JUN 1 1998

MRL
DIAGNOSTICS

K971007

510(k) Safety and Effectiveness Summary (Page 1 of 6)

Applicant:	MRL Diagnostics 10703 Progress Way Cypress, California 90630
Establishment Registration No:	2023365
Contact Person:	Michael J. Wagner
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Summary Date:	May 20, 1998
Device Name:	Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgM
Classification:	Lyme Disease *Borrelia burgdorferi* Serological Reagents 21 CFR §866.3830 Class II
Predicate Device:	MRL Diagnostics Lyme Disease IFA IgM kit (K883767)

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Device Description:

MRL Diagnostics separates *B. burgdorferi* proteins by polyacrylamide gel electrophoresis and electrophoretically transfers the fractionated proteins from the gel to a nitrocellulose membrane. The nitrocellulose membrane is dried and cut into strips. The antigen strips are numbered and packaged.

The MRL Diagnostics Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgM test is a two stage procedure. In the first stage, the patient sera is diluted and incubated with individual antigen strips. If antibodies to *B. burgdorferi* are present in the sera, they will bind to the Borrelia antigens immobilized on the nitrocellulose membranes. In the second stage, visualization of the bound antibodies is accomplished by incubating the blots with alkaline phosphatase—conjugated goat anti-human IgM, (F_c fragment specific) followed by the addition of substrate (BCIP/NBT) which forms a colored precipitate at each site (antigen band) where the anti-human conjugate has bound. The resulting pattern of band reactivity is then interpreted.

Intended Use:

MRL Diagnostics' Lyme Disease *Borrelia burgdorferi* Genogroup 1 Western Blot IgM test allows the qualitative detection of IgM class antibody in human serum to individual proteins of the genogroup 1 (*B. burgdorferi* sensu stricto) of *B. burgdorferi* sensu lato. The MRL Diagnostics Lyme Disease *B. burgdorferi* Western Blot assay is intended to provide supportive evidence of infection with *B. burgdorferi*, the causative agent of Lyme disease, using serum samples which have been found positive or equivocal by another *B. burgdorferi* detection methodology (e.g. IFA or ELISA).

The MRL Diagnostics Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgM can be used alone during the acute phase (0-4 weeks of symptoms onset) of *B. burgdorferi* infection. After the acute phase, infected patients are usually found to be Western Blot positive for IgG. For persons beyond the acute phase, a positive IgM test alone is not recommended for determining active disease in patients. Therefore, both IgG and IgM Western Blots should be used after the acute phase.

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Expected Values:

Three investigational sites (2 independent off-site investigators and 1 on-site investigator) studied the following 3 distinct populations:

1) a Lyme Disease population (n=181) consisting of serum samples from patients with EM, a late stage symptom per the CDC case definition and *B. burgdorferi* seropositive, or *B. burgdorferi* culture positive;

2) a Normal population (n=325) consisting of serum samples from donors with no known history or symptoms of Lyme Disease (including persons from Lyme disease endemic and non-endemic areas), and;

3) a Cross-reactivity population (n=281) consisting of serum samples from patients with potentially cross-reactive conditions or infections.

The frequency of criteria bands observed in the three populations are described in the following table:

				Criteria Bands (kDa)		
Disease State	n	%Pos	Any Band	23	39	41
Lyme Disease (By Disease Stage) (n=181)						
Lyme Stage I	72	69%	86%	71%	49%	55%
Lyme Stage II	42	66%	83%	59%	56%	76%
Lyme Stage III	67	30%	70%	27%	31%	42%
Lyme Disease (By Months Post Infection Onset) (n=181)						
< 1 month	40	78%	80%	73%	53%	80%
1 to 2 months	25	72%	92%	72%	60%	76%
3 to 12 months	63	48%	71%	45%	39%	58%
> 12 months	53	34%	81%	34%	36%	49%
Normal Population (n=325)						
Endemic	81	0%	7%	1%	0%	2%
Non-Endemic	244	2%	23%	11%	2%	9%
Potential Cross-reactives (n=281)						
Spirochetal	104	3%	40%	19%	5%	12%
Auto-Immune	22	18%	55%	41%	0%	23%
Tick Borne	21	24%	38%	29%	5%	29%
Muscular Skeletal	33	3%	24%	9%	0%	6%
Neurologic	27	4%	41%	7%	0%	22%
Viral	32	0%	13%	3%	0%	9%
Symptomology	15	0%	27%	13%	0%	13%
Misc. Disease	27	4%	15%	4%	4%	11%

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Sensitivity:

To determine assay Sensitivity, two independent off-site investigators (Investigational Sites 1 and 2) and one on-site investigator (Investigational Site 3), assayed well characterized Lyme disease positive patient sera (n=176) from patients (n=155) with EM, a late stage symptom per the CDC case definition and *B. burgdorferi* seropositive, or *B. burgdorferi* culture positive. Investigational Sites 1 and 2 used retrospective serum samples from their own well-characterized serum banks, and Investigational Site 3 used a retrospective well characterized serum panel supplied by the CDC. The CDC panel results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply an endorsement of the assay by the CDC.

For the CDC panel, sensitivity results are provided in the following table for 1) the IgM Western Blot, and 2) the number of samples which were IgM negative but IgG positive by MRL Diagnostics' *B. burgdorferi* Western blots ("IgM Negative & IgG Positive"):

Months Post Infection Onset	IgG Sensitivity	IgG 95% CI	IgG Negative & IgM Positive
<1	100% (4/4)	40 to 100%	0
1 to 2	79% (7/9)	40 to 97%	1
3 to 6	75% (12/16)	48 to 97%	2
>6	36% (4/11)	11 to 69%	6
Overall Sensitivity	66% (27/40)	51 to 84%	9

For all three sites, sensitivity results are provided in the following table for 1) the IgM Western Blot and 2) the number of samples which were IgM negative but IgG positive by MRL Diagnostics' *B. burgdorferi* Western blots ("IgM Negative & IgG Positive"):

Months Post Infection Onset	IgM Sensitivity	IgM 95% CI	IgG Positive & IgM Negative
<1	77% (30/39)	61 to 89%	1
1 to 2	72% (18/25)	51 to 88%	4
3 to 6	63% (25/40)	46 to 77%	7
>6	32% (23/71)	22 to 45%	29
Unspecified	0% (0/1)		1
Overall Sensitivity	55% (97/176)	47 to 63%	42

Eighteen patients were drawn more than once, i.e., three patients were drawn three times and the other patients twice. One of those patients was drawn at 99 and 105 months post onset, and both draws were found IgG positive IgM negative. The other seventeen patients were initially drawn less than one month post onset, and the results for those multiple draws are summarized in the following table:

	Initial Draw	Subsequent Draw Sensitivity		
	Sensitivity	<1 Mo.	1-2 Mo.	3-6 Mo.
	76% (13/17)	100% (1/1)	90% (9/10)	67% (6/9)

Specificity

To determine assay Specificity, Investigational Sites 1, 2, and 3 assayed 606 sera consisting of 325 serum samples from persons with no known history of Lyme disease (from endemic and non-endemic areas) (Investigational Sites 1, 2, and 3) and 284 disease state serum samples from potentially cross-reactive diseases (including diseases likely to produce similar clinical presentation) (Investigational Sites 1 and 3). Where specimen quantities were sufficient, the investigators assayed each specimen on both the IgG and the IgM Western Blots. For persons with no known history of Lyme disease (Normals), specificity results are provided in the following table for 1) the IgM Western Blot and 2) the number of samples which were IgM negative but IgG positive by MRL Diagnostics' *B. burgdorferi* Western blots ("IgM Negative & IgG Positive"):

Condition	IgM Positivity	IgG Positive & IgM Negative
Normal Population (n=325)		
Endemic	0% (0/81)	0
Non-endemic	2%(5/244)	0
Overall Normal Positivity	2%(5/325)	0

Condition	IgM Cross-reactivity	IgG Positive & IgM Negative
Spirochetal Disease Population (n=104)		
Syphilis	1%(1/74)	0
Periodontal	10%(2/20)	0
Leptospirosis	0%(0/10)	0
Auto Immune Disease Population (n=22)		
RF	20%(2/10)	0
ANA	18%(2/11)	0
SLE (Lupus)	0% (0/1)	0
Tickborne Disease Population (n=21)		
Rickettsia	0% (0/9)	0
E. chaffeensis	63% (5/8)	0
HGE	0% (0/3)	0
Tickborne Relapsing	0% (0/1)	0
Muscular Skeletal Disease (n=33)		
Arthritis	0%(0/15)	1
Arthralgia	9%(1/11)	1
JRA	0% (0/4)	0
Misc. Muscular	0% (0/3)	0
Misc. Neurologic Disease (n=27)	4%(1/27)	1
Viral Disease Population (n=36*)		
EBV*	0%(0/13)	0
CMV*	0%(0/11)	0
HSV-1/2*	0% (0/2)	0
HIV	0%(0/10)	0
Misc. Disease/Similar Symptoms (n=42)		
Fatigue	0%(0/15)	0
Misc.	4%(1/27)	0

*** includes 2 sera with antibody response to EBV, CMV, and HSV-1/2**

Reproducibility

Intra-laboratory Reproducibility was assessed by assaying 10 serum samples once per day on 3 days using a single MRL Diagnostics Western Blot Genogroup 1 Strip lot. All 3 runs yielded identical screening interpretations for all 10 selected sera. Overall, the 3 criteria bands yielded identical interpretations on 89 of 90 (99%) criteria band readings.

Inter-lot Reproducibility was assessed using 10 serum samples on 3 lots of MRL Diagnostics Western Blot Genogroup 1 Strips. All 3 lots produced identical screening interpretations for all 10 selected sera. Overall, the 3 criteria bands yielded identical interpretations on 89 of 90 (99%) criteria band readings.

Inter-reader Reproducibility was assessed by assaying 18 patient sera with a single lot of strips. The sera were assayed at the three Investigational Sites, and read by two readers at each site. Overall, interpretation was identical 94% (51/54), and criteria band readings were identical 96% (155/162).

Inter-site Reproducibility was assessed by assaying 18 patient sera with a single lot of strips. The sera were assayed at the three Investigational Sites, and read by two readers at each site. Overall, interpretation was identical 95% (97/108), and criteria band readings were identical 96% (311/324).

The following table summarizes the reproducibility studies by interpretation and band reproducibility.

Study	n	Interp	23	39	41
Intra-lab	10	100%	100%	90%	100%
Inter-lot	10	100%	100%	100%	90%
Inter-reader	18	96%	96%	94%	96%
Inter-site	18	95%	98%	94%	96%

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 1 1998

Michael J. Wagner
Regulatory Affairs Specialist
MRL Diagnostics
10703 Progress Way
Cypress, CA 90630

Re: K971007
Trade Name: Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgM
Regulatory Class: II
Product Code: LSR
Dated: March 23, 1998
Received: March 25, 1998

Dear Mr. Wagner:

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 (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 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.

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 (if known): K971007

Device Name: Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgM

Indications for Use:

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K971007

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

(Optional Format 1-2-96)