

JUN 1 1998

MRL
DIAGNOSTICS

K971006

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 IgG

Classification: Lyme Disease *Borrelia burgdorferi* Serological Reagents
21 CFR §866.3830
Class II

**Predicate
Device:** MRL Diagnostics Lyme Disease IFA IgG kit (K883487)

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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 IgG 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 IgG, (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 *B. burgdorferi* Genogroup 1 Western Blot IgG test is intended for the qualitative detection of IgG class antibodies, in human serum, to the genogroup 1 (*Borrelia burgdorferi sensu stricto*) of *B. burgdorferi sensu lato*. The MRL Diagnostics Lyme Disease *B. burgdorferi* Western Blot IgG test is intended to provide supportive evidence of infection with *B. burgdorferi*, the causative agent of Lyme disease as an aid in the diagnosis of Lyme disease, using serum samples which have been found positive or equivocal by a *B. burgdorferi* screening method (e.g., IFA or ELISA). The MRL Diagnostics Lyme Disease *B. burgdorferi* Western Blot IgG can be used at any time following onset of symptoms provided the IFA or ELISA is positive or equivocal. Also, it should be used for follow up when: 1) only IgM antibodies were originally detected, 2) IgG antibodies were detected, but were not considered significant by Western blot, or 3) previously seronegative patients subsequently test positive by IFA or ELISA.

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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=183) 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=326) 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=282) 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:

Disease State	n	%Pos	Any Band	Criteria Bands (kDa)									
				21	23	28	30	39	41	45	58	66	93
<u>Lyme Disease (By Disease Stage) (n=183)</u>													
Lyme I	72	21%	96%	17%	39%	7%	14%	54%	93%	7%	24%	22%	11%
Lyme II	41	37%	95%	32%	27%	24%	49%	73%	95%	39%	41%	24%	34%
Lyme III	70	71%	97%	59%	54%	54%	64%	86%	94%	33%	73%	59%	61%
<u>Lyme Disease (By Months Post Infection Onset) (n=183)</u>													
< 1 month	40	28%	93%	17%	35%	13%	20%	60%	90%	20%	28%	28%	13%
1 to 2 months	25	28%	100%	28%	48%	20%	32%	64%	96%	12%	24%	24%	32%
3 to 12 months	64	44%	95%	39%	38%	30%	47%	70%	94%	27%	52%	33%	36%
> 12 months	54	63%	98%	50%	50%	44%	54%	81%	96%	30%	65%	54%	54%
<u>Normal Population (n=326)</u>													
Endemic	82	0%	49%	0%	0%	0%	1%	7%	32%	0%	9%	2%	0%
Non-Endemic	244	0%	61%	0%	1%	0%	2%	8%	48%	3%	4%	6%	1%
<u>Possible Cross-reactives (n=281)</u>													
Spirochetal	104	0%	85%	0%	4%	3%	5%	16%	66%	11%	5%	10%	3%
Auto-Immune	22	0%	77%	0%	0%	0%	5%	0%	55%	0%	5%	9%	5%
Tick Borne	21	0%	43%	0%	0%	0%	5%	14%	38%	14%	5%	14%	0%
Musc. Skeletal	33	6%	88%	9%	9%	6%	12%	15%	79%	21%	9%	6%	9%
Neurologic	27	4%	78%	4%	0%	0%	7%	11%	59%	4%	22%	15%	4%
Viral	32	0%	66%	0%	3%	3%	6%	0%	44%	9%	6%	0%	0%
Symptomology	15	0%	93%	7%	0%	0%	13%	7%	73%	7%	7%	7%	0%
Misc. Disease	29	0%	93%	0%	0%	0%	7%	21%	72%	10%	17%	3%	0%

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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=184) from patients (n=158) 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 IgG Western Blot, and 2) the number of samples which were IgG negative but IgM positive by MRL Diagnostics' *B. burgdorferi* Western Blots ("IgG Negative & IgM Positive"):

Months Post Infection Onset	IgG Sensitivity	IgG 95% CI	IgG Negative & IgM Positive
<1	25% (1/4)	1 to 81%	3
1 to 2	22% (2/9)	3 to 60%	6
3 to 6	31% (5/16)	11 to 59%	9
>6	82% (9/11)	48 to 98%	1
Overall Sensitivity	43% (17/40)	27 to 59%	19

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

Months Post Infection Onset	IgG Sensitivity	IgG 95% CI	IgG Negative & IgM Positive
<1	28% (11/39)	15 to 45%	20
1 to 2	28% (7/25)	12 to 49%	15
3 to 6	41% (17/42)	26 to 57%	15
>6	65% (47/72)	53 to 76%	5
Unspecified	100% (1/1)		
Overall Sensitivity	46% (83/179)	39 to 54%	55

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 Sensitivity	Subsequent Draw Sensitivity		
	<1 Mo.	1-2 Mo.	3-6 Mo.
12% (2/17)	0% (0/1)	10% (1/10)	0% (0/9)

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Specificity

To determine assay Specificity, Investigational Sites 1, 2, and 3 assayed 606 sera consisting of 326 serum samples from persons with no known history of Lyme disease (from endemic and non-endemic areas) (Investigational Sites 1, 2, and 3) and 286 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), and those with potentially cross-reactive diseases (Potential Cross-reactives), specificity results are provided in the following table for 1) the IgG Western Blot and 2) the number of samples which were IgG negative but IgM positive by MRL Diagnostics' *B. burgdorferi* Western Blots ("IgG Negative & IgM Positive"):

Condition	IgG Positivity	IgG Negative & IgM Positive
Normal Population (n=326)		
Endemic Normals	0% (0/82)	0
Non-Endemic Normals	0% (0/244)	5

Condition	IgG Crossreactivity	IgG Negative & IgM Positive
Spirochetal Disease Population (n=103)		
Syphilis	0% (0/73)	1
Periodontal	0% (0/20)	2
Leptospirosis	0% (0/10)	0
Auto Immune Disease Population (n=22)		
RF	0% (0/10)	2
ANA	0% (0/11)	2
SLE (Lupus)	0% (0/1)	0
Tickborne Disease Population (n=21)		
Rickettsia	0% (0/9)	0
<i>E. chaffeensis</i>	0% (0/8)	5
HGE	0% (0/3)	0
Tickborn Relapsing	0% (0/1)	0
Muscular Skeletal Disease (n=33)		
Arthritis	7% (1/15)	0
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=44)		
Fatigue	0% (0/15)	0
Misc.	0% (0/29)	1

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

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Reproducibility Intra-laboratory Reproducibility was assessed by assaying 10 serum samples (of varying reactivity) once per day on 3 days using a single Antigen Strip lot. All 3 runs yielded identical screening interpretations for 9 of 10 selected sera. The remaining discrepant sample (a weakly reactive sample) produced identical interpretations on 8 of the 10 criteria bands. Overall, the 10 criteria bands yielded identical interpretations on 288 of 300 (96%) criteria band readings.

Inter-lot Reproducibility was assessed using 10 serum samples (of varying reactivity) on 3 lots of Antigen Strips. All 3 lots produced identical screening interpretations for 9 of the 10 selected sera. The discrepant sample (a weakly reactive sample) produced identical interpretations on 7 of the 10 criteria bands. Overall, the 10 criteria bands yielded identical interpretations on 284 of 300 (95%) criteria band readings.

Inter-reader Reproducibility was assessed by assaying 18 patient sera with a single lot of strips. The sera were assayed at up to three Investigational Sites (two sera were tested at two sites only), and read by two readers at each site. Overall, interpretation was identical 94% (49/52), and criteria band readings were identical 94% (491/520).

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 88% (91/104), and criteria band readings were identical 87% (900/1040).

The results indicate that for strongly reactive and negative specimens the assay reproducibility is high. Weakly reactive (borderline) specimens decrease the kit's reproducibility.

The following table summarizes reproducibility by interpretation and band reproducibility.

Study	n	Interp	21	23	28	30	39	41	45	58	66	93
Intra-lab	10	90%	90%	90%	90%	90%	100%	90%	90%	100%	90%	100%
Inter-lot	10	90%	90%	90%	90%	90%	100%	90%	90%	90%	90%	100%
Inter-reader	18	94%	90%	92%	94%	98%	98%	98%	92%	96%	90%	90%
Inter-site	18	88%	88%	83%	84%	80%	91%	84%	73%	94%	92%	97%



JUN 1 1998

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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

Re: K971006
Trade Name: Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgG
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 (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.

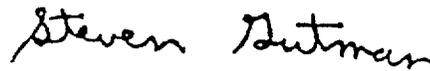
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Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

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 (if known): K971006

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

Indications for Use:

MRL Diagnostics' Lyme Disease *B. burgdorferi* Genogroup 1 Western Blot IgG test is intended for the qualitative detection of IgG class antibodies, in human serum, to the genogroup 1 (*Borrelia burgdorferi sensu stricto*) of *B. burgdorferi sensu lato*. The MRL Diagnostics Lyme Disease *B. burgdorferi* Western Blot IgG test is intended to provide supportive evidence of infection with *B. burgdorferi*, the causative agent of Lyme disease as an aid in the diagnosis of Lyme disease, using serum samples which have been found positive or equivocal by a *B. burgdorferi* screening method (e.g., IFA or ELISA). The MRL Diagnostics Lyme Disease *B. burgdorferi* Western Blot IgG can be used at any time following onset of symptoms provided the IFA or ELISA is positive or equivocal. Also, it should be used for follow up when: 1) only IgM antibodies were originally detected, 2) IgG antibodies were detected, but were not considered significant by Western blot, or 3) previously seronegative patients subsequently test positive by IFA or ELISA.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Debois
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K971006

Prescription Use X
(Per 21 CFR 801.109)

OR

Over-The-Counter Use _____

(Optional Format 1-2-96)