K971393

Summary of Safety and Effectiveness Information
Mycoplasma IgG ELISA Test Kit

JUL 14 1997

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Date of preparation: June 11, 1997

II. Description of Device

The Mycoplasma IgG ELISA kit is an Enzyme-Linked Immunosorbent Assay (ELISA) for semi-quantitative or qualitative determination of IgG antibodies in human serum to *Mycoplasma pneumoniae* for the determination of immunological experience. The Mycoplasma IgG ELISA kit may be used to evaluate paired sera for the presence of seroconversions and a significant increase in specific IgG as an aid in the diagnosis of *Mycoplasma pneumoniae* infection in the adult population. **For In Vitro Diagnostic Use Only.**

The Mycoplasma IgG ELISA test is an enzyme linked immunosorbent assay to detect IgG antibodies to *Mycoplasma pneumoniae*. Purified *Mycoplasma pneumoniae* antigen is attached to a solid phase microtiter well. Diluted test sera is added to each well. If the antibodies are present that recognize the antigen, they will bind to the antigen in the well. After incubation the wells are washed to remove unbound antibody. An enzyme labeled anti-human IgG is added to each well. If antibody is present it will bind to the antibody attached to the antigen on the well. After incubation the wells are washed to remove unbound conjugate. A substrate solution is added to each well. If enzyme is present the substrate will undergo a color change. After an incubation period the reaction is stopped and the color intensity is measured photometrically, producing an indirect measurement of specific antibody in the patient specimen.

III. Predicate Device

The Mycoplasma IgG ELISA test is substantially equivalent to the IFA test. Equivalence is demonstrated by the following comparative results:

PERFORMANCE CHARACTERISTICS

Relative Sensitivity and Specificity

Two different sites compared the Wampole Mycoplasma IgG ELISA test relative to a commercial IFA kit. The two sites were R&D laboratories at commercial companies located in Maryland and New York, and affiliated with the manufacturer of the kit. The 187 frozen retrospective sera from the first study were from normal individuals of various ages, gender, from Lyme diseases endemic and non-endemic areas. The results of the first study are summarized in Table 2. The 176 frozen retrospective sera from the second study were randomly selected sera from normal inividuals of various ages, gender, and geographical location. The results of the second study are summarized in Table 3. None of the performance characteristics were established with specimens from patients having documented mycoplasma infections.

Table 2
Comparison of Wampole Mycoplasma IgG ELISA and IFA
Study 1

		Wampole Mycoplasma IgG ELISA			
		+	**eq**	**-**	**Total**
Mycoplasma IFA (1:32)	**+**	117	13	6	136
	-	20*	6	25	51
	Total	137	19	31	187

Relative Sensitivity = 117/123 = 95.1% 95% Confidence interval = 91.2% - 99.0%
Relative Specificity = 25/45 = 55.6% 95% Confidence interval = 40.7% - 70.4%
Relative Agreement = 142/168 = 84.5% 95% Confidence interval = 78.19 - 90.1%

* All 20 sera were found to be positive by an alternate ELISA.
Equivocals were not included in the above calculations.
The 95% Confidence Intervals were calculated using the normal method.

Table 3
Comparison of Wampole Mycoplasma IgG ELISA and IFA
Study 2

Wampole Mycoplasma IgG ELISA

		+	eq	-	Total
	+	132	5	2	139
Mycoplasma IFA (1:32)	-	20*	0	17	37
	Total	152	5	19	176

Relative Sensitivity = 132/134 = 98.5% 95% Confidence interval = 96.4% -100.0%
Relative Specificity = 17/37 = 45.9% 95% Confidence interval = 29.6% - 62.3%
Relative Agreement = 149/171 = 87.1% 95% Confidence interval = 82.0% - 92.3%

* All 20 sera were found to be positive by an alternate ELISA.
Equivocals were not included in the above calculations.
The 95% Confidence Intervals were calculated using the normal method.

Please be advised that 'relative' refers to the comparison of this 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 judgment can be made on the comparison assay's accuracy to predict disease.

PRECISION
Seven sera were assayed ten times each on three different assays at two different sites. Both sites were affiliated with the manufacturer of the kit. The intra and inter assay precision at each site is shown in Tables 4 and 5. The intersite precision is shown in Table 6. With appropriate technique the user should obtain precision of <15% CV.

Table 4 Mycoplasma IgG ELISA Intra and Inter Assay Precision Study 1

	Assay 1 (n=10)			Assay 2 (n=10)			Assay 3 (n=10)			Inter-Assay(n=30)		
Sera#	X	SD	CV	X	SD	CV	X	SD	CV	X	SD	CV
1	0.42	0.054	12.86%	0.36	0.033	9.18%	0.47	0.025	5.48%	0.42	0.054	13.02%
2	0.29	0.043	14.58%	0.23	0.026	11.38%	0.29	0.034	11.91%	0.27	0.043	15.93%
3	3.54	0.274	7.73%	3.24	0.244	7.53%	3.50	0.273	7.78%	3.43	0.274	7.98%
4	1.89	0.133	7.05%	1.76	0.142	8.09%	1.90	0.103	5.42%	1.85	0.133	7.21%
5	0.42	0.059	13.93%	0.33	0.051	15.21%	0.42	0.044	10.45%	0.39	0.059	15.02%
6	1.09	0.103	9.49%	1.03	0.088	8.56%	1.16	0.096	8.28%	1.09	0.103	9.45%
7	2.31	0.218	9.44%	2.21	0.286	12.98%	2.41	0.160	6.66%	2.31	0.218	9.46%
HPC										4.51	0.078	1.72*
Cal										2.50	0.072	2.89%**
LPC										1.31	0.135	10.33%*
NC										0.49	0.049	10.14%*

* n = 3
** n = 9

Table 5 Mycoplasma IgG ELISA Intra and Inter Assay Precision Study 2

	Assay 1 (n=10)			Assay 2 (n=10)			Assay 3 (n=10)			Inter-Assay(n=30)		
Sera#	X	SD	CV	X	SD	CV	X	SD	CV	X	SD	CV
1	0.23	0.013	5.74%	0.22	0.024	10.76%	0.25	0.028	11.04%	0.24	0.025	10.75%
2	0.17	0.022	12.71%	0.17	0.023	13.58%	0.19	0.018	9.45%	0.18	0.023	12.90%
3	3.58	0.199	5.56%	3.58	0.161	4.51%	3.70	0.154	4.17%	3.62	0.176	4.87%
4	1.84	0.102	5.57%	1.84	0.173	9.41%	2.07	0.135	6.55%	1.91	0.174	9.07%
5	0.35	0.016	4.54%	0.33	0.028	8.37%	0.37	0.029	7.90%	0.35	0.029	8.29%
6	1.15	0.070	6.09%	1.14	0.074	6.47%	1.27	0.078	6.15%	1.19	0.092	7.78%
7	2.22	0.147	6.64%	2.16	0.154	7.13%	2.31	0.105	4.56%	2.23	0.148	6.63%
HPC										3.48	0.191	5.48%*
Cal										2.51	0.056	2.21%**
LPC										1.43	0.140	9.78%
NC										0.13	0.03	23.08%

* n = 3
** n = 9

Table 6
Wampole Mycoplasma IgG ELISA Inter Site Precision Study

Inter-Assay

Sera#	X	SD	CV	n
1	0.33	0.101	30.89%	60
2	0.22	0.057	25.73%	60
3	3.52	0.247	7.01%	60
4	1.88	0.157	8.33%	60
5	0.37	0.050	13.43%	60
6	1.14	0.108	9.50%	60
7	2.27	0.189	8.34%	60
HPC	4.00	0.581	14.53%	6
CAL	2.51	0.063	2.50%	18
LPC	1.37	0.140	10.24%	6
NC	0.31	0.199	64.46%	6

A total of 456 determinations were made at the two sites. The only sera to change status was sera # 6 which was positive 38 times and equivocal 22 times.

X = Mean
SD = Standard Deviation
CV = Coefficient of Variation = SD/X x 100

The methods in NCCLS EP5 were utilized for precision parameters.

LINEARITY

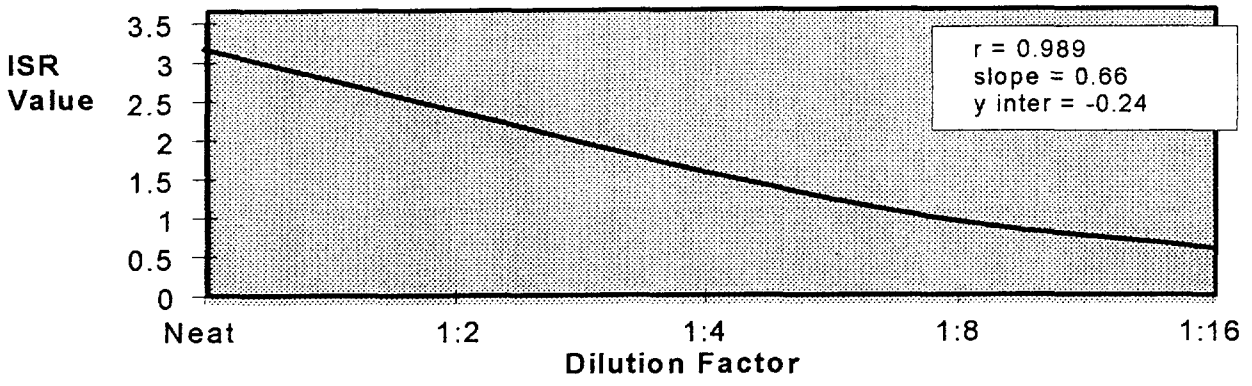
Simulated paired sera evaluation

To evaluate the linearity of the assay 20 positive sera were serially two-fold diluted and run on the assay. The ISR values were compared to $\log_2$ of dilution by standard linear regression. The r values were all ≥ 0.974. The data indicates that the antibody can be semi-quantitated by using a single serum dilution. The detection of a significant antibody increase may be made only by an evaluation of paired specimens, acute and convalescent. To validate the sensitivity of the paired sera procedure the percent rise in ISR values were calculated for 56 pairs that had a four-fold dilution where the acute sera had a value of less than 2.18. All 56 pairs demonstrated a >46% rise in ISR value, showing a significant rise in antibody. Therefore, the paired sera procedure demonstrated 100% sensitivity in being able to detect a four-fold increase in antibody level when the acute sera has a value of <2.18.

Figure 1 illustrates the linearity of a representative serum. The ISR values were compared to $\log_2$ of dilution by standard linear regression

Figure 1

Linearity of Mycoplasma ELISA



Complement Fixation Paired Serum Study

Eleven serum pairs tested by CF from patients suspected of having acute *Mycoplasma pneumoniae* infection were assayed on the Wampole Mycoplasma IgG ELISA assay. Each serum pair was evaluated to determine a significant rise in antibody. Four serum pairs could not be used due to the acute serum being too high. The remaining seven pairs all demonstrated a >46% rise in ISR values thus giving a 100% sensitivity versus CF for showing a significant rise in antibody for serum meeting the paired sera criteria.

Reproducibility Study

Fifty different sera with various levels of activity were assayed at three different sites. Two sites were R&D laboratories at commercial companies located in Maryland and New York. The third site was a large clinical laboratory located in Pennsylvania. The data from the three sites show good correlation with Pearson product moment correlation coefficients of >0.987 between the sites. Excluding equivocals (n = 4) one determination varied from its expected result (negative result for a positive specimen) giving a percent agreement of expected results between the three sites of 99.3% (145/146). The expected results were derived from previous Wampole ELISA testing of the samples. Three sera changed status in this study: one serum was equivocal at one site and negative at the other two sites; the second serum was equivocal at two sites and positive at the third; and the third serum was positive at one site, equivocal at second site, and negative at the third site.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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JUL 14 1997

Re: K971393
Trade Name: Mycoplasma IgG ELISA Test Kit
Regulatory Class: I
Product Code: LJZ
Dated: June 11, 1997
Received: June 11, 1997

Dear Mr. Boteler:

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 (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 Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP 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 at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/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: Not known

Device Name: Mycoplasma IgG ELISA

Indications For Use: The Mycoplasma IgG ELISA kit is an Enzyme-Linked Immunosorbent Assay (ELISA) for semi-quantitative or qualitative determination of IgG antibodies in human serum to *Mycoplasma pneumoniae* for the determination of immunological experience. The Mycoplasma IgG ELISA kit may be used to evaluate paired sera for seroconversions and the presence of a significant increase in specific IgG as an aid in the diagnosis of *Mycoplasma pneumoniae* infection in the adult population.

PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The Counter Use____
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K971393