

K983605

DEC 16 1998

510k 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:

Applicant Information:

Date Prepared: Oct 11, 1998
Name: Columbia Bioscience, Inc.
Address: 8775 M Centre Park Drive, #559
Columbia, MD 21045

Contact Person: Norman Jenkins
Phone Number: 410-995-0450
Fax Number: 410-995-0448

Device Information:

Trade Name:  *Borrelia burgdorferi* IgG/IgM ELISA Kit
Common Name: *Borrelia burgdorferi* EIA Test
Classification Name: Borrelia Serological Reagent

Univalent Device:
Lyme Elisa

Device Description: The  *Borrelia burgdorferi* IgG/IgM ELISA Kit is an enzyme-linked immunosorbent assay (ELISA) for the detection of IgG/IgM to *Borrelia burgdorferi* antigen in human serum.

Intended Use: For the qualitative presumptive detection of total (IgG/IgM) antibodies to *Borrelia burgdorferi* in human serum. This ELISA should only be used for patients with signs and symptoms that are consistent with Lyme disease. Equivocal or positive results must be supplemented by testing with a standardized Western blot procedure. Positive supplemental results are supportive evidence of exposure to *B. burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. The test can be performed either manually or in conjunction with the MAGO™ PLUS Automated EIA Processor.

Principle of Procedure:

The  *Borrelia burgdorferi* IgG/IgM ELISA Kit is an enzymelinked immunosorbent assay to detect IgG/IgM to *Borrelia burgdorferi* in human serum. Partially purified *Borrelia burgdorferi* antigen is attached to a solid phase (microtiter well). Diluted test sera are added to each well. If antibodies which recognize the, *Borrelia burgdorferi* antigen are present in the patient sample they will bind to the antigen 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 detection of the specific antibody present in the patient sample.

Performance Characteristics

1. Clinical Sensitivity and Specificity :

The following information is from a panel of characterized sera obtained from the CDC (Centers for Disease Control and Prevention) and assayed by Diamedix Corp. using the Is-anti *B.burgdorferi* IgG/IgM Test Kit. The panel consists of 5 normal sera and 42 sera with a clinical diagnosis of Lyme disease and obtained at different times from onset of disease. The results are presented as a means to convey further information on the performance of the assay with a masked, characterized serum panel. This does not imply an endorsement of the assay by the CDC. Table 1 illustrates the performance of the assay with this serum panel.

Table 1 : Results of the CDC Serum Panel Stratified by Time After Onset

Elapsed Time From Onset	Positive	Equiv.	Negative	Total	% Agreement
> 1 Yr	8	0	0	8	100.0%
3 - 12 Months	9	3	8	20	60.0%
1 - 2 Months	4	1	4	9	55.6%
<1 Month	3	0	2	5	60.0%
Negatives	0	0	5	5	100.0%
Total	24	4	19	47	70.2%

Note that equivocal samples were considered positive for the above calculations due to the fact that all equivocal samples would be tested by immunoblotting in a 2-step system.

The following information is from a panel of characterized sera obtained from a clinical lab in Wisconsin and assayed by Diamedix Corp. using the Is-anti *B.burgdorferi* IgG/IgM Test Kit. The panel consists of 72 sera with a clinical diagnosis of Lyme disease and obtained at different times from onset of disease. Table 2 illustrates the performance of the assay with this serum panel.

Table 2 : Results of the Characterized Lyme Sera Stratified by Time After Onset

Elapsed Time From Onset	+	E	-	Total	% Agreement
> 1 Yr	3	0	0	3	100%
3 - 12 Months	11	2	0	13	100%
1 - 2 Months	8	2	3	13	76.9%
<1 Month	24	8	11	43	74.4%
Total	46	12	14	72	80.6%

Note that equivocal samples were considered positive for the above calculations due to the fact that all equivocal samples would be tested by immunoblotting in a 2-step system.

2. Prospective Sample Study

One hundred and seventy three prospective sera from patients of various ages and gender from an endemic area that were submitted to a clinical laboratory for *B. burgdorferi* antibody testing were assayed using the Is-anti-*B. burgdorferi* IgG/IgM test kit and another commercially available EIA kit. Positive and equivocal results from both assays were supplemented by testing with a Western Blot method. Table 3, and the summary that follows, shows the prevalence of positive and equivocal results obtained in both EIAs (first-step) and percentage of these sera positive by the Western Blot method (second-step).

Table 3 : Prospective Sample Study Results

		Western Blot	
		Pos	Neg
Is- EIA	Pos	7	2
	Equiv	4	1
Other EIA	Pos	11	12
	Equiv	3	10

The results from Table 3 are summarized as follows :

Result	Is-EIA	(95% CI)	Other EIA	(95% CI)
EIA Pos. or Equiv.	14/173 = 8.09%	(3.95-12.20%)	36/173 = 20.8%	(14.6-27.0%)
Western Blot Pos.	11/173 = 6.36%	(2.65-10.07%)	14/173 = 8.09%	(3.95-12.24%)
% Western Blot Pos. among EIA Pos. or Equiv.	11/14 = 78.6%	(56.6%-100%)	14/36 = 38.9%	(22.64-55.14%)

3. Precision

To determine the precision of the Is-anti-*B. burgdorferi* IgG/IgM Test Kit, four positive and two negative sera were assayed ten times each in three different runs at three different sites. The intra- and interassay precision obtained at each site is shown in Tables 4, 5 and 6.

TABLE 4 : Is-anti-*B. burgdorferi* IgG/IgM Precision Site 1

	RUN 1		RUN 2		RUN 3		INTER ASSAY	
SERUM	Mean Index	CV	Mean Index	CV	Mean Index	CV	Mean Index	CV
1 (POS)	1.31	6.03%	1.38	10.55%	1.20	6.80%	1.29	9.80%
2 (POS)	1.40	6.86%	1.49	5.03%	1.24	6.31%	1.38	9.62%
3 (POS)	1.34	8.17%	1.42	6.07%	1.19	4.49%	1.32	9.69%
4 (POS)	2.26	5.00%	2.36	5.98%	1.82	7.53%	2.15	12.52%
5 (NEG)	0.20	16.26%	0.24	22.30%	0.20	14.76%	0.21	20.68%
6 (NEG)	0.16	14.78%	0.17	21.19%	0.20	15.81%	0.18	19.20%
						CAL	0.97	12.81%
						PC	1.29	11.06%
						NC	0.29	11.95%

n = 30
 PC and NC n = 3
 CAL n = 9

TABLE 5 : Is-anti-*B. burgdorferi* IgG/IgM Precision Site 2

	RUN 1		RUN 2		RUN 3		INTER ASSAY	
SERUM	Mean Index	CV	Mean Index	CV	Mean Index	CV	Mean Index	CV
1 (POS)	1.34	6.19%	1.24	6.18%	1.19	8.13%	1.25	8.26%
2 (POS)	1.52	8.80%	1.36	3.51%	1.33	5.18%	1.40	8.55%
3 (POS)	1.50	8.56%	1.28	7.50%	1.26	9.53%	1.35	11.64%
4 (POS)	2.60	4.81%	2.30	7.27%	2.27	6.56%	2.39	8.66%
5 (NEG)	0.21	18.40%	0.20	12.31%	0.20	8.72%	0.20	13.38%
6 (NEG)	0.15	9.21%	0.14	14.02%	0.15	16.87%	0.15	13.51%
						CAL	1.00	3.22%
						PC	1.42	8.54%
						NC	0.33	6.34%

n = 30
 PC and NC n = 6
 CAL n = 9

TABLE 6 : Is-anti-*B. burgdorferi* IgG/IgM Precision Site 3

SERUM	RUN 1		RUN 2		RUN 3		INTER ASSAY	
	Mean Index	CV	Mean Index	CV	Mean Index	CV	Mean Index	CV
1 (POS)	1.27	5.54%	1.31	3.64%	1.35	4.86%	1.31	5.21%
2 (POS)	1.42	4.55%	1.44	6.30%	1.49	6.84%	1.45	6.18%
3 (POS)	1.36	7.01%	1.40	6.80%	1.42	6.69%	1.39	6.79%
4 (POS)	2.26	5.64%	2.29	5.58%	2.31	6.77%	2.29	5.91%
5 (NEG)	0.22	15.92%	0.22	12.49%	0.23	18.81%	0.23	15.45%
6 (NEG)	0.18	6.84%	0.16	5.67%	0.17	8.49%	0.17	8.70%
						CAL	1.00	8.04%
						PC	1.39	7.19%
						NC	0.33	12.37%

n = 30
 PC and NC n = 3
 CAL n = 9

4. Specificity with Potentially Cross-Reactive Sera

To evaluate the performance of the Is-anti-*B. burgdorferi* IgG/IgM Test Kit with potentially cross reactive sera, a group of sera with laboratory results that may cross-react or interfere with the assay were tested. Table 7 summarizes the results obtained.

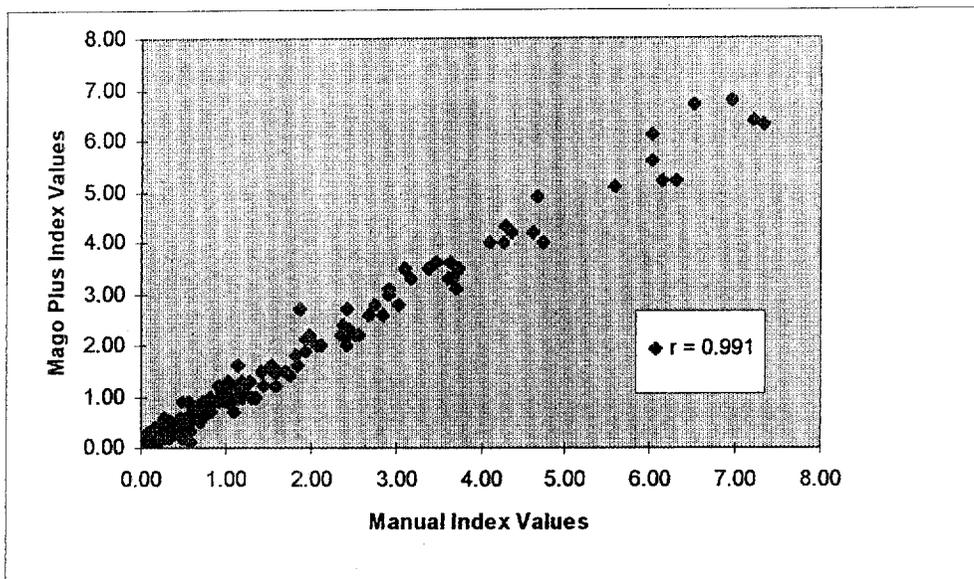
Table 7 : Results with Potentially Cross-Reactive Sera.

Laboratory Test	Lab Results	N	# equivocal	# positive
RPR +	1:2 - 1:32	20	7	1
ds-DNA +	52 - 1072 IU	15	0	1
RF +	245 - 338 IU	5	0	0
Lipemic +	+++	5	1	1
Bilirubin +	2.8 - 11.2 mg/dl	5	0	0
Elevated ESR	43-78	4	0	0
Elevated CRP	4.2-22.2 mg/dl	5	0	0
EBV +	+	7	1	1
CMV +	0.72 - 2.31 OD	6	2	1
Rocky MT Spotted Fever	1:64 G	4	0	0

5. Correlation of Manual and MAGO Plus Results

The Is-anti-*B. burgdorferi* IgG/IgM 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 296 sera tested by both methods were plotted. Figure 3 illustrates the correlation between manual and MAGO Plus results. The data indicate good correlation with a Pearson Correlation Coefficient of 0.991.

Figure 3 : Correlation of Mago Plus and Manual Results



6. Mago Plus Precision

The precision of the assay when performed on the Mago Plus Automated EIA Processor was determined by assaying 6 sera 10 times each in three different runs. Table 8 shows the intra-and interassay precision obtained using the MAGO Plus.

TABLE 8 : MAGO Plus Is-anti-*B. burgdorferi* IgG/IgM Precision

	RUN 1		RUN 2		RUN 3		INTER ASSAY	
SERUM	Mean Index	CV	Mean Index	CV	Mean Index	CV	Mean Index	CV
1 (POS)	1.11	6.65%	1.15	8.45%	1.30	8.11%	1.19	10.32%
2 (POS)	1.31	9.82%	1.39	6.30%	1.51	5.80%	1.41	9.26%
3 (POS)	1.24	11.53%	1.28	4.94%	1.47	5.60%	1.33	10.66%
4 (POS)	2.13	5.88%	2.29	5.39%	2.40	4.39%	2.27	7.05%
5 (NEG)	0.14	36.89%	0.19	16.64%	0.21	15.06%	0.18	26.90%
6 (NEG)	0.11	28.75%	0.13	37.16%	0.18	23.42%	0.14	35.59%
						CAL	0.98	9.67%
						PC	1.23	4.68%
						NC	0.3	0.00%

30
and NC n = 3
CAL n = 9



DEC 16 1998

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Norman Jenkins
President
Columbia Bioscience, Inc.
8775 M Centre Park Drive #559
Columbia, MD 21045

Re: K983605
Trade Name: *Is-Borrelia burgdorferi* IgG/IgM ELISA Test
Regulatory Class: II
Product Code: LSR
Dated: October 11, 1998
Received: October 14, 1998

Dear Mr. Jenkins:

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 (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 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.

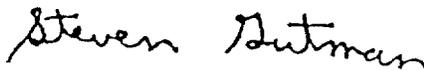
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

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: not known

Device Name: ~~Z~~ *Borrelia burgdorferi* IgG/IgM ELISA Test

Indications For Use: For the qualitative presumptive detection of total (IgG/IgM) antibodies to *Borrelia burgdorferi* in human serum. This ELISA should only be used for patients with signs and symptoms that are consistent with Lyme disease. Equivocal or positive results must be supplemented by testing with a standardized Western blot procedure. Positive supplemental results are supportive evidence of exposure to *B. burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. The test can be performed 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)

Prescription Use X
(Per 21 CFR 801.109)

OR

Over-The Counter Use _____
(Optional Format 1-2-96)

Woody Dehaes
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K983605