January 29, 2019

DiaSorin Inc.
Mari Meyer
Vice President of Regulatory & Clinical Affairs
1951 Northwestern Ave
Stillwater, Minnesota 55082-0285

Re: K193051
Trade/Device Name: LIAISON Lyme Total Antibody Plus, LIAISON Lyme Total Antibody Plus Control Set
Regulation Number: 21 CFR 866.3830
Regulation Name: Treponema pallidum treponemal test reagents
Regulatory Class: Class II
Product Code: LSR, QCH
Dated: October 31, 2019
Received: November 1, 2019

Dear Mari Meyer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Steven Gitterman, M.D., Ph.D.
Deputy Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

5.0 510(k) SUMMARY

SUBMITTED BY:

Mari Meyer
VP Regulatory and Clinical Affairs, North America, DiaSorin Inc.
1951 Northwestern Avenue
Stillwater, MN 55082-0285
Phone (651) 439-9710
Fax (651) 351-5669
Email: mari.meyer@diasorin.com

DATE PREPARED: January 11, 2020

NAME OF DEVICE:

Trade Name:	LIAISON® Lyme Total Antibody Plus LIAISON® Lyme Total Antibody Plus Control Set
Common Names/Descriptions:	*Borrelia burgdorferi IgG/IgM* assay and *Borrelia burgdorferi IgG/IgM* controls
Classification Names:	Treponema pallidum; treponemal test reagents Class II, 21 CFR: 866.3830; Microbiology
Product Code:	LSR
Predicate Device:	Zeus ELISA Borrelia VlsE1/pepC10 IgG/IgM Test System (K113397)

INTENDED USE:

LIAISON® Lyme Total Antibody Plus: The LIAISON® Lyme Total Antibody Plus assay uses chemiluminescent immunoassay (CLIA) technology for the qualitative determination of lgG and IgM antibodies to *Borrelia burgdorferi* in human serum and plasma (K_2-EDTA, Li-heparin) samples. This assay is intended for use 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 *B. burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. Negative results by LIAISON® Lyme Total Antibody Plus assay should not be used to exclude Lyme disease. The test has to be performed on the LIAISON® XL Analyzer.

The LIAISON® Lyme Total Antibody Plus Control Set: The LIAISON® Lyme Total Antibody Plus Control Set is intended for use as assayed quality control samples to monitor the performance of the LIAISON® Lyme Total Antibody Plus assay. The performance characteristics of LIAISON® Lyme Total Antibody Plus Control Set have not been established for any other assays or instrument platforms different from the LIAISON® XL.

KIT DESCRIPTION:

The method for qualitative determination of IgG and IgM antibodies 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 Analyzer. The principal components of the test are magnetic particles (solid phase) coated with recombinant Borrelia 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, antigen-specific antibodies present in calibrators, samples or controls bind to the solid phase. During the second incubation, the conjugates react with *Borrelia burgdorferi* IgG and IgM antibodies captured by the solid phase. Unbound material is removed with a wash cycle following incubations. 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.

COMPARISON TO PREDICATE DEVICE

Table 1: Table of Similarities

Characteristic	**Candidate Device LIAISON® *Lyme Total Antibody Plus***	**Predicate Device Zeus ELISA Borrelia VlsE1/pepC10 IgG/IgM Test System – K113397**
Intended Use	LIAISON® Lyme Total Antibody Plus: The LIAISON® Lyme Total Antibody Plus assay uses chemiluminescent immunoassay (CLIA) technology for the qualitative determination of lgG and IgM antibodies of *Borrelia burgdorferi* in human serum and plasma (K_2-EDTA, Li-heparin) samples. This assay is intended for use 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 *B. burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. Negative results by LIAISON® Lyme Total Antibody Plus assay should not be used to exclude Lyme disease. The test has to be performed on the LIAISON® XL Analyzer.	Qualitative detection of lgG and IgM class antibodies to VlsE1 and pepC10 antigens from *Borrelia burgdorferi* in human serum. The assay is intended for testing serum samples from symptomatic patients or those with a history of Lyme Borreliosis. All positive and equivocal specimens should be tested with a second-tier test such as Western Blot, which if positive, is supportive evidence of infection with *Borrelia burgdorferi*. Diagnosis of Lyme Borreliosis should be made based on the presence of *B. burgdorferi* antibodies, history, symptoms, and other laboratory data. Negative first or second tier results should not be used to exclude Borreliosis. This kit is for *in vitro* diagnostic use.
Results	Qualitative	Same

Measurand	IgG and IgM antibodies to *Borrelia burgdorferi*	Same
Intended Population	Patients with signs and symptoms consistent with *Borrelia* infection (Lyme disease)	Same
Assay Principle	Uses *Borrelia* antigens coated on a solid phase to capture specific patient antibodies.	Uses *B. burgdorferi* antigen coated on a solid phase to capture specific patient antibodies.
Sample Type	Human serum, serum separator tubes, K_2-EDTA, lithium heparin plasma	Human serum
Conjugate antibody specificities	Anti-human IgG and anti-human IgM	Anti-human IgG/IgM
Assay Output	Index	Same

Table 2: Table of Differences

Feature	**Candidate Device LIAISON® *Lyme Total Antibody Plus***	**Predicate Device Zeus ELISA Borrelia VlsE1/pepC10 IgG/IgM Test**
Test Format	CLIA (indirect chemiluminescent assay)	ELISA
Reporter Molecule	Isoluminol derivative conjugated to anti-human IgG and IgM	TMB (as a substrate for Horseradish peroxidase conjugated to anti-human IgG/IgM).
Antigen	Recombinant VlsE antigen from *B. burgdorferi* strain B31 and from *B. garinii* strain Pbi, and OspC antigen from *Borrelia afzelii*,	VlsE1 and pepC10 antigens of *B. burgdorferi*
Assay Procedure	Automated (on the LIAISON® XL Analyzer)	Manual
Calibration	Two-point verification (in triplicate) of stored 10-point master curve	Single Cut-off Calibrator assayed in triplicate
Output Signal	Flash chemiluminescent response is integrated over a 3 second reading period to generate a relative light unit (RLU) value.	Microtiter well O.D. (450 nm) is measured after the enzyme reaction is halted by sulfuric acid.
Measurement System	Photomultiplier (flash chemiluminescence reader)	Spectrophotometer (EIA Microtiter plate reader)

PERFORMANCE DATA:

Prospective Study/Method Comparison Agreement:

One thousand five hundred fifty (1550) samples collected from subjects sent to the lab for Lyme disease testing, were de-identified and numbered. The collection consisted of subjects from five (5) geographical regions of the U.S. The samples were tested with the LIAISON® Lyme Total Antibody Plus assay on the LIASON® XL and performed in three (3) laboratories (2 external and internally at DiaSorin). Results were evaluated for first tier testing.

Table 3: First Tier Percent Agreement with Predicate Device

	Predicate Assay (IgG/IgM)

LIAISON® Lyme Total Antibody Plus	Positive	Equivocal	Negative	Total
Positive	62	1	9	72
Equivocal	2	0	10	12
Negative	42	8	1416	1466
Total	106	9	1435	1550

Positive % Agreement* 56.5% (65/115) 95% CI: 47.4% - 65.2%
Negative % Agreement 98.7% (1416/1435) 95% CI: 97.9% - 99.2%
*****Includes Positive and Equivocal combined

Table 4: Second Tier Testing
Western blot testing was performed on the samples positive or equivocal by the test device and the predicate. The following results were obtained:

Test System	Tier 1 + or Eqv	Western Blot IgG/IgM +	Western Blot IgG/IgM -
LIAISON® Lyme Total Antibody Plus	84	48	36
Predicate Assay	115	48	67
Predicate + LIAISON® Lyme Total Antibody Plus	65	47	18

Agreement Results:
2nd Tier PPA 97.9% (47/48) 95% CI: 89.1%-99.6%

15.2 Characterized Lyme Panel
Two hundred eighty samples of various reactivity were acquired from the CDC and evaluated internally at the manufacturer's site. The results of the testing are presented here as a means of conveying further information on the performance of the LIAISON® Lyme Total Ab Plus assay with a characterized serum panel. This does not imply an endorsement of the assay by the CDC.

Table 5: Testing of CDC Lyme Reference Sera

Sample Category (CDC Reference Classification)		Candidate			Predicate			N	LIAISON Lyme Total AB Plus % Agreement/ 95% Wilson CI	Predicate % Agreement/ 95% Wilson CI
		Pos	Neg	Eqv	Pos	Neg	Eqv			
Stage I	Acute	27	9	3	30	9	0	39	76.9% (30/39) 61.7% - 87.4%	76.9% (30/39) 61.7% - 87.4%
Stage II	Convalescent	29	2	0	29	2	0	31	93.5% (29/31) 79.3% - 98.2%	93.5% (29/31) 79.3% - 98.2%
Stage III	Late	20	0	0	20	0	0	20	100.0% (20/20) 83.9% - 100.0%	100.0% (20/20) 83.9% - 100.0%
Look-alike Diseases		2	86	2	4	85	1	90	95.6% (86/90) 89.1% - 98.3%	94.4% (85/90) 87.6% - 97.6%
Healthy Controls		2	98	0	3	95	2	100	98.0% (98/100) 93.0% - 99.4%	95.0% (95/100) 88.8% - 97.8%

15.3 PRECISION STUDY

A 12-day precision/repeatability study was conducted at DiaSorin on the LIAISON® Lyme Total Antibody Plus assay. Six (6) serum samples and one (1) lot of LIAISON® Lyme Total Antibody Plus Controls were tested for 12 days, 2 runs/day, and 2 replicates per run by multiple technologists for a total of 48 replicates. These test days span 2 calibration cycles. CLSI document EP05-A3 was consulted in the preparation of the testing protocol.

Sample ID	N	Mean (Index)	Within Run		Between Run		Between Day		TOTAL	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Control	48	0.09	0.01	9.4	0.01	8.0	0.00	0.0	0.01	11.3
Pos Control	48	1.96	0.13	6.7	0.03	1.6	0.15	7.7	0.20	10.4
Sample 1	48	0.09	0.00	5.6	0.01	6.0	0.00	2.2	0.01	8.5
Sample 2	48	0.84	0.04	4.5	0.02	2.8	0.05	5.6	0.07	7.7
Sample 3	48	1.59	0.12	7.7	0.00	0.0	0.10	6.0	0.15	9.4
Sample 4	48	4.51	0.21	4.7	0.24	5.4	0.25	5.5	0.41	9.0
Sample 5	48	0.82	0.06	7.3	0.07	8.4	0.06	7.0	0.11	13.2
Sample 6	48	1.39	0.08	6.0	0.12	8.7	0.07	5.2	0.16	11.8

15.4 REPRODUCIBILITY STUDY

A five (5) day precision/reproducibility study was performed internally at DiaSorin Inc. and at two (2) external U.S. laboratories with one (1) lot of LIAISON® Lyme Total Antibody Plus assay. The study was performed for 5 days, 2 runs/day, and 3 replicates/run. Each day, two operators, at each testing site performed the testing for a total of 30 replicates at each site. CLSI document EP15-A3 was consulted in the preparation of the testing protocol.

Sample ID	n	mean	Within Run		Between Day		Between Run		Between Site		TOTAL	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Neg Control	90	0.0509	0.002	4.7	0.002	3.4	0.002	3.4	0.002	4.7	0.004	8.2
Pos Control	90	1.8	0.118	6.5	0.04	2.2	0.039	2.2	0.000	0.0	0.13	7.2
Sample 1	90	0.0463	0.002	4.6	0.002	4.3	0.001	3.1	0.000	0.0	0.003	7.0
Sample 2	90	0.654	0.028	4.2	0.036	5.5	0.026	3.9	0.024	3.7	0.057	8.8
Sample 3	90	1.55	0.07	4.5	0.055	3.6	0.046	3.0	0.077	5.0	0.126	8.2
Sample 4	90	4.66	0.207	4.4	0.161	3.5	0.107	2.3	0.000	0.0	0.283	6.1
Sample 5	90	0.86	0.052	6.1	0.04	4.6	0.000	0.0	0.035	4.1	0.074	8.7
Sample 6	90	1.42	0.065	4.6	0.075	5.3	0.041	2.9	0.064	4.5	0.125	8.8

15.5 Cross-Reactivity Study

The cross-reactivity study was designed to evaluate 238 specimens from twenty four (24) disease states either known to contain potentially cross-reactive antibodies to *B. burgdorferi* or from patients with diagnoses that can exhibit signs and symptoms similar to late manifestations of Lyme disease and cause false positive results.

Organism Infected or Disease State	Samples Tested (n)	Pos or Eqv
Tick Borne Diseases		
Babesiosis	10	4
Tick Borne Relapsing Fever (TBRF)	8	2
Autoimmune Disorders		
Anti-Nuclear Antibodies (ANA)	10	0
Multiple Sclerosis	10	0
Sjogrens Syndrome	10	1
Viral Diseases		
Cytomegalovirus (CMV) IgM	10	0
Cytomegalovirus (CMV) IgG	10	0
Epstein-Barr Virus (EBV) VCA, and/or heterophile Ab IgM	10	0
Epstein-Barr Virus (EBV) VCA, NA-1 and/or EA-D IgG	10	0
Epstein-Barr Virus (EBV) EBNA IgG	10	1
Epstein-Barr Virus (EBV) VCA IgM	10	2
Epstein-Barr Virus (EBV) VCA IgG	10	0
Human Immunodeficiency Virus (HIV)	10	0
Influenza Virus	10	0
Parvovirus	10	3
Bacterial Diseases		
E. coli	10	0
H. pylori	10	0
Syphilis	10	0
Rheumatic Diseases		
Fibromyalgia	10	0
Rheumatoid Arthritis	10	0
Rheumatoid Factor	10	0
Systemic Lupus Erythematosus (SLE)	10	0
Additional Markers		
Chronic Fatigue Syndrome	10	0
Human Anti-mouse Antibodies (HAMA)	10	0
Total	238	13

15.6 Interfering Substances

Controlled studies of potentially interfering substances from endogenous interferents spiked into equivocal *B. burgdorferi* serum specimens showed that assay performance was not affected at the concentration for each substance listed below. The testing was based on CLSI-EP7-A3.

Substance	Concentration
Hemoglobin	1000 mg/dL
Triglycerides	1500 mg/dL
Bilirubin	40 mg/dL
Total protein	12 g/dL
Cholesterol	500 mg/dL
Biotin	3600 ng/mL

15.7 Matrix Equivalence Study

Thirty-two (32) matched patient sets of serum, SST serum, K_2-EDTA plasma and lithium heparin plasma samples were tested to determine if these sample types provide equivalent results. Sample regression analysis was done by Passing and Bablok method. All sample types met acceptance criteria for use in the LIAISON® Lyme Total Antibody Plus assay. A summary of the results is shown in the following table.

Sample Equivalence Results:

Comparison to Serum	Bias	CI: 95%	
SST Serum Constant	0.00	0.01	0.01
SST Serum Proportional	0.99	0.97	1.01
K_2-EDTA Constant	0.01	0.03	0.01
K_2-EDTA Proportional	0.99	0.95	1.01
Lithium Heparin Constant	0.01	0.02	0.01
Lithium Heparin Proportional	0.95	0.92	0.97

CONCLUSION:

The material submitted in this premarket notification supports a substantial equivalence decision.