

Summary of Safety and Effectiveness Information
Borrelia burgdorferi IgG/IgM ELISA Test Kit

K965131

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II. Description of Device

The *Borrelia burgdorferi* IgG/IgM ELISA kit is an Enzyme-Linked Immunosorbent Assay (ELISA) 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 patients with symptoms that are consistent with Lyme disease. Equivocal or positive results should 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 *Borrelia burgdorferi* IgG/IgM ELISA test is an enzyme linked immunosorbent assay to detect IgG/IgM antibodies to *Borrelia burgdorferi*. Purified *Borrelia burgdorferi* 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/IgM 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 *Borrelia burgdorferi* IgG/IgM ELISA test is substantially equivalent to BioWhittaker's Lyme STAT test. Equivalence is demonstrated by the following comparative results:

Performance Characteristics

Table 1 The CDC Lyme Disease Serum Panel Stratified by Time After Onset.

The following information is from a serum panel obtained from the CDC and tested by Wampole. The 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.

Wampole *B. burgdorferi* IgG/IgM ELISA Result

Time From Onset	+	Equivocal	-	Total	% Agreement with Clinical Diagnosis
normals	0	0	5	5	100%
<1 month	2	0	3	5	40.0%
1-2 months	6	2	2	10	80.0%
3-12 months	9	3	7	19	63.3%
> 1yr	8	0	0	8	100.0%
Total	25	5	17	47	

Because the equivocals would have been tested by immunoblotting in a 2-step test system, they were considered 1-step positive for purposes of calculating % agreement. The Wampole *Borrelia burgdorferi* IgG/IgM ELISA demonstrated 71% (30/42) agreement (sensitivity) with clinical diagnosis of Lyme disease.

Study 2: 176 fresh sera from patients of various ages and genders that were submitted to a large clinical lab for *B. burgdorferi* antibody testing were tested on the Wampole *B. burgdorferi* IgG/IgM ELISA and Lyme Stat. Any serum found positive or equivocal was tested by Mardx Diagnostics Western Blot on both IgG and IgM.

Table 2: Western blot results

		<u>Western Blot</u>	
		+	-
Wampole	+	6	3
	eq.	1	6
Lyme Stat	+	5	3
	eq.	0	5

<u>Type of Result</u>	<u>Wampole (95%CI)</u>	<u>Lyme Stat (95%CI)</u>
1-step (ELISA) pos. or eq.	9.1% (4.8%-13.4%) (16/176)	7.4% (3.4%-11.3%) (13/176)
1-step pos. or eq. & 2-step (WB) pos.	4% (1.0%-6.9%) (7/176)	2.8% (0.3%-5.3%) (5/176)
2-step pos. among 1-step pos. or eq.	44% (18.9%-68.6%) (7/16)	39% (11.5%-65.4%) (5/13)

2. Precision. Seven sera were assayed ten times each on three different plates at three different sites. An additional three serum were assayed ten times each on three different plates at two different sites. The intersite precision is shown in Table 3. With appropriate technique the user should obtain precision of <15% CV.

Table 3
***Borrelia burgdorferi* IgG/IgM ELISA Inter Assay Precision Between Sites**

#	Inter-Assay (n=90)				n
	<u>X</u>	<u>SD</u>	<u>CV</u>		
1.	1.18	0.113	9.58%		90
2.	2.26	0.226	10.02%		90
3.	3.85	0.278	7.21%		90
4.	5.36	0.402	7.50%		90
5.	2.04	0.186	9.11%		90
6.	0.33	0.132	40.57%		90
7.	0.34	0.234	68.93%		90
8.	1.47	0.152	10.34%		60
9.	1.47	0.104	7.10%		60
10.	1.65	0.131	7.95%		60
HPC	5.31	0.314	5.91%		15
LPC	2.70	0.107	3.96%		15
NC	0.20	0.043	21.97%		15
CAL	3.34	0.103	3.08%		45

A total of 810 determinations were made at the three sites. In all 810 determinations there was not a case a positive result for a negative serum or a negative result for a positive serum.

X = Mean ISR

SD = standard deviation

CV = coefficient of variation = $SD/X \times 100$

The methods in NCCLS EP5 were utilized for precision parameters.

3. Cross-Reactivity. The following potentially cross-reactive sera were run on the *Borrelia burgdorferi* IgG/IgM ELISA assay to assess cross-reactivity with the assay: lipemic, bilirubinemic, RPR +, dsDNA +, RF +, EBV +, CMV +, RMS +, elevated ESR, and CRP. The data in Table 4 illustrates the amount of reactivity with the sera.

TABLE 4
Cross Reactivity

<u>Laboratory result (Titer)</u>	<u># of samples</u>	<u># of positives</u>
Lipemic (+++)	5	0
Bilirubinemic (1.9-16.9)	5	1
RPR + (1:2 - 1:64)	10	0
Rheumatoid Factor + (1:40-1:320)	3	0
Epstein Barr Virus Antibody + (1:40-1:2560)	7	0
Cytomegalovirus Antibody + (O.D. 0.718-2.308)	6	1
Rocky Mt Spotted Fever Antibody + (1:256-1:16,384)	4	0
CRP + (2.79-8.61 mg/dl)	5	0
Elevated ESR (40-115)	10	0
dsDNA + (52.3-1072 IU)	16	0