

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K062473

B. Purpose for Submission:

New device

C. Measurand:

Borrelia burgdorferi IgG/IgM antibodies

D. Type of Test:

Chemiluminescent immunoassay

E. Applicant:

DiaSorin, Inc.

F. Proprietary and Established Names:

DiaSorin LIAISON® *Borrelia burgdorferi*

DiaSorin LIAISON® *Borrelia burgdorferi* Serum Controls

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:

The LIAISON® *Borrelia burgdorferi* assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer (Model 15970) for the qualitative presumptive detection of IgG and IgM antibodies to VlsE (variable major protein-like sequence, expressed) protein antigen of *Borrelia burgdorferi* in human serum. This assay should be used only on samples from patients with signs and

symptoms that are consistent with Lyme disease. Positive or equivocal results should be supplemented by testing with a standardized Western blot procedure. Positive supplemental results provide evidence of exposure to *Borrelia burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. Negative results by LIAISON® *Borrelia burgdorferi* Assay should not be used to exclude Lyme disease.

Controls

The LIAISON® *Borrelia burgdorferi* Serum Controls (negative, positive) are used to monitor the performance of the LIAISON® *Borrelia burgdorferi* chemiluminescent immunoassay (CLIA) for the qualitative determination of IgG/IgM antibodies to *B. burgdorferi* in human serum. The performance of the LIAISON® *Borrelia burgdorferi* Serum Controls has not been established with any other Lyme disease assay.

2. Indication(s) for use:

The LIAISON® *Borrelia burgdorferi* assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the qualitative presumptive detection of IgG and IgM antibodies to VlsE (variable major protein-like sequence, expressed) protein antigen of *Borrelia burgdorferi* in human serum. This assay should be used only on samples from patients with signs and symptoms that are consistent with Lyme disease. Positive or equivocal results should be supplemented by testing with a standardized Western blot procedure. Positive supplemental results provide evidence of exposure to *Borrelia burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. Negative results by LIAISON® *Borrelia burgdorferi* should not be used to exclude Lyme disease.

Controls

The LIAISON® *Borrelia burgdorferi* Serum Controls contains two assayed quality control sera (negative and positive) that are used to monitor the performance of the LIAISON® *Borrelia burgdorferi* assay.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

None

I. Device Description:

The method for qualitative determination of IgG and IgM to *Borrelia burgdorferi* is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the

exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with recombinant *Borrelia VlsE* antigens and a conjugate reagent containing two mouse monoclonal antibodies (anti-human IgG and anti-human IgM) linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, anti-Borrelia antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, the antibody conjugates react with anti-Borrelia IgG and IgM antibodies that have bound to the solid phase. After each incubation, unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and hence the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of *Borrelia burgdorferi* antibodies present in calibrators, samples or controls.

Controls Description:

Positive and negative serum controls are made from defibrinated human plasma.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Immunitics® C6 *B. burgdorferi* (Lyme) ELISA™ Kit
2. Predicate 510(k) number(s):
K003754
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Specimen Type Method and type	Human serum Qualitative	Human serum Qualitative
Differences		
Item	Device	Predicate
Method and Type Instrumentation Antigens	Chemiluminescent Immunoassay Automated Proteins from <i>B. burgdorferi</i> and <i>B. garinii</i>	ELISA Manual Proteins from <i>B. burgdorferi</i>

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

Not applicable

L. Test Principle:

Chemiluminescent immunoassay

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Study 1: Assay precision performance was established at DiaSorin following a protocol outlined in CLSI document, EP5-A2. Six (6) serum samples and one lot of LIAISON® *Borrelia* Serum Controls (2) were tested in four replicates per day over 20 working days on two LIAISON® instruments. The panel members were selected to represent negative to high-positive analyte levels. The results indicated a %CV of 8 to 14 for positive samples.

Study 2: An assay reproducibility study was conducted at two external US laboratories and at DiaSorin using the same serum samples described above in a five-day protocol outlined in CLSI document, EP15-A2. The samples were tested at all three sites, in four replicates per day for five days. Each site used a different LIAISON® *Borrelia burgdorferi* IgG/IgM Assay lot. The results indicated a %CV of 8 to 11 for positive samples.

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:

The LIAISON® *Borrelia burgdorferi* assay was used to test samples from apparently healthy adult blood donors collected in a region in which Lyme disease is endemic (Pennsylvania) and in a region in which Lyme disease is rare (Arizona).

	N	Negative	Equivocal	Positive	% positive
Endemic	300	297	1	2	0.7%
Non-endemic	300	299	0	1	0.3%

Cross-reactivity: The cross-reactivity studies for the LIAISON® *Borrelia burgdorferi* IgG/IgM Assay were done by testing closely related members of the spirochete genera (*T. pallidum*), tick-borne diseases (Babesiosis, HGE, TBRF and RMSF), organisms that may cause infectious disease, (CMV, EBV, HIV), *H.pylori*, and other conditions that may result from atypical immune system activity such as RF, RA, Autoimmune diseases, SLE, MS as well as HAMA and anti-*E.Coli*. Eleven specimens out of 300 total specimens tested from the cross-reaction panel were positive. Potential assay interference due to circulating antibodies against Human Ehrlichiosis (HGE) and Tick Borne Relapsing Fever (TBRF) has been detected.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Sixty (60) samples from an archived collection consisted of clinically-defined (culture confirmed) Lyme disease patients were tested with the LIAISON® *Borrelia* IgG/IgM Assay. These samples consisted of early, convalescent, and neurologic stages.

Sensitivity: 73.3% (44/60)

Percent Agreement with predicate ELISA device

Positive	93.2%	(41/44)
Negative	81.3%	(13/16)
Overall	90.0%	(54/60)

Vaccine Recipients: Eleven (11) frozen banked samples were tested from adults treated with a licensed recombinant OspA vaccine (LYMERix™, manufactured by GlaxoSmithKline Biologics). All samples were negative by the test indicating no cross reactivity with the vaccine antigens.

CDC Serum Panel: A serum panel was obtained from the Centers for Disease Control and Prevention and tested by the LIAISON® *Borrelia burgdorferi* IgG/IgM Assay. The panel consists of 5 normal sera and 37 sera with confirmed Lyme disease and obtained at different times from onset of disease. It was assayed using the test kit and the positive agreement was found to be 73% (27/37) and the negative agreement to be 100% (5/5).

Prospective Samples: A total of 1038 which were prospectively collected and tested. LIAISON® *Borrelia burgdorferi* IgG/IgM Assay showed 41 samples as positive and 4 as equivocal.

Agreement with predicate ELISA

Positive	70.0%	(35/50)
Negative	99.1%	(973/982)
Overall	97.1%	(1008/1038)

The samples that were found to be positive or equivocal in the ELISA are tested on a second step Western blot.

			Western Blot	
			+	-
LIAISON	+	41	22	19
	±	4	0	4
Predicate	+	50	23	27
	±	6	0	6

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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

Not applicable

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