May 2, 2018

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

Re: K180264
Trade/Device Name: Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit
Regulation Number: 21 CFR 866.3830
Regulation Name: Treponema pallidum treponemal test reagents
Regulatory Class: Class II
Product Code: LSR
Dated: January 26, 2018
Received: January 30, 2018

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR

Part 820); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/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 for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K180264

Device Name
Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit

Indications for Use *(Describe)*
The Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit is intended as a qualitative presumptive (first-step) test for the detection of IgG and 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: January 26, 2018

2) **Product and Trade Name:**
   Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM 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 Captia™ *Borrelia burgdorferi* IgG/IgM ELISA Test Kit (K033070).

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/IgM antibodies conjugated with horseradish peroxidase are 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/IgM 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 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. The purity of each antigen is assayed by SDS-PAGE followed by Coomassie staining and/or Western blotting.

5) Intended Use of the Device:

The Gold Standard Diagnostics *Borrelia* burgdorferi IgG/IgM ELISA Test kit is intended as a qualitative presumptive (first step) test for the detection of IgG and IgM antibodies to *B. burgdorferi sensu stricto* in human serum from symptomatic patient 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/IgM ELISA Test kit with the Trinity Biotech Captia™ *Borrelia burgdorferi* IgG/IgM ELISA Test kit (predicate device: K033070).

Similarities		
Item	**Subject Device: Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit**	**Predicate Device: Trinity Biotech Captia™ *Borrelia burgdorferi* IgG/IgM ELISA Test Kit**
Intended Use	The Gold Standard Diagnostics *Borrelia* burgdorferi IgG/IgM ELISA Test kit is intended as a qualitative presumptive (first step) test for the detection of IgG and 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.	Trinity Biotech Captia™ *Borrelia burgdorferi* IgG/IgM ELISA Test kit is intended for the qualitative presumptive (first-step) detection of total (IgG/IgM) antibodies to *B. burgdorferi* in human serum. This ELISA should only be used for patients with signs and symptoms that are consistent with Lyme disease. Equivocal or positive results must be supplemented by testing with a standardized Western-blot (second step) procedure. Positive supplemental (second-step) results are supportive evidence of exposure to *B. burgdorferi* and can be used to support a clinical diagnosis of Lyme disease. The diagnosis of Lyme disease must be made based on history, signs (such as erythema migrans), symptoms, and other laboratory data, in addition to the presence of antibodies to *B.*

		burgdorferi. Negative results (either first or second step) 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
Controls Provided	Positive, Cutoff, Negative	Same
Reagents Provided	Diluent, Wash, Conjugate, Substrate, Stop Solution	Same
Reported Results	Positive, Equivocal, Negative	Same
Interpretation	Optical density readings from Spectrophotometer	Same

Differences		
Item	**Subject Device: Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit**	**Predicate Device: Trinity Biotech Captia™ *Borrelia burgdorferi* IgG/IgM ELISA Test Kit**
Sample Processing	Dilute Samples 1:100 in Diluent	Dilute Samples 1:20 in Diluent
Volumes	100ul sample, 50ul substrate, 50ul stop solution	100ul sample, 100ul substrate, 100ul stop solution
Incubation	15/15/15 minutes at room temperature	25/25/10-15 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 ≤0.90 Equivocal 0.91-1.09 Positive ≥1.10

6(b1): Nonclinical Studies:

Determination of the Assay Cutoff

The cutoff was determined by testing a total of 200 normal sera which consisted of 100 sera from an endemic region of Lyme disease and 100 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. After the cutoff was determined 125 characterized Lyme disease samples were tested. An ROC analysis was then generated with the 325 samples (200 normal and 125 characterized samples) to verify the chosen cutoff. The analysis confirmed that the assay cutoff provided an optimal level of sensitivity and specificity.

Precision

To determine the precision of the *Borrelia burgdorferi* IgG/IgM 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 sample panel was masked and randomized. The results are summarized in the following table:

Sample	N	Mean Units		Within-Run	Between-Run	Between-Day	Total
Moderate Positive	48	19.6	SD	0.815	1.534	1.472	1.737
			CV	4.2%	7.8%	7.5%	8.9%
Low Positive	48	12.1	SD	0.267	1.417	1.248	1.442
			CV	2.2%	11.7%	10.3%	11.9%
High Negative	48	6.1	SD	0.211	0.662	0.642	0.695
			CV	3.4%	10.8%	10.5%	11.4%
Negative	48	1.7	SD	0.113	0.164	0.151	0.199
			CV	6.6%	9.6%	8.8%	11.6%

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-Sites	Total
Moderate Positive	90	21.1	SD	1.117	1.543	1.434	0.386	1.905
			CV	5.3%	7.3%	6.8%	1.8%	9.0%
Low Positive	90	13.8	SD	0.591	1.155	1.026	0.404	1.297
			CV	4.3%	8.4%	7.5%	2.9%	9.4%
High Negative	90	6.4	SD	0.323	0.756	0.715	0.237	0.822
			CV	5.0%	11.7%	11.1%	3.7%	12.8%
Negative	90	1.6	SD	0.145	0.335	0.312	0.347	0.365
			CV	9.1%	21.1%	19.6%	21.8%	23.0%

Analytical Specificity

The analytical specificity was determined by testing 210 asymptomatic individuals' samples from endemic (Pennsylvania) and non-endemic (Arizona) regions. The Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test results are summarized in the following table:

	Number of Samples	Number Positive/Equivocal	Analytical Specificity
Endemic Region	110	3	97.3%
Non-endemic Region	100	2	98.0%

Cross Reactivity

A study using 221 samples was conducted to evaluate potential cross reactivity from different disease conditions. The samples were obtained from serum vendors who confirmed their positivity for each respective marker. The samples were tested on the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test. The results are summarized in the following table:

Infection / Diagnosis	Number of Sera Tested	# Positive / (%)
Tick-borne Relapsing Fever	26	2 / (7.7%)
Treponemal Infections	23	2* (8.7%)
Rickettsia	10	0 / (0%)
Ehrlichiosis	10	0 / (0%)
Babesiosis	11	0 / (0%)
Leptospirosis	11	0 / (0%)
Parvovirus B19	12	0 / (0%)
Influenza A&B	10	0 / (0%)
Epstein-Barr Virus	10	0 / (0%)
Cytomegalovirus	19	0 / (0%)
H. pylori	11	0 / (0%)
Fibromyalgia	10	1/ (10%)
Rheumatoid Arthritis	11	0 / (0%)
Herpes Simplex Virus	13	0 / (0%)
Varicella Zoster Virus	12	0 / (0%)
Autoimmune Disease	22	0 / (0%)

*Also positive on the predicate device

Interfering Substances

The effect of potential interfering substances on samples using the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test was evaluated. Three samples, a negative, a low positive and a moderate 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 EP7-A2" 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/IgM ELISA Test.

Substance	Concentration	Interference
Albumin	120 g/L	None detected
Bilirubin	342 µmol/L	None detected
Cholesterol	13 mmol/L	None detected
Hemoglobin	2 g/L	None detected
Triglycerides	37 mmol/L	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 and twenty (520) serum samples were tested on both the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test and on the predicate *B. burgdorferi* IgG/IgM ELISA Test. The results are summarized in the following table:

		Predicate IgG/IgM ELISA			
		Positive	Equivocal*	Negative	**Total**
Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit	Positive	55	7	2	**64**
	Equivocal*	8	2	9	**19**
	Negative	2	1	434	**437**
	Total	**65**	**10**	**445**	**520**

*Equivocal samples counted as positive

Positive percent agreement = 96.0% (72/75) 95% CI (88.8% - 99.2%)
Negative percent agreement = 97.5% (434/445) 95% CI (95.6% - 98.8%)

Clinical Sensitivity

Sensitivity Study

A sensitivity study was performed on 89 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/IgM ELISA Test and on the predicate *B. burgdorferi* IgG/IgM ELISA Test. The results are summarized in the following table:

Disease Stage	**n**	**Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit**	**Predicate IgG/IgM ELISA**
Early	38	76.3% (29/38)	78.9% (30/38)
Disseminated	15	100.0% (15/15)	100.0% (15/15)
Late	36	97.2% (35/36)	94.4% (34/36)

CDC Panel

Forty samples of various reactivity were acquired from the Centers for Disease Control (CDC). Of the 40 samples, five were from healthy individuals and 35 were from patients diagnose with Lyme disease and stratified by disease stage. All samples were tested on the Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test and on the predicate *Borrelia burgdorferi* IgG/IgM ELISA Test. The results are summarized in the following table:

Disease Stage	n	Gold Standard Diagnostics *Borrelia burgdorferi* IgG/IgM ELISA Test Kit		Predicate IgG/IgM ELISA	
		Positive or Equivocal	% Agreement with Clinical Diagnosis	Positive or Equivocal	% Agreement with Clinical Diagnosis
Healthy	5	0	100%	0	100%
Early (0-2 months)	15	13	86.7%	12	80.0%
Convalescent (3-12 months)	13	7	53.8%	7	53.8%
Late (>1 year)	7	7	100%	7	100%

Expected Values

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

Population	# Samples	Unit Results			Qualitative Results	
		Mean	Range	Std. Dev.	# Positive/ Equivocal	% Positive/ Equivocal
Normal Endemic	110	5.8	0.6 – 11.3	2.075	3	2.7%
Normal Non-Endemic	100	4.2	0.9 – 12.3	2.077	2	2.0%
Prospective Study	520	6.3	0.70 – 32.3	5.407	83	16.0%
Sensitivity Study	89	25.0	3.6 – 34.9	8.449	79	88.8%

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/IgM ELISA Test is substantially equivalent to the Trinity Biotech Captia™ *Borrelia burgdorferi* IgG/IgM ELISA Test kit (predicate device: K033070).