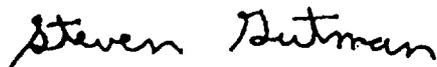
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

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 at (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>"

Sincerely yours,



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

510(k) Number (if known): K974889

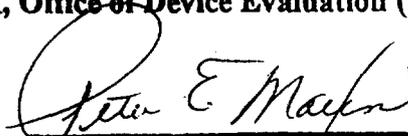
Device Name: _____

Indications For Use:

Indications for Use :The Diamedix Is-RF an Enzyme Immunoassay (EIA) for the detection and quantitative determination of RF-IgM antibodies in human serum as an aid in the diagnosis of rheumatoid arthritis. These reagents can be used either manually or in conjunction with the MAGO® 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 K974889
510(k) Number _____

Prescription Use
(Per 21 CFR 801.109)

OR Over-The-Counter Use _____

(Optional Format 1-2-96)