510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K080012

B. Purpose for Submission:

New 510(k)

C. Measurand:

Borrelia burgdorferi IgG antibodies

D. Type of Test:

Enzyme immunoassay

E. Applicant:

Bio-Rad, Inc.

F. Proprietary and Established Names:

Platelia™ Lyme IgG assay

G. Regulatory Information:

1. Regulation section:

   21CFR 866.3830; Treponema pallidum treponemal test reagents

2. Classification:

   Class: II

3. Product code:

   LSR; Reagent, Borrelia Serological Reagent

4. Panel:

   83 Microbiology

H. Intended Use:

1. Intended use(s):

   The Platelia™ Lyme IgG Assay is a qualitative test intended for use in the presumptive detection of human IgG antibodies to *Borrelia burgdorferi* in human serum or plasma (K_3 EDTA, sodium heparin or sodium citrate). The EIA system should be used to test serum or plasma from patients with a history and symptoms of infection with *B. burgdorferi*. All positive and equivocal specimens should be re-tested with a specific second-tier test such as Western blot. Positive second-tier results are supportive evidence of infection with *B. burgdorferi*. The diagnosis of Lyme disease should be made based on history and symptoms (such as erythema migrans), and other laboratory data, in addition to the presence of antibodies to *B. burgdorferi*. Negative results (either first or second-tier) should not be used to exclude Lyme disease.

2. Indication(s) for use:

   The Platelia™ Lyme IgG Assay is a qualitative test intended for use in the presumptive detection of human IgG antibodies to *Borrelia burgdorferi* in human serum or plasma (K_3 EDTA, sodium heparin or sodium citrate). The EIA system should be used to test serum or plasma from patients with a history and symptoms of infection with *B. burgdorferi*. All positive and equivocal specimens should be re-tested with a specific second-tier test such as Western blot. Positive second-tier results are supportive evidence of infection with *B. burgdorferi*. The diagnosis of Lyme disease should be made based on history and symptoms (such as erythema migrans), and other laboratory data, in addition to the presence of antibodies to *B. burgdorferi*. Negative results (either first or second-tier) should not be used to exclude Lyme disease.

3. Special conditions for use statement(s):

   For prescription use

4. Special instrument requirements:

   None

I. Device Description:

Platelia™ Lyme IgG Assay is a qualitative test for detection of IgG antibodies to *Borrelia burgdorferi* in human serum or plasma. Platelia™ Lyme IgG uses an indirect ELISA immuno-enzymatic method. Inactivated antigens of *Borrelia burgdorferi* B31 are used for coating the microplate. A monoclonal antibody labeled with peroxidase which is specific for human gamma chains (anti-IgG) is used as the conjugate. Patients samples and controls are diluted 1/101 and then distributed to the wells of the microplate. During this incubation of one hour at 37°C, IgG antibodies to *Borrelia burgdorferi* present in the

sample bind to the *Borrelia* antigen coated on microplate wells. After incubation, unbound non-specific antibodies and other serum proteins are removed by washings. The conjugate (peroxidase-labeled monoclonal antibody specific for human gamma chains) is added to the microplate wells. During this incubation of one hour at 37°C, the labeled monoclonal antibody binds to the serum IgG captured by the *Borrelia* antigen. The unbound conjugate is removed by washings at the end of the incubation. The presence of immuno-complexes (*Borrelia* Antigen, IgG antibodies to *Borrelia burgdorferi*, anti-IgG conjugate) is demonstrated by the addition of an enzymatic development solution to each well. After incubation at room temperature (+18-30°C), the enzymatic reaction is stopped by addition of 1N sulfuric acid solution. The optical density reading obtained with a spectrophotometer set at 450/620 nm is proportional to the amount of IgG antibodies to *Borrelia burgdorferi* present in the sample.

Controls Description:
The positive and negative controls are made from human serum.

J. Substantial Equivalence Information:

1. Predicate device name(s):

    Mardx Lyme Disease EIA (IgG) Test

2. Predicate K number(s):

    K894224

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Method	ELISA	ELISA
Type	Qualitative	Qualitative
Antigens	Inactivated antigens of *Borrelia burgdorferi* B31	Inactivated antigens of *Borrelia burgdorferi* B31

Differences		
Item	Device	Predicate
Specimen type	Human Plasma or Serum	Human Serum

K. Standard/Guidance Document Referenced (if applicable):

Not applicable

L. Test Principle:

Chemiluminescent immunoassay

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. *Precision/Reproducibility:*
   Study 1: Assay precision was established at Bio-Rad. To confirm the inter assay precision of the Platelia™ Lyme IgG assay, six samples were run twice a day for 20 days. Each sample (2 positive, 2 low positive and 2 negative samples) was tested according to the assessed kit's protocol (same batch used throughout the experiment). Coefficients of variation obtained for positive samples were less than 10%. Higher CV was obtained in the grey zone.

   Study 2: Assay precision was established at Bio-Rad. To confirm the intra assay precision of the Platelia™ Lyme IgG assay two studies were run:
   o Three samples close to the cut off value were tested 20 times during the same run, according to the assessed kit's protocol.
   o Various samples spanning the assay range were tested 30 times during the same run, according to the assessed kit's protocol.
   The coefficient of variation was less than 10% for positive samples as well as those samples close to the cut off.

   Study 3: Assay reproducibility was established at two external sites and at Bio-Rad through a panel of samples containing Lyme IgG. NYMC assayed 111 samples in triplicate and one sample in duplicate. There were six discrepancies. MDL had three technicians assay 90 samples each. There were four discrepancies.

   The studies were acceptable for this type assay.

   b. *Linearity/assay reportable range:*

   Not applicable

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

   Not applicable

   d. *Detection limit:*

   Not applicable

   e. *Analytical specificity:*
   A study to confirm the analytical specificity of the assay was performed using normal blood bank donor samples. Samples were collected from endemic and

non-endemic regions and tested on the Bio-Rad Platelia™ Lyme assays. Medical Diagnostic Laboratories (MDL) tested 100 samples from Nevada, Oregon, and Louisiana; all considered non-endemic areas. New York Medical College (NYMC) tested 83 samples from the northeastern United States, considered an endemic area. NYMC found a prevalence of 1.2 % for IgG. MDL found no IgG positive samples. The results are summarized below.

Prevalence of Lyme IgG antibodies using Platelia™ Lyme IgG Assay

	Endemic	Non-Endemic	Total
Number of samples tested	83	100	183
Positive or Equivocal	1.2% (1/83)	0.0% (0/100)	0.5% (1/183)
95% CI	0.0% - 6.5 %	0.0% - 3.6 %	0.0 % - 3.0 %

Cross-reactivity: The cross-reactivity studies for the Platelia™ Lyme IgG Assay were done by testing a panel of sixteen disease conditions including syphilis, *H. pylori*, viral infections (EBV, HSV, Rubella, Toxoplasmosis, Measles, Mumps, VZV, HIV, CMV), and inflammatory syndromes (CRP, SLE, HAMA, RF, ANA). One specimen (syphilis) out of a total of 161 samples tested from the cross-reaction panel was positive.

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Prospective study: A prospective study of discarded samples collected for routine Lyme disease testing was conducted at Medical Diagnostic Laboratories (MDL) and New York Medical College (NYMC). All samples with positive or equivocal results on the Bio-Rad Platelia™ Lyme assays were further tested by western blot (MDL -- Borrelia B31 Vira Blot from ViraMed; NYMC -- Mardx). A summary of the results is presented below.

	Platelia™ Lyme IgG		
	Positive	Equivocal	Negative
Site 1 (n=339)	45	18	276
Site 2 (n=100)	10	7	83
Total (n=439)	**55**	**25**	**359**

	Lyme IgG		
	Platelia™ Lyme IgG Positive or Equivocal	Western Blot IgG Positive	Positive Agreement samples (%)
Site 1 (n=339)	61 [1]	6 [1]	9.8%
Site 2 (n=100)	17	3	17.6%
Total (n=439)	**78**	**9**	**11.5%**

[1] *Two samples were not interpretable on Western Blot IgG and were not considered for calculation.*

CDC Serum Panel: The following information is from a serum panel obtained from the CDC and tested by the Platelia™ Lyme IgG Kit. The results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. The table below summarizes results obtained on Platelia™ Lyme IgG and a marketed device.

Time from onset	Platelia™ Lyme IgG				Predicate Lyme IgG EIA Assay			
	Positive or equivocal	Negative	Total	% agreement with clinical diagnosis [1]	Positive or equivocal	Negative	Total	% agreement with clinical diagnosis [1]
Normals	0	5	5	**100.0%** (5/5)	0	5	5	**100.0%** (5/5)
0-1 Month	2	3	5	**40.0%** (2/5)	3	2	5	**60.0%** (3/5)
1-2 Months	5	3	8	**62.5%** (5/8)	3	5	8	**37.5%** (3/8)
3-12 Months	10	7	17 [2]	**58.8%** (10/17)	10	8	18	**55.6%** (10/18)

> 1 Year	8	0	8	100.0% (8/8)	7	1	8	87.5% (7/8)
Total	25	18	43 [2]	69.8% (30/43)	23	21	44	63.6% (28/44)

[1] *Equivocal samples considered as positive*
[2] *One sample not tested due to insufficient sample volume*

b. *Matrix comparison:*

Serum and plasma correlation studies were performed at Bio-Rad. Serum and plasma samples collected from a given individual were tested in parallel. Since it was impossible to obtain Lyme positive serum and plasma samples, negative samples were supplemented with high positive Lyme IgG sample in order to obtain various concentration levels. Plasma *versus* serum comparisons were performed with a panel of 25 samples (12 negative and 13 positive or equivocal samples). See table below for a distribution of percent difference of different types of plasma *versus* serum.

		<10%	≥10% to ≤20%	>20%	Mean of differences
Negative samples (n=12)	K3 EDTA	16.7%	8.3%	75.0%	-16.7%
	Na Heparin	33.3%	0.0%	66.7%	-12.4%
	Na Citrate	8.3%	8.3%	83.4%	-20.9%
Equivocal or Positive samples (n = 13)	K3 EDTA	46.1%	15.4%	38.5%	2.9%
	Na Heparin	61.5%	15.4%	23.1%	0.6%
	Na Citrate	38.5%	46.1%	15.4%	0.0%

A large variation has been observed on negative plasma compared to negative sera but without a change in results interpretation. However, the variation within the positive or equivocal samples is small and did not change the results interpretation.

3. Clinical studies:

a. *Clinical Sensitivity:*
   Sensitivity: A retrospective study to confirm the sensitivity of the assay was conducted at NYMC. All retrospective patient samples were from their Lyme culture studies; all were culture positive and all were seen by one of the

infectious disease physicians or a nurse practitioner who specializes in Lyme disease. Skin biopsied from leading edge of the Lyme rash and/or 9 ml plasma was cultured. Tissue was ground in a micro tissue grinder with incomplete BSK media, and a 0.3 to 0.4 mL aliquot of that was cultured in 60 mL of modified complete BSK media. Plasma cultures were 3 mL of plasma to 60 mL of modified BSK. All positive cultures were confirmed by restriction fragment length polymorphism (RFLP) typing. The samples were run on the Bio-Rad Platelia™ Lyme IgG assay. A summary of the data is provided below.

		Positive	Equivocal	Negative	Total	% Sensitivity [1]
Platelia™ Lyme IgG	Early Stage	55	16	49	120	**59.2%** (71/120)
	Disseminated Stage	18	2	13	33	**60.6%** (20/33)
	Late Stage	13	0	0	13	**100.0%** (13/13)
	All Stages	86	18	62	166	**62.7%** (104/166)

[1] *Equivocal results were considered as positive for calculation of sensitivity.*

b. *Clinical specificity:*

See item 3 a.

c. Other clinical supportive data (when a. and b. are not applicable):

None

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The information submitted in this premarket notification is complete and supports a substantial equivalence decision.