SEP 2 8 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: K012795

**Applicant Information:**


| | |
|---|---|
| Date Prepared: | September 18, 2001 |
| 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 anti-Gliadin IgG Test System |
| Common Name: | Anti-Gliadin ELISA test |
| Classification Name: | Anti-Gliadin immunological test system |

**Equivalent Device:**
Inova QUANTA Lite Gliadin IgG ELISA

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

**Intended Use:** The assay is intended for the semi-quantitative measurement of IgG antibodies to gliadin in human serum. The results of the assay can be used as an aid in the diagnosis of celiac disease.

**Principle of the Procedure:**

The Is-anti-Gliadin IgG Test System is an indirect solid-phase enzyme immunoassay. Purified gliadin is coated onto plastic microwells. Standards, controls and diluted patient samples are added to the wells. Any IgG antibodies in the patient sample bind to the well. Anti-human IgG 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 gliadin IgG antibodies in the patient sample.

# SUMMARY OF SAFETY AND EFFECTIVENESS

## Performance Characteristics

### A. Relative Sensitivity and Specificity

One hundred and ninety frozen retrospective sera were tested for IgG antibodies using the Is-anti-Gliadin IgG Test Kit and a commercially available ELISA kit for detecting gliadin IgG antibodies. These sera consisted of normal samples, clinical samples and samples submitted to a large reference laboratory for celiac disease evaluation. A number of these submitted samples were from pediatric patients. 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 twelve samples that were negative in the Is-anti-Gliadin IgG Test Kit and positive by the other EIA, ten were positive and two were negative by a referee EIA method .

**TABLE 1**

**Is-anti-Gliadin IgG**

| Other EIA | Positive | Negative | *Equivocal |
|---|---|---|---|
| Positive | 84 | 12 | 8 |
| Negative | 0 | 86 | 0 |
| *Equivocal | 0 | 0 | 0 |

| | | | **95% CI* |
|---|---|---|---|
| Relative Sensitivity | 84/96 | = 87.5 % | 79.2-93.4% |
| Relative Specificity | 86/86 | = 100.0% | 95.8-100.0% |
| Overall Agreement | 170/182 | = 93.4% | 88.8-96.6% |

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

The minimum detection limit for this assay is 3.0 U/ml

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.

## B. Clinical Sensitivity and Specificity

A total of four hundred and eighty-four frozen retrospective, clinically characterized sera were assayed using the Is anti-Gliadin IgG Test Kit in order to assess both the clinical sensitivity and clinical specificity of the assay system. These samples consisted of 214 normal sera, 72 sera from patients with possible celiac disease that had been sent to a large reference laboratory for celiac disease evaluation (primarily gliadin IgG antibody testing), 61 sera from patient with diagnosed celiac disease, 54 sera from patients with other gastrointestinal diseases, 10 sera from patients with systemic lupus erythematosus (SLE), 12 sera from patients with polymyositis, 20 sera from patients with scleroderma, 13 sera from patients with Sjogren's Syndrome, 11 sera from patients with autoimmune thyroid disease and 10 sera from patients with microscopic polyangiitis. Results for the Is-anti-Gliadin IgG Test Kit are summarized in TABLE 2. These results also indicate that the potential for cross-reactvity due to various autantibodies is unlikely with these test kits.

**TABLE 2**

| Patient Group | Total | Positive | Negative | Equivocal |
|---|---|---|---|---|
| Normals | 214 | 6 | 203 | 5 |
| *Possible Celiac Disease | 72 | 68 | 4 | 0 |
| Diagnosed Celiac Disease | 61 | 42 | 14 | 5 |
| Other Gastrointestinal Diseases | 54 | 0 | 53 | 1 |
| SLE | 10 | 0 | 10 | 0 |
| Polymyositis | 12 | 0 | 11 | 1 |
| Scleroderma | 20 | 5 | 15 | 0 |
| Sjogrens Syndrome | 13 | 0 | 12 | 1 |
| Thyroid Disease | 11 | 0 | 11 | 0 |
| Microscopic Polyangiitis | 10 | 0 | 10 | 0 |
| Anti-Phospholipid Syndrome | 7 | 0 | 6 | 1 |

**Clinical Specificity:**

| | |
|---|---|
| Normals | 203/209 = 97.1% |
| Others | 128/133 = 96.2% |

**Clinical Sensitivity:**

| | |
|---|---|
| *Possible Celiac Disease | 68/72 = 94.4% |
| Diagnosed Celiac Disease | 42/56 = 75.0% |

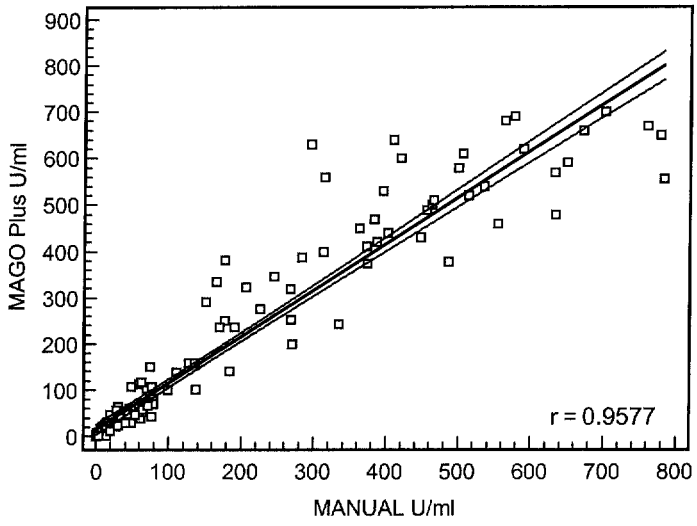
*Samples primarily tested for IgG antibodies

(Equivocal samples excluded from calculations)

## C. Correlation of Manual and MAGO Plus results

The Is-anti-Gliadin IgG 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 174 serum samples tested for anti-Gliadin IgG 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 1. Results were obtained using 6-point calibration. The data indicate good correlation with a Correlation Coefficient (r) of 0.9577

**FIGURE 1: Is anti-Gliadin IgG**
**Manual vs MAGO Plus Correlation**




## D. Precision

To assess the precision of the Is anti-Gliadin IgG 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-Gliadin 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 | 10.0 | 0.90 | 8.99 | 7.8 | 0.30 | 3.85 | 9.9 | 0.82 | 8.27 | 9.2 | 1.24 | 13.41 |
| B | 45.6 | 0.17 | 0.38 | 37.5 | 1.05 | 2.80 | 43.6 | 1.01 | 2.33 | 42.2 | 3.71 | 8.79 |
| C | 85.8 | 3.33 | 3.88 | 69.4 | 1.97 | 2.83 | 78.8 | 3.68 | 4.66 | 78.0 | 7.61 | 9.76 |
| D | 111.6 | 3.33 | 2.98 | 94.8 | 4.92 | 5.19 | 99.9 | 2.20 | 2.20 | 102.1 | 8.09 | 7.93 |
| E | 92.1 | 0.65 | 0.71 | 82.4 | 1.93 | 2.34 | 85.2 | 0.55 | 0.65 | 86.5 | 4.44 | 8.01 |
| F | 209.2 | 4.85 | 2.32 | 188.5 | 5.26 | 2.79 | 195.3 | 3.80 | 1.95 | 197.7 | 9.98 | 5.05 |

**TABLE 4** : MAGO Plus Intra-Assay and Interassay Precision for Is-anti-Gliadin 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 | 9.9 | 0.65 | 6.55 | 9.1 | 0.71 | 7.77 | 11.7 | 0.53 | 4.52 | 10.3 | 1.26 | 12.32 |
| B | 46.6 | 4.75 | 10.21 | 39.6 | 1.17 | 2.95 | 51.2 | 6.15 | 12.00 | 45.8 | 6.43 | 14.04 |
| C | 79.5 | 9.90 | 12.45 | 72.2 | 2.77 | 3.84 | 93.8 | 3.62 | 3.86 | 81.8 | 10.99 | 13.43 |
| D | 115.9 | 3.56 | 3.07 | 102.6 | 1.25 | 1.22 | 120.6 | 9.42 | 7.81 | 113.0 | 9.55 | 8.45 |
| E | 92.9 | 2.65 | 2.85 | 90.7 | 6.40 | 7.05 | 111.1 | 11.86 | 10.67 | 98.2 | 11.88 | 8.01 |
| F | 199.1 | 26.56 | 13.34 | 216.5 | 27.85 | 12.87 | 221.5 | 41.66 | 18.81 | 212.4 | 30.13 | 14.19 |

# Expected Values

The prevalence of anti-gliadin IgG 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-gliadin should generally have a low incidence in the normal healthy population. Increased incidence can occur in first-degree relatives of celiacs, in patients with other autoimmune disorders, in patients with Down syndrome and in patients with unexplained anemia, osteoporosis, epilepsy or cerebral calcifications.

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-Gliadin IgG Test Kit. One hundred and forty sera (94.6%) were negative for IgG antibodies, five sera (3.4%) were positive and three sera(2.0%) 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 sixty-one sera from patients with celiac disease. Of this group forty-two (68.9%) were positive, fourteen (22.9%) were negative and five (8.2%) were equivocal for anti-gliadin IgG antibodies.

Histograms showing the distribution of values for these normal and clinical populations are shown in FIGURES 2 and 3. Results shown were obtained using the 6-point calibration system.

**TABLE 5: Age Distribution and Prevalence of anti-Gliadin IgG in a Normal S. Florida Population**

| | Number of Donors | Prevalence |
|---|---|---|
| **Total Number** | 148 | |
| **Geographic Location:** | South Florida : 148 | 3.4% |
| **Age** | | |
| 10-19 | 7 | 0.0% |
| 20-29 | 36 | 8.3% |
| 30-39 | 73 | 1.4% |
| 40-49 | 22 | 4.5% |
| 50-59 | 8 | 0.0% |
| 60-69 | 2 | 0.0% |

**FIGURE 2**

**Distribution of anti-Gliadin IgG in a Normal Population**

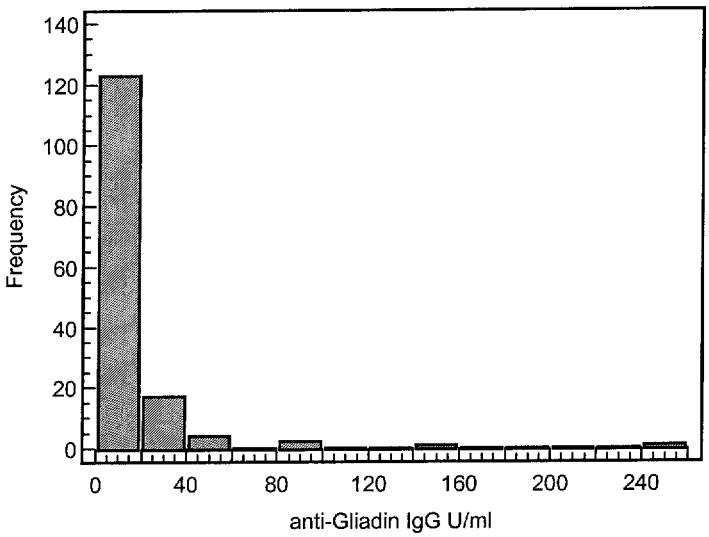
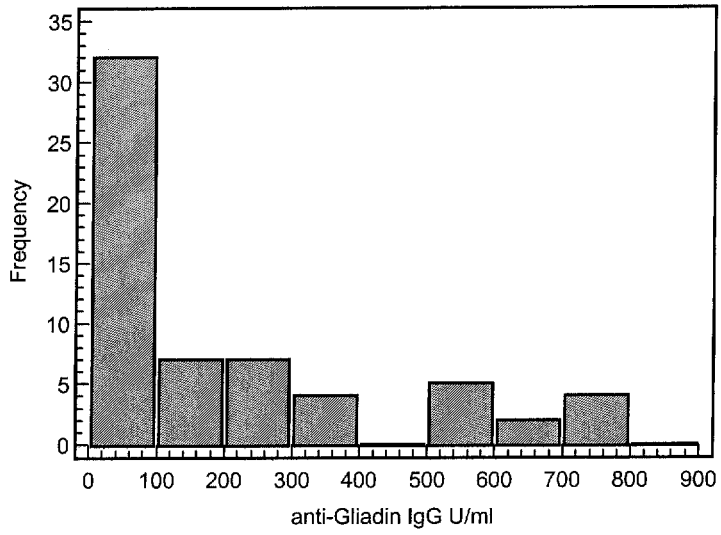



**FIGURE 3**

**Distribution of anti-Gliadin IgG in a Clinical Population**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 2 8 2001

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

Re: K012795
Trade/Device Name: Diamedix Is-anti-Gliadin IgG Test System
Regulation Number: 21 CFR 866.5750
Regulation Name: Radioallergosorbent (RAST) Immunological Test System
Regulatory Class: Class II
Product Code: MST
Dated: August 20, 2001
Received: August 21, 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 :** K012795

**DEVICE NAME : Is anti-Gliadin IgG Test System**

***Indications for Use :*** The Diamedix Is anti-Gliadin IgG Test Kit is an indirect enzyme immunoassay (EIA) for the semi-quantitative measurement of IgG antibodies to gliadin in human serum as an aid in the diagnosis of celiac disease. These reagents can be used either manually or in conjunction with the MAGO® Plus Automated EIA Processor.

Susan S. Alpaire

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K012795

For prescription use only ✓