April 21, 2020

Gold Standard Diagnostics
Napoleon Monce
Director, Product Development
2851 Spafford St.
Davis, California 95618

Re: K200025
Trade/Device Name: Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit
Regulation Number: 21 CFR 866.3830
Regulation Name: Treponema Pallidum Treponemal Test Reagents
Regulatory Class: Class II
Product Code: LSR
Dated: December 27, 2019
Received: January 6, 2020

Dear Napoleon Monce:

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 R. Gitterman -S

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

K200025

Device Name

Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit

Indications for Use *(Describe)*

The Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit is intended as a qualitative presumptive (first-step) test for the detection of IgM antibodies to *B. burgdorferi sensu stricto* in human serum from symptomatic patients or people suspected of infection. Positive and equivocal results must be supplemented by testing with a second-step Western blot assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This 510(k) Summary is being submitted in accordance with the requirement of SMDA 1990 and 21 CFR 807.92.

1) **Submitter's Name:** Gold Standard Diagnostics
   Address: 2851 Spafford St. Davis, CA. 95618
   Phone Number: 530-759-8000
   Contact Person: Napoleon Monce
   Date: December 27, 2019

2) **Product and Trade Name:**
   Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit

   Common Name:
   Lyme ELISA Test

   Regulation Section:
   21 CFR 866.3830; Treponema pallidum treponemal test reagents.

   Classification:
   Class II

   Product Code:
   LSR; Reagent, Borrelia Serological Reagent

3) **Legally Marketed Device to Which the Submitter Claims Equivalence:**
   Trinity Biotech MarDx *Borrelia burgdorferi* EIA IgG Test Kit (K894224).

4) **Description of the Device:**
   The kit includes 12 x 8 well Antigen Coated strips, Conjugate, Substrate, Stop Solution, Wash Buffer, Diluent, Negative Control, Positive Control, and Cutoff Control. The controls are provided to determine if the assay is functioning properly and to determine the antibody level. The reagents are sufficient for 96 determinations.

   During the test procedure, antibodies to *B. burgdorferi* (*sensu stricto*) if present in the human serum sample will bind to the antigens coated onto the wells forming antigen-antibody complexes. Excess antibodies are removed by washing. A conjugate of goat anti-human IgG antibodies conjugated with horseradish peroxidase is then added, which binds to the antigen-antibody complexes. Excess conjugate is removed by washing. This is followed by the addition of a chromogenic substrate, tetramethylbenzidine (TMB). If specific antibodies to the antigen are present in the patients' serum, a blue color will develop. The enzymatic reaction is then stopped with a stopping solution causing the contents of the well to turn yellow. The wells are read photometrically with a microplate reader at 450nm.

The antigens used in the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test kit is a combination of *B. burgdorferi sensu stricto* strain B31 lysate, *B. burgdorferi sensu stricto* strain 2591 lysate, and a recombinant VlsE protein from *B. burgdorferi sensu stricto* strain B31. The lysates use spirochetes growing in BSK-H complete medium until mid-exponential phase. The recombinant VlsE protein is produced in *E. coli* SURE2 cells and purified by affinity chromatography.

5) Intended Use of the Device:

The Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test kit is intended as a qualitative presumptive (first step) test for the detection of IgG antibodies to *B. burgdorferi sensu stricto* in human serum from symptomatic patients or people suspected of infection. Positive and equivocal results must be supplemented by testing with a second-step Western blot assay.

6) Comparison with the Predicate Device:

The tables below provide a comparison of the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test kit with the Trinity Biotech MarDx *Borrelia burgdorferi* EIA IgG Test kit (predicate device: K894224).

Similarities		
Item	**Subject Device: Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit**	**Predicate Device: Trinity Biotech MarDx *Borrelia burgdorferi* EIA IgG Test Kit**
Intended Use	The Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test kit is intended as a qualitative presumptive (first step) test for the detection of IgG antibodies to *B. burgdorferi sensu stricto* in human serum from symptomatic patients or people suspected of infection. Positive and equivocal results must be supplemented by testing with a second-step Western blot assay.	Trinity Biotech MarDx *Borrelia burgdorferi* EIA IgG Test System is a qualitative test intended for use in the presumptive detection of human IgG antibodies to *Borrelia burgdorferi* in human serum. This EIA system should be used to test serum from patients with a history and symptoms of infection with *B. burgdorferi.* All positive and equivocal specimens should be retested with a highly 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.
Assay Format	Antigen coated microtiter plate – 96 wells.	Same
Technology	ELISA	Same

Sample Matrix	Human serum	Same
Sample Processing	Dilute Samples 1:100 in Diluent	Same
Controls Provided	Positive, Cutoff, Negative	Same
Reagents Provided	Diluent, Wash, Conjugate, Substrate, Stop Solution	Same
Reported Results	Positive, Equivocal, Negative	Same
Assay Output	Optical density readings from Spectrophotometer	Same

Differences		
Item	**Subject Device: Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit**	**Predicate Device: Trinity Biotech MarDx *Borrelia burgdorferi* EIA IgG Test Kit**
Volumes	100ul sample, 50ul substrate, 50ul stop solution	100ul sample, 100ul substrate, 100ul stop solution
Incubation	15/15/15 minutes at room temperature	30/30/10 minutes at room temperature
Antigens	*B. burgdorferi* B31 strain, *B. burgdorferi* 2591 strain, *B. burgdorferi* recombinant VlsE B31 strain	*B. burgdorferi* B31 strain
Results Interpretation	Convert to units. Negative <9 Equivocal 9.0-11.0 Positive >11.0	Convert to units. Negative <0.80 Equivocal 0.80-1.19 Positive ≥1.2

6(b1): Nonclinical Studies:

Determination of the Assay Cutoff

The cutoff was determined by testing a total of 210 normal sera which consisted of 105 sera from an endemic region of Lyme disease and 105 sera from a non-endemic region of Lyme disease. The mean plus two standard deviations was used to determine the assay cutoff. A known positive sample was then diluted to produce a ready to use cutoff control. An additional 194 samples consisting of 114 samples from different phases of Lyme disease, 8 negative healthy samples, 72 negative Lyme disease samples but do have other diseases that may cause serologic cross-reactivity, were tested. A receiver operating characteristics (ROC) analysis was performed to evaluate the performance of the assay and confirm that the chosen cutoff provided the best compromise between sensitivity and specificity.

Precision

To determine the precision of the *Borrelia burgdorferi* IgG ELISA Test, a within-lab precision study was conducted. A precision panel consisting of a negative sample, a high negative sample, a low positive sample, and a moderate positive sample, along with the kit controls, was tested in-house. The sample panel was masked and randomized. Each of the panel

members was tested in duplicate, twice per day, for 12 days. The results are summarized in the following table:

Sample	N	Mean Units		Within-Run	Between-Run	Between-Day	Total
Moderate Positive	48	20.3	SD	1.488	1.312	1.257	1.439
			CV	7.3%	6.5%	6.2%	7.1%
Low Positive	48	11.5	SD	0.845	0.718	0.718	0.816
			CV	7.4%	6.2%	6.2%	7.1%
High Negative	48	8.3	SD	0.880	0.646	0.615	0.857
			CV	10.6%	7.8%	7.4%	10.4%
Negative	48	0.8	SD	0.116	0.049	0.076	0.113
			CV	14.2%	6.5%	10.0%	14.8%
Positive Control	48	17.2	SD	0.947	0.649	0.739	.932
			CV	5.5%	3.8%	4.3%	5.4%
Cutoff Control	48	10.1	SD	0.241	0.115	0.285	0.264
			CV	2.7%	1.1%	2.8%	2.6%
Negative Control	48	0.4	SD	0.052	0.424	0.144	0.051
			CV	12.9%	10.6%	11.0%	12.7%

Reproducibility

A reproducibility panel consisting of a negative sample, a high negative sample, a low positive sample, and a moderate positive sample, along with the kit controls, was tested at three different sites. The sample panel was masked and randomized. Each of the panel members was tested in triplicate, twice per day, for five days. The Within-Run, Between-Run, Between-Days, and Between-Sites Standard Deviation and Coefficients of Variation (CV) were calculated. The sample panel was masked and randomized. The results are summarized in the following table:

Sample	N	Mean Units		Within-Run	Between-Run	Between-Day	Between-Site	Total
Moderate Positive	90	21.0	SD	1.54	0.40	1.07	0.91	1.29
			CV	7.3%	1.9%	5.1%	4.3%	6.1%
Low Positive	90	13.7	SD	0.72	0.34	1.09	1.24	1.28
			CV	5.5%	2.6%	8.0%	9.1%	9.3%
High Negative	90	6.6	SD	0.76	0.27	0.46	0.68	0.67
			CV	11.7%	4.1%	7.0%	10.3%	10.2%
Negative	90	3.0	SD	0.33	0.56	0.49	0.56	0.55
			CV	21.1%	18.7%	16.4%	18.8%	18.3%
Positive Control	30	19.1	SD	0.65	0.67	0.67	0.63	0.62
			CV	3.5%	3.5%	3.5%	3.3%	3.2%

Cutoff Control	60	10.0	SD	0.25	0.22	0.23	0.22	0.22
			CV	2.4%	2.2%	2.3%	2.2%	2.2%
Negative Control	30	0.5	SD	0.08	0.06	0.06	0.50	0.50
			CV	11.0%	11.0%	11.0%	9.5%	9.6%

Analytical Specificity

The analytical specificity was determined by testing 208 asymptomatic individuals' samples from endemic and non-endemic regions. The Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test results are summarized in the following table:

	Number of Samples	Number Positive/Equivocal	Analytical Specificity
Endemic Region	103	4	96.1%
Non-endemic Region	105	0	100%

Cross Reactivity

A study using 377 samples was conducted to evaluate potential cross reactivity from different infections and disease conditions. The samples were obtained from serum vendors who confirmed their positivity for each respective marker or clinical diagnosis. The samples were tested on the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test. The results are summarized in the following table:

Infection / Diagnosis	Number of Sera Tested	# Positive / (%)
Tick-borne Relapsing Fever IgG	21	0 / (0%)
Treponemal Infections (TPPA)	23	0 / (0%)
Rickettsiosis IgG	25	6 / (24%)
Ehrlichiosis IgG	10	2 / (20%)
Babesiosis IgG	12	0 / (0%)
H. pylori IgG	11	0 / (0%)
Parvovirus B19 IgG	12	0 / (0%)
Influenza A&B IgG	12	0 / (0%)
Epstein-Barr Virus IgG	34	1 / (3%)
Cytomegalovirus IgG	31	0 / (0%)
Herpes Simplex Virus IgG	21	0 / (0%)
Varicella Zoster Virus	16	1 / (6%)
Fibromyalgia	32	0 / (0%)
Rheumatoid Arthritis	12	0 / (0%)
Autoimmune Disease	59	0 / (0%)
Multiple Sclerosis	23	0 / (0%)
Severe Periodontitis	23	0 / (0%)

Interfering Substances

The effect of potential interfering substances on samples using the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test was evaluated. Three samples, a high negative, an equivocal and a low positive were spiked with high levels of interferants and were tested along

with serum without spiked interferants. The recommended concentrations from the guideline "Interference Testing in Clinical Chemistry" EP07-A3 from the Clinical and Laboratory Standards Institute were used (see table below). The tested substances did not affect the performance of the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test.

Substance	Concentration	Interference
Albumin	60 mg/ml	None detected
Bilirubin	0.4 mg/ml	None detected
Cholesterol	4.0 mg/ml	None detected
Hemoglobin	10 mg/ml	None detected
Triglycerides	15 mg/ml	None detected

6(b2): Clinical Studies:

Comparison with Predicate Device

Comparison studies were conducted at three sites (one internal and two external reference laboratories) using prospective samples submitted for Lyme serology testing. Five hundred twenty three (523) serum samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test and on the predicate *B. burgdorferi* IgG ELISA Test. The results are summarized in the following table:

		Predicate IgG ELISA			
		Positive	Equivocal*	Negative	**Total**
Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit	Positive	40	5	2	**47**
	Equivocal*	3	7	0	**10**
	Negative	2	4	460	**466**
	Total	**45**	**16**	**462**	**523**

*Equivocal samples counted as positive

Positive percent agreement = 90.2% (55/61) 95% CI (79.8% - 96.3%)
Negative percent agreement = 99.6% (460/462) 95% CI (98.5% - 99.9%)

Second Tier Testing: All positive and equivocal samples by the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test and by the Predicate IgG ELISA were tested by an FDA cleared IgG Western blot assay. The results are summarized in the following table:

	Tier 1 Positive or Equivocal	IgG Blot Positive	IgG Blot Negative
Predicate IgG ELISA	61	37	24
Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit	57	37	20

Predicate IgG ELISA + Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit	55	37	18

2nd Tier Percent Agreement		
2nd Tier PPA (95% CI)	100% (92.2% - 100%)	37/37

Clinical Sensitivity

Sensitivity Study

A sensitivity study was performed on 114 clinically characterized samples. The samples encompass early, disseminated, and late stages of Lyme disease. The samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test and on the predicate *B. burgdorferi* IgG ELISA Test. The results are summarized in the following table:

Disease Stage	**n**	**Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit**	**Predicate IgG ELISA**
Early	58	46.6% (27/58)	27.6% (16/58)
Disseminated	17	82.4% (14/17)	52.9% (9/17)
Late	39	97.4% (38/39)	97.4% (38/39)

CDC Panel

A panel of 280 positive and negative specimens from the Center of Disease Control (CDC) for Lyme disease detection was tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test and on the predicate device. The results are presented as a means to convey further information on the performance of the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test with a masked characterized serum panel. This does not imply an endorsement of the assay by the CDC. The results are summarized in the following table:

Disease Stage	**n**	**Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test Kit**		**Predicate IgG ELISA**	
		Positive or Equivocal	**% Agreement with Clinical Diagnosis**	**Positive or Equivocal**	**% Agreement with Clinical Diagnosis**
Healthy	100	1	99.0%	1	99.0%
Early Lyme	60	41	68.3%	21	35.0%

Cardiac Lyme	3	2	66.7%	3	100%
Neurological Lyme	7	6	85.7%	3	42.9%
Late	20	20	100%	20	100%
Look-alike Disease	90	11	87.8%	10	88.9%

Expected Values

The range of values and positivity rate among different studies and population for the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test are as follows:

Population	**# Samples**	**Unit Results**			**Qualitative Results**	
		Mean	Range	Std. Dev.	# Positive/ Equivocal	% Positive/ Equivocal
Normal Endemic	103	3.7	0.5 – 14.3	2.452	4	3.9%
Normal Non-Endemic	105	3.9	0.6 – 8.9	2.002	0	0.0%
Prospective Study	523	4.3	0.1 – 22.2	4.409	57	10.9%
Sensitivity Study	114	13.6	0.9 – 40.4	7.994	81	71.1 %

Note: It is recommended that each laboratory determine its own normal range based on the population.

7) Conclusion:

From the comparison data, we conclude that the Gold Standard Diagnostics *Borrelia burgdorferi* IgG ELISA Test is substantially equivalent to the Trinity Biotech MarDx *Borrelia burgdorferi* EIA IgG Test kit (predicate device: K894224).