JUL 9 2002

# 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: K021394

**Applicant Information:**

| | |
|---|---|
| Date Prepared: | June 27, 2002 |
| Name: | Diamedix Corporation |
| Address: | 2140 N. Miami Avenue<br>Miami, FL 33127 |
| Contact Person: | Dr. Lynne Stirling |
| Phone Number: | 305-324-2354 |
| Fax Number: | 305-324-2388 |

**Device Information:**

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

**Equivalent Device:**
Is-RF Test System

**Device Description:** The Is-Rheumatoid Factor 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 the quantitative detection of RF IgM-class antibodies in human serum by indirect enzyme immunoassay as an aid in the diagnosis of rheumatoid arthritis (RA). This test kit can be used either manually or in conjunction with the MAGO Plus Automated EIA processor.

**Principle of the Procedure:**

The Is-Rheumatoid Factor 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 intesnity is measured photometrically producing an indirect measure of the specific antibody present in the patient sample.

# SUMMARY OF SAFETY AND EFFECTIVENESS

## Performance Charactistics

### Comparisons with Other Methods

#### A. Relative Sensitivity and Specificity versus Another EIA Test

One hundred and eighty-five frozen retrospective sera were tested using the Is-Rheumatoid Factor Test Kit and another commercially available EIA kit for detecting RF. Based upon the results of this testing the relative sensitivity, relative specificity and overall agreement were calculated. The results obtained are summarized in TABLE 1 and reveal excellent agreement with no discordant/discrepant sample results.

**TABLE 1**
**Is-Rheumatoid Factor**

| Other EIA | Positive | Negative | *Equivocal |
|---|---|---|---|
| Positive | 89 | 0 | 2 |
| Negative | 0 | 91 | 1 |
| * Equivocal | 2 | 0 | 0 |

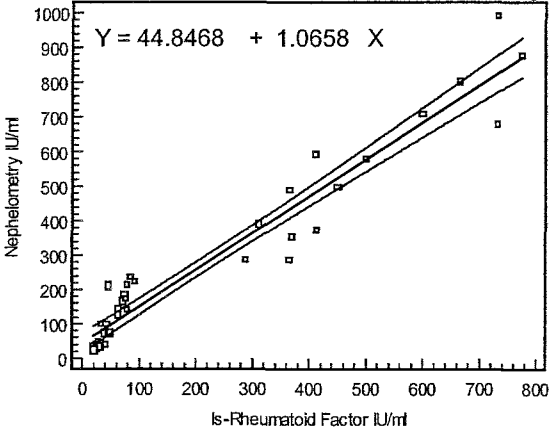
| | | | **95% CI |
|---|---|---|---|
| Relative Sensitivity | 89/89 | = 100% | 95.9-100.0% |
| Relative Specificity | 91/91 | = 100% | 96.0-100.0% |
| Overall Agreement | 190/190 | = 100% | 98.1-100.0% |

* Equivocal results were excluded from calculations ** 95% Confidence Intervals (CI) calculated by the Exact Method (11)

#### B. Correlation with Nephelometry Results

Forty samples containing varying levels of RF as determined by nephelometry were tested using the Is-Rheumatoid Factor Test Kit. Samples whose results exceeded the Calibrator value were diluted and results obtained were then multipied by the dilution factor. IU/ml values determined by both methods were then subjected to linear regression analysis. The correlation between IU/ml values determined by both methods is shown below.

**FIGURE 1 : Correlation with Nephelometry**




| |
|---|
| Intercept 44.8468 |
| Slope 1.0658 |
| Coefficient of determination = 0.9355 |
| Correlation Coefficient r = 0.9672 |
| 95% CI for r = 0.9384 to 0.9826 |

## C. Comparison with Latex Agglutination

The performance of the Is-Rheumatoid Factor Test Kit was also compared to that of the latex agglutination test which is another commonly used method for detecting RF. A total of 71 sera were tested by both methods. These consisted of 40 normal samples, 18 known clinical samples and 13 samples containing other autoantibodies with or without RF. The results are summarized in TABLE 2 below.

**TABLE 2 : Comparison with a Latex Agglutination Test**

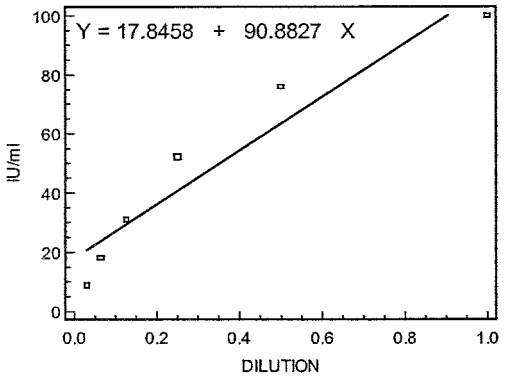
| Sample Type | # | Latex Results | Is- Results | Comments |
|---|---|---|---|---|
| Normal Sera | 40 | 40/40 Negative | 40/40 Negative | Specificity: Latex & Is- 100% |
| Clinical Sera | 18 | 9/18 Positive | 18/18 Positive | Sensitivity: Latex 50% |
| | | | | Sensitivity: Is- 100% |
| Other Sera | 13 | 4/13 Positive | 10/13 Positive | Other ELISA 9/13 Positive |

It should be note that the screening dilution for the latex is 1:20. A positive result at this dilution is considered equivalent to 60 IU/ml. Therefore, all samples less than 60 IU/ml by either ELISA or nephelometry were negative by latex.

## D. Linearity

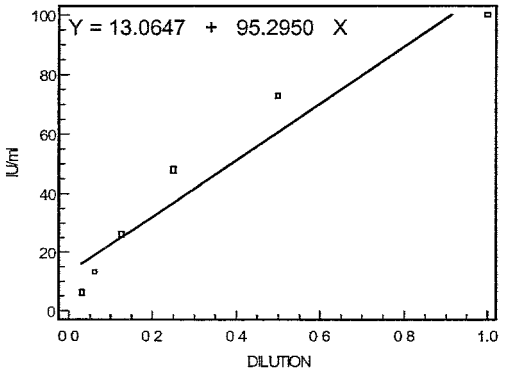
To assess the linearity of the Is-Rheumatoid Factor Test Kit several highly positive samples were serially diluted using Sample Diluent and each dilution was then tested in the assay system. In addition to this testing, the WHO Standard and the Diamedix in-house Reference Standard, both assigned values of 100 IU/ml, were also serially diluted and each dilution then tested with the assay system. FIGURES 2 and 3 show the titration of these materials. The Correlation Coefficients of the other samples were in close agreement with those shown below.

**FIGURE 2 : Linearity of WHO Standard**




Intercept 17.8458
Slope 90.8827
Coefficient of determination = 0.9133
Correlation Coefficient r = 0.9557

**FIGURE 3 : Linearity of In-House Standard**




Intercept 13.0647
Slope 95.2950
Coefficient of determination = 0.9282
Correlation Coefficient r = 0.9634

## E. Lack of Crossreactivity with Other Antinuclear Antibodies

Antinuclear antibodies (ANA) have been found in 14 to 28% of patients with RA and are usually found in patients with more advanced disease (1). Several RF-negative samples (as determined by testing in an commercially available RF kit) containing various ANA were evaluated to ensure lack of interference from these antibodies in RF-negative sera. These results are shown in TABLE 3 and show that only one sample containing anti-SSB gave a very low positive result.

**TABLE 3 : Crossreactivity Results**

| # of Samples | Primary ANA Specificity | Is-Rheumatoid Factor IU/ml values | Interp |
|---|---|---|---|
| 5 | SSA | 1.8, 1.9, 4.4, 1.3, 1.4 | 5/5 NEG |
| 4 | Sm | 9.1, 1.7, 1.6, 1.3 | 4/4 NEG |
| 5 | RNP | 4.0, 0.9, 1.2, 0.8, 1.6 | 5/5 NEG |
| 3 | Scl-70 | 0.8, 1.6, 3.2 | 3/3 NEG |
| 4 | Jo-1 | 1.9, 2.6, 2.7, 1.8 | 3/3 NEG |
| 3 | dsDNA | 1.6, 3.8, 3.7 | 3/4 NEG |
| 1 | SSB | 21.2 | 1/1 POS |

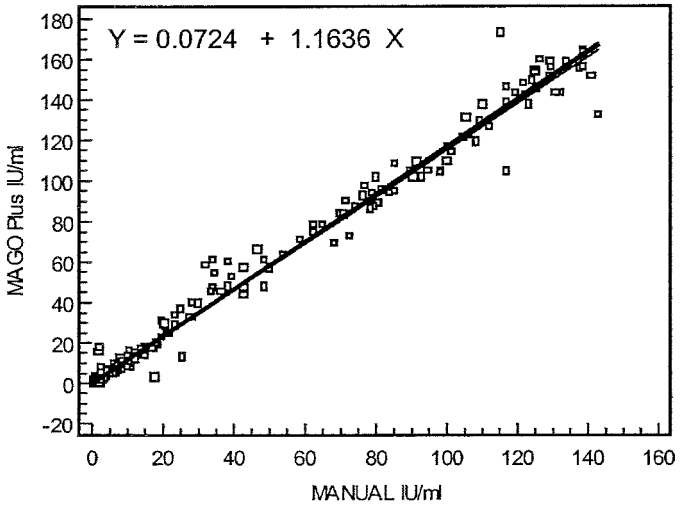
## F. Lack of Prozone/High-Dose Hook Effects

The lack of interference from prozone/high-dose hook effects was determined by testing several sera, serially diluted and undiluted in the Is-Rheumatoid Factor test Kit. A total of 8 sera were evaluated, 4 contained the highest concentrations available as established by nephelometry, 2 contained levels in the mid range and 2 were in the negative range. No prozone or high-dose hook effects were evidenced by any of the results obtained from the samples tested in the assay system.

## G. Correlation of Manual and MAGO Plus Results

The Is-Rheumatoid Factor Test Kit has been developed for both automated as well as manual use. To demonstrate the equivalence of the manual and MAGO Plus procedures, the results of a total of 303 normal and clinical serum samples tested for RF by both the manual and MAGO Plus methods were plotted. A scattergram and regression line of the results obtained with 95% confidence intervals is shown in FIGURE 6. The data indicate excellent correlation with a Correlation Coefficiient (r) = 0.9933.

**FIGURE 4 : Manual vs MAGO Plus Correlation**




Intercept = 0.0724

Slope = 1.1636

Coefficient of determination = 0.9866

Correlation Coefficient r = 0.9933

95% CI for r = 0.9916 to 0.9946

## H. Precision

To assess the precision of the Is-Rheumatoid Factor Test Kit six serum samples of varying reactivity as well as the kit Calibrator and controls were tested in triplicate in two runs per day for three days. Precision was assessed both manually and using the MAGO Plus Automated EIA Processor. Results are summarized in TABLES 4 and 5.

**TABLE 4** : Manual Intra-Assay and Interassay Precision for Is-Rheumatoid Factor

| | Intra-assay (n=6) | | | | | | | | | Interassay (n=18) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DAY 1 | | | DAY 2 | | | DAY 3 | | | | | |
| SERUM | Mean | SD | %CV | Mean | SD | %CV | Mean | SD | %CV | Mean | SD | %CV |
| A (Neg) | 0.7 | 0.21 | 30.00 | 1.0 | 0.10 | 10.00 | 0.8 | 0.05 | 6.25 | 0.8 | 0.16 | 20.00 |
| B (Neg) | 0.4 | 0.33 | >50.00 | 0.7 | 0.09 | 12.86 | 0.5 | 0.05 | 10.00 | 0.5 | 0.23 | 46.00 |
| C (Pos) | 34.1 | 1.25 | 3.67 | 35.1 | 2.94 | 8.38 | 34.2 | 1.94 | 5.67 | 34.5 | 2.08 | 6.03 |
| D (Pos) | 57.6 | 1.80 | 3.13 | 60.0 | 1.50 | 2.50 | 57.9 | 2.05 | 3.54 | 58.5 | 2.01 | 3.44 |
| E (Pos) | 82.2 | 1.93 | 2.35 | 84.9 | 3.57 | 4.20 | 79.6 | 1.57 | 1.97 | 82.2 | 3.23 | 3.93 |
| F (Pos) | 98.4 | 2.18 | 2.22 | 102.3 | 2.07 | 2.02 | 96.7 | 1.86 | 1.92 | 99.1 | 3.10 | 3.13 |
| Cal. | 98.8 | 2.03 | 2.05 | 101.6 | 1.25 | 1.23 | 98.4 | 1.16 | 1.18 | 101.0 | 3.98 | 3.94 |
| Pos. | 41.6 | 1.43 | 3.44 | 46.5 | 0.44 | 0.95 | 43.2 | 1.44 | 3.33 | 43.8 | 2.39 | 5.46 |
| Neg. | 0.7 | 0.18 | 25.71 | 0.9 | 0.05 | 5.78 | 0.6 | 0.09 | 15.00 | 0.7 | 0.16 | 22.86 |

**TABLE 5**: MAGO Plus Intra-Assay and Interassay Precision for Is-Rheumatiod Factor

| | Intra-assay (n=6) | | | | | | | | | Interassay (n=18) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | DAY 1 | | | DAY 2 | | | DAY 3 | | | | | |
| SERUM | Mean | SD | %CV | Mean | SD | %CV | Mean | SD | %CV | Mean | SD | %CV |
| A (Neg) | 0.9 | 0.26 | 28.89 | 0.9 | 0.95 | >50.00 | 0.2 | 0.18 | >50.00 | 0.6 | 0.65 | >50.00 |
| B (Neg) | 0.3 | 0.25 | >50.00 | 0.4 | 0.40 | >50.00 | 0.4 | 0.63 | >50.00 | 0.4 | 0.43 | >50.00 |
| C (Pos) | 33.7 | 3.75 | 11.13 | 34.9 | 1.67 | 4.79 | 35.1 | 2.00 | 5.70 | 34.5 | 2.56 | 7.42 |
| D (Pos) | 69.6 | 1.18 | 1.70 | 70.3 | 3.05 | 4.34 | 69.9 | 1.96 | 2.80 | 69.9 | 2.09 | 2.99 |
| E (Pos) | 87.0 | 4.42 | 5.08 | 85.0 | 1.91 | 2.25 | 85.7 | 3.26 | 3.80 | 85.9 | 3.27 | 3.81 |
| F (Pos) | 102.0 | 1.84 | 1.80 | 101.2 | 2.52 | 2.49 | 101.6 | 2.91 | 2.86 | 101.6 | 2.33 | 2.29 |
| Cal. | 108.1 | 3.38 | 3.13 | 102.0 | 2.76 | 2.71 | 103.9 | 4.24 | 4.08 | 104.7 | 4.21 | 4.02 |
| Pos. | 43.3 | 7.29 | 16.84 | 40.5 | 2.54 | 6.27 | 40.2 | 2.02 | 5.02 | 41.3 | 4.56 | 11.04 |
| Neg. | 0.4 | 0.40 | >50.00 | 0.7 | 0.60 | >50.00 | 0.2 | 0.48 | >50.00 | 0.4 | 0.50 | >50.00 |

# Expected Values

The prevalence of RF 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. The expected value in the normal population is negative. However, a small but variable percentage of apparently healthy asymptomatic individuals may have RF. These individuals usually have low titers. The incidence of false positives tends to increase with age and is similar in males and females.

In the present study the expected values for a normal healthy population were assessed by testing sera from one hundred and eighteen S. Florida blood donors in the Is-Rheumatoid Factor Test Kit. One hundred and twelve sera (94.9%) were negative, two sera (1.7%) were positive and four sera (3.4%) were equivocal. The age distribution and prevalences for this population are shown in TABLE 6. Note that similar results were obtained for both manual and MAGO Plus testing.

The expected values for a clinical population were assessed by testing ninety-three sera from patients with a diagnosis of rheumatoid arthritis in the Is-Rheumatoid Factor Test Kit. For this population eighty-seven sera (93.5%) were positive, four (4.3%) were negative and two (2.2%) were equivocal.

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

**TABLE 6: Age Distribution and Prevalence of Rheumatoid Factor in a Normal S. Florida Population**

| | Number of Donors | Prevalence |
|---|---|---|
| **Total Number** | 118 | 1.69% |
| **Geographic Location** | South Florida : 118 | |
| **Age** | | |
| 10-19 | 5 | 0.0% |
| 20-29 | 25 | 4.0% |
| 30-39 | 61 | 1.6% |
| 40-49 | 20 | 0.0% |
| 50-59 | 7 | 0.0% |

**FIGURE 5**

**Distribution of IgM-RF Values in a Normal Population**

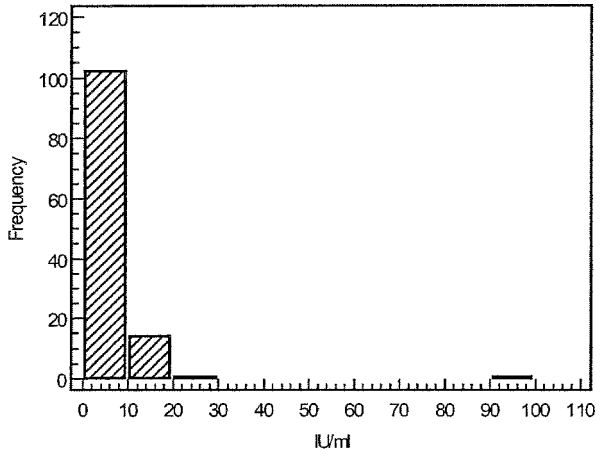
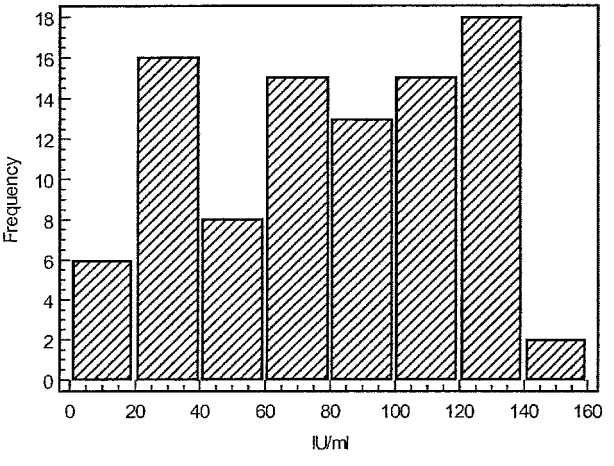



**FIGURE 6**

**Distribution of IgM-RF Values in a Clinical Population**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 9 2002

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

Re: k021394
Trade/Device Name: Diamedix *Is*-Rheumatoid Factor Test System
Regulation Number: 21 CFR § 866.5775
Regulation Name: Rheumatoid Factor Immunological Test System
Regulatory Class: II
Product Code: DHR
Dated: May 1, 2002
Received: May 2, 2002

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

510(k) Number (if known): K021394

## DEVICE NAME : Is-Rheumatoid Factor Test System

***Indications for Use :****For the quantitative detection of RF IgM-class antibodies in human serum by indirect enzyme immunoassayas an aid in the diagnosis of rheumatoid arthritis (RA). This test kit 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)**

J. P. Reeves for S. Attaie

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K021394

**Prescription Use** X OR **Over-The-Counter Use**____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)