October 2, 2019

DiaSorin Inc.
Mari Meyer
Regulatory Affairs Specialist
1951 Northwestern Ave.
P.O. Box 285
Stillwater, MN 55082-0285

Re: K192064
Trade/Device Name: LIAISON® Vitamin B12
Regulation Number: 21 CFR 862.1810
Regulation Name: Vitamin B12 test system
Regulatory Class: II
Product Code: CDD
Dated: July 31, 2019
Received: August 5, 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,

Kellie B. Kelm, Ph.D.
Acting Director
Division of Chemistry
and Toxicology 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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

k192064

Device Name
LIAISON® Vitamin B12

Indications for Use *(Describe)*

The DiaSorin LIAISON® Vitamin B12 assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of Vitamin B12 in human serum, SST serum and lithium heparin plasma. Measurements obtained by this device are used in the diagnosis and treatment of anemia's of gastrointestinal malabsorption. Assay results should be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions.

The assay must be performed on the LIAISON® XL Analyzer.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

LIAISON® Vitamin B12

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

1. **510(k) Number:** k192064

2. **Applicant:** Mari Meyer
DiaSorin Inc.
1951 Northwestern Avenue, P.O. Box 285**,** Stillwater, MN 55082-0285
Office Number: 651-351-5635; Fax Number: 651-351-5669
Email: mari.meyer@diasorin.com

3. **Date:** September 25, 2019

4. **Proprietary and Established Names:**

LIAISON® Vitamin B12

5. **Regulatory Information:**

LIAISON® Vitamin B12

Regulation Section: 21 CFR 862.1810
Classification: Class II
Product Code: CDD
Panel: Clinical Chemistry (75)

6. **Predicate Device(s):**

The predicate device used to demonstrate substantial equivalence to the LIAISON® Vitamin B12 assay is the Beckman Coulter Access Vitamin B12 assay previously FDA cleared under (K140496).

7. **Device Description:**

The LIAISON® Vitamin B12 assay is a competitive chemiluminescence immunoassay (CLIA) for quantitative determination of Vitamin B12 is serum, SST serum and lithium heparin plasma. During the first incubation, Vitamin B12 is dissociated from its binding protein. After the initial incubation of 10.5 minutes, Vitamin B12 binds to an intrinsic factor on the solid phase. After a second incubation of 10.5 minutes, a Vitamin B12 linked to an isoluminol derivative is added to compete with the Vitamin B12 in the sample. After a third incubation of 5.25 minutes, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added to initiate a flash chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLU) and is inversely proportional to the concentration of Vitamin B12 present in calibrators, controls, or samples.

8. Intended Use:

The DiaSorin LIAISON® Vitamin B12 assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of Vitamin B12 in human serum, SST serum and lithium heparin plasma. Measurements obtained by this device are used in the diagnosis and treatment of anemia's of gastrointestinal malabsorption. Assay results should be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions.

The assay must be performed on the LIAISON® XL Analyzer.

9. Indication(s) for Use:

Same as Intended Use

10. Substantial Equivalence Information:

A comparison of the similarities and differences between the LIAISON® Vitamin B12 assay and the predicate Beckman Coulter Access Vitamin B12 assay is provided in the following table:

Assay Similarities and Differences		
Characteristic	**Candidate Device LIAISON® Vitamin B12**	**Predicate Device Beckman Coulter Access Vitamin B12 (K140496)**
Intended Use	The DiaSorin LIAISON® Vitamin B12 assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of Vitamin B12 in human serum, SST serum and lithium heparin plasma. Measurements obtained by this device are used in the diagnosis and treatment of anemia's of gastrointestinal malabsorption. Assay results should be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions. The assay must be performed on the LIAISON® XL Analyzer.	The Access Vitamin B12 assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of vitamin B12 levels in human serum and plasma (heparin) using the Access Immunoassay Systems.
Measured Analyte	Vitamin B12	Same
Assay Type	Chemiluminescence immunoassay	Same
Results	Quantitative	Same

Characteristic	Candidate Device LIAISON® Vitamin B12	Predicate Device Beckman Coulter Access Vitamin B12 (K140496)
Sample Type	Human serum, SST serum and lithium heparin plasma	Human serum and heparin plasma
Sample Size	100 µL	45 µL
Storage	2-8°C	2-10°C
Operating Principle	Automated Chemiluminescent Immunoassay (CLIA)	Same
Solid Phase	Magnetic particles coated intrinsic factor	Paramagnetic particles coated with goat anti-mouse IgG
Conjugate	Proprietary polymer conjugated with Vitamin B12 and an isoluminol derivative, in MES buffer	Porcine intrinsic factor-alkaline phosphate (bovine) conjugate in TRIS buffered saline
Analytical Measuring Range	55 - 1500 pg/mL	50 -1500 pg/mL
Calibrators	2 Levels, on board	5 Levels

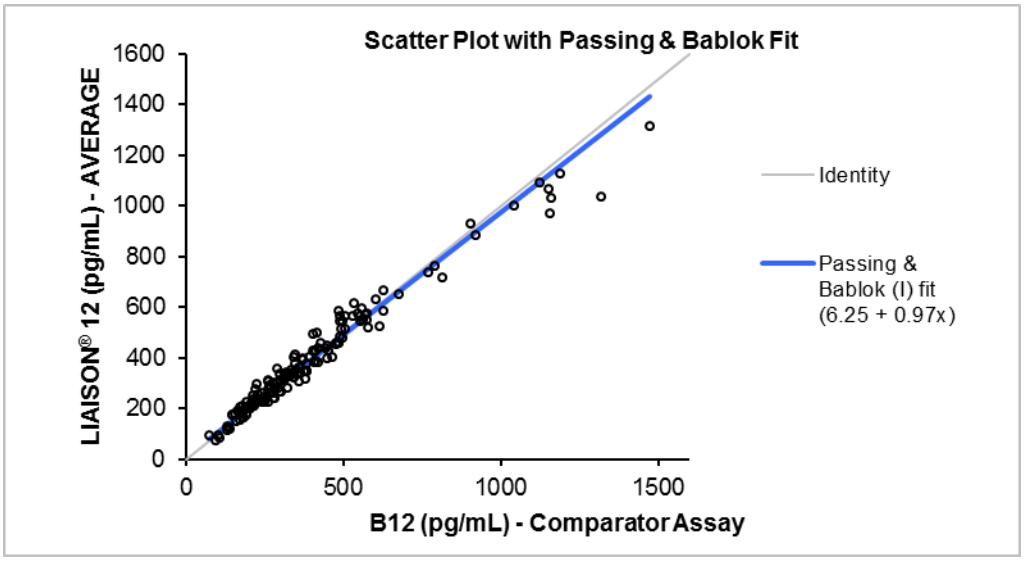
11. Standard/guidance Document Reference:

- CLSI Guideline EP5-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline.
- CLSI Guideline EP15-A3, User Verification of Precision and Estimation of Bias; Approved Guideline.
- CLSI Guideline EP EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline.
- CLSI Guideline EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline.
- CLSI Guideline EP 17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline.
- CLSI Guideline EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline.
- CLSI Guideline EP28-A3C, Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline.

12. Performance Characteristics:

<u>Method Comparison</u>
A total of 155 samples spanning the assay range, were tested by the LIAISON® Vitamin B12 and by another commercially available method following CLSI EP09-A3, and yielded the following Passing & Bablok regression analysis:
LIAISON® Vitamin B12 = 0.97 (Reference Method) + 6.25; R = 0.985.

Assay	N	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient
Vitamin B12	155	0.97 (0.94-1.00)	6.25 (-3.50-18.29)	0.985



Sample Matrix Comparison

Forty eight (48) matched patient sets of serum, SST serum and lithium heparin plasma samples were tested to determine if these sample types provide equivalent results on the LIAISON® Vitamin B12 assay.

Sample Equivalence SST serum compared to Serum

N = 48	Bias	95% CI
Constant	8.21	2.14 to 16.56
Proportional	0.97	0.94 to 0.99
R^2	0.996	N/A

Sample Equivalence Lithium Heparin compared to Serum

N = 48	Bias	95% CI
Constant	14.78	1.09 to 29.87
Proportional	1.10	1.05 to 1.15
R^2	0.988	N/A

Reference Range

It is recommended that each laboratory establish its own range of expected values for the population taken into consideration.

Observed Reference Ranges

Population (n=166)	Median	Observed Range 2.5th to 97.5th Percentile
United States	318.5 (pg/mL)	107.2 pg/mL – 653.3 pg/mL

Prospectively collected serum samples from 166 apparently healthy adults aged 21-59 who had been fasting for at least 8 hours were obtained. Apparently healthy status of the adults were determined by the Inclusion/Exclusion criteria listed below. Samples were collected, centrifuged and removed from cells within 2 hours. Once serum was removed from the cells, the sample was frozen immediately and stored at -70°C in order to maintain integrity. Samples were shipped frozen and kept frozen until tested.

To assess the expected reference range for the LIAISON® Vitamin B12 assay, a study was performed with serum samples from 166 apparently healthy adults aged 21 - 59 years of age from mixed ethnic backgrounds (30% Caucasian, 31% African Americans, 39% Hispanics) who were fasting for at least 8 hrs. Apparently healthy status was determined by subjects who had no history of anemias, Folic acid or B12 deficiency, IBD or suspected IBD, celiac disease, gastrointestinal malabsorption disorders, or eating disorders. No oral contraceptive use within 3 months, and no alcohol within 48 hrs of blood draw or excessive alcohol usage. No pregnant women or anyone taking B12 supplementation were included in the study population.
Based on the 95% Confidence Interval, the following values were established following CLSI guideline C28-A3.

Precision

One (1) lot of kit controls and six (6) serum samples spanning the range of the assay measuring range were tested twice per day in duplicate, over 20 operating days using one (1) reagent lot at DiaSorin Inc. The testing was performed according to CLSI EP5-A3.

Sample ID	Mean (pg/mL)	Intra-Run Within One Lot and Site		Total Within One Lot and Site	
		SD	%CV	SD	%CV
Sample #1 (KC)	642	21.56	3.4%	42.99	6.7%
Sample #2 (KC)	1262	48.79	3.9%	86.28	6.8%
Sample #3	240	10.16	4.2%	20.36	8.5%
Sample #4	417	21.85	5.2%	39.76	9.5%
Sample #5	646	24.83	3.8%	57.55	8.9%
Sample #6	773	29.36	3.8%	60.12	7.8%
Sample #7	1039	39.87	3.8%	103.87	10.0%
Sample #8	1093	47.96	4.4%	93.89	8.6%

Linearity

One (1) high sample of each specimen type (serum, SST serum, lithium heparin plasma) containing endogenous and/or spiked Vitamin B12 above the measuring range of the assay at 1500 pg/mL was diluted and tested by the LIAISON® Vitamin B12 assay following CLSI EP6-A. The results for each sample were analyzed by regression of observed concentration versus expected concentration.

The resulting equations for each sample type are:
Serum: Observed Vitamin B12 = 1.076x + 6.896; R = 0.998
SST Serum: Observed Vitamin B12 = 1.009x + 0.224; R = 0.999
Lithium Heparin plasma: Observed Vitamin B12 = 1.029x – 0.095; R = 0.996

Recovery Study

Five (5) high concentration (endogenous or spiked) serum samples and five (5) low concentration serum samples were analyzed neat. Recovery samples were then prepared by mixing defined ratios of the high and low samples and tested in replicates of five (5). The mean results of the five (5) replicates are provided in the table below.

	Defined Concentration	Expected (pg/mL)	Observed (pg/mL)	% Recovery
Sample				
High	1484	-		-
2 H:1 L		1129	1144	101%
1 H:1 L		946	940	99%
1 H:2 L		763	752	99%
Low neat	108	-		-
Sample				
High	1280	-		-
2 H:1 L		974	946	97%
1 H:1 L		816	773	95%
1 H:2 L		658	633	96%
Low neat	352	-		-
Sample				
High	1112	-		-
2 H:1 L		827	816	99%
1 H:1 L		680	683	100%
1 H:2 L		533	553	104%
Low neat	247	-		-
Sample				
High	1098	-		-
2 H:1 L		794	775	98%
1 H:1 L		637	641	101%
1 H:2 L		480	499	104%
Low neat	176	-		-
Sample				
High	1184	-		-
2 H:1 L		853	904	106%
1 H:1 L		682	707	104%
1 H:2 L		512	534	104%
Low neat	180	-		-
			Mean Recovery	**100%**

Analytical Specificity

Cross-Reactivity Studies

Controlled Studies of potentially cross-reacting substances were performed on the LIAISON® Vitamin B12 assay at the concentrations listed below. The testing was based on CLSI-EP7-A2.

Cross-Reactant	Spiked Concentration	% Cross Reactivity
Dicyanocobinamide	10,000 pg/mL	-0.19%

The cross reactivity study for the LIAISON® Vitamin B12 was designed to evaluate potential interference from other closely analytes with similar structure.

Interference Studies

Controlled studies of potentially interfering substances performed in serum at two (2) levels (200 and 800 pg/mL) demonstrated no interference in the LIAISON® Vitamin B12 at the highest concentration for each substance listed below.

Drug/Substance	Concentration Tested
Hemoglobin	300 mg/dL
Bilirubin (conjugated)	40 mg/dL
Bilirubin (unconjugated)	40 mg/dL
Triglycerides	3,000 mg/dL
Cholesterol	500 mg/dL
Albumin	12 g/dL
Human IgG	12 g/dL
HAMA	1387.5 ng/mL
Rheumatoid Factor	1035 IU/mL
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	65 mg/dL
Ibuprofen	50 mg/dL
Biotin	2 mg/mL

Limit of Blank, Limit of Detection and Limit of Quantitation

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined according to CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline June 2012- Second Edition.

The following limits were determined with the LIAISON® Vitamin B12 assay:
The limits are reported in the following table:

LoB	LoD	LoQ
≤ 38.7 pg/mL	51.2 pg/mL	55 pg/mL

Stability

Product	Storage Conditions		Claimed stability
Reagent Integral	Open vial	on system	42 days
Reagent Integral	Open vial	2-8°C	28 days
Calibration curve	N/A	N/A	21 days

Traceability

The LIAISON® Vitamin B12 Calibrators are traceable to an in-house standard preparation (pg/mL).

13. Conclusion:

The LIAISON® Vitamin B12 assay is substantially equivalent in principle and performance to the Beckman Coulter Access Vitamin B12 assay.