

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k141463

B. Purpose for Submission:

New device

C. Measurand:

1, 25-dihydroxyvitamin D

D. Type of Test:

Quantitative chemiluminescent immunoassay

E. Applicant:

DiaSorin Inc.

F. Proprietary and Established Names:

LIAISON XL 1,25 Dihydroxyvitamin D

LIAISON XL 1,25 Dihydroxyvitamin D Control Set

LIAISON XL 1,25 Dihydroxyvitamin D Calibration Verifiers

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1825, Vitamin D Test System

21 CFR 862.1660, Quality Control Material

2. Classification:

Class II

Class I, reserved

3. Product code:

MRG-Vitamin D Test System

JJX- Single (specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The LIAISON[®] XL 1,25 Dihydroxyvitamin D is an *in vitro* chemiluminescent immunoassay (CLIA) intended for the quantitative determination of 1,25 dihydroxyvitamin D (1,25(OH)₂ D) in serum, EDTA and Lithium Heparin plasma. Results of the 1,25 Dihydroxyvitamin D are used in the assessment of vitamin D sufficiency. Assay results should be used in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions in adult populations. The test is to be performed on the LIAISON[®] XL Analyzer.

The LIAISON[®] XL 1,25 Dihydroxyvitamin D Control Set is intended for use as assayed quality control samples to monitor the performance of the LIAISON[®] XL 1,25 Dihydroxyvitamin D assay.

The LIAISON[®] XL 1,25 Dihydroxyvitamin D Calibration Verifiers are assayed quality control materials intended for the quantitative verification of calibration and reportable range of the LIAISON[®] XL 1,25 Dihydroxyvitamin D assay.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use on the DiaSorin, LIAISON XL Analyzer

I. Device Description:

The LIAISON[®] XL 1,25 Dihydroxyvitamin D assay is an *in vitro* diagnostic device consisting of reagents provided in individual compartment within a plastic container called the Reagent Integral. All reagents in the Integral are supplied ready to use. The LIAISON[®] XL 1,25 Dihydroxyvitamin D assay Reagent Integral consists of the

following:

- Magnetic particles coated with mouse monoclonal antibody, phosphate buffers, BDS, Tween 20, 0.09% sodium azide.
- TCEP (TRIS (2-carboxyethyl) phosphine), Citrate buffer and 0.09% sodium azide.
- Conjugate: mouse monoclonal antibody conjugated to an isoluminol derivative in phosphate buffer, BSA, Tween 20, 0.01% gentamicin sulfate and 0.2% Proclin 300.
- Assay Buffer: Phosphate buffer with blockers, mouse IgG, BSA, Tween 20, 0.01% gentamicin sulfate, and 0.2% Proclin 300.

Additional components included in the reagent kit but not on the Reagent Integral:

- Calibrator 1: Two vials of lyophilized human serum and phosphate buffer spiked with low level 1,25 dihydroxyvitamin D, 0.2 % ProClin 300, 0.01% gentamicin sulfate.
- Calibrator 2: Two vials of lyophilized human serum and phosphate buffer spiked with high level 1,25 dihydroxyvitamin D, 0.2 % ProClin 300, 0.01% gentamicin sulfate.
- Binding Agent: Four vials of lyophilized recombinant fusion protein, TRIS buffer with mannitol and detergent.
- Binding Agent Reconstitution Buffer: Water with 0.09% sodium azide.

LIAISON[®] XL 1,25 Dihydroxyvitamin D Control (provided separately) consists of two levels of lyophilized controls, one low level and one high level of 1,25 dihydroxyvitamin D in human serum with phosphate buffer, 0.01% gentamicin sulfate and 0.2% Proclin 300. The range of concentrations of each control is reported on the certificate of analysis provided with each LIAISON[®] XL 1,25 Dihydroxyvitamin D Control set.

LIAISON[®] XL 1,25 Dihydroxyvitamin D Calibration Verifier set (provided separately) consists of 4 levels of lyophilized material containing human serum spiked with 1,25 dihydroxyvitamin D, and preservatives. The range of concentrations of each calibration verifier is reported on the certificate of analysis provided with each LIAISON[®] XL 1,25 Dihydroxyvitamin D Calibration Verifier set.

The DiaSorin XL 1,25 Dihydroxyvitamin D Diluent Kit (provided separately) consists of charcoal stripped human serum, phosphate buffers, 0.01% gentamicin sulphate and 0.2% Proclin 300. The diluent is used to dilute samples that read above the upper measuring range of the assay.

Each serum/plasma donor unit used in the preparation of these products has been tested by an U.S. FDA approved method and found to be non-reactive for the presence of the antibody to Human Immunodeficiency Virus 1 and 2, the Hepatitis B surface antigen, and the antibody to Hepatitis C.

J. Substantial Equivalence Information:

1. Predicate device name(s):
 DiaSorin 1,25 Dihydroxyvitamin D ¹²⁵ I RIA
 LIAISON N-TACT PTH Gen II Control Set
 LIAISON N-TACT PTH Gen II Calibration Verifiers
2. Predicate 510(k) number(s):
 k014030
 k132515
3. Comparison with predicate:

Assay:

Similarities		
Item	Predicate device DiaSorin 1,25- Dihydroxyvitamin D ¹²⁵ I RIA (k014030)	Candidate device LIAISON XL 1,25 Dihydroxyvitamin D
Intended Use	For in vitro quantitative determination of 1,25 dihydroxyvitamin D	Same
Analyte	1, 25-Dihydroxy Vitamin D	Same
Reagent Storage	2-8 °C	Same
Measuring Range	5-200 pg/mL	Same

Differences		
Item	Predicate device DiaSorin 1,25- Dihydroxyvitamin D ¹²⁵ I RIA (k014030)	Candidate device LIAISON XL 1,25 Dihydroxyvitamin D
Test Principle	Radioimmunoassay	Chemiluminescent immunoassay
Sample Matrix	Serum and EDTA plasma	Serum, SST serum, EDTA and Lithium Heparin plasma
Primary Extraction	Yes	No

Differences		
Item	Predicate device DiaSorin 1,25- Dihydroxyvitamin D ¹²⁵ I RIA (k014030)	Candidate device LIAISON XL 1,25 Dihydroxyvitamin D
Antibodies	Rabbit polyclonal	Mouse monoclonal
Calibration interval	Every run	14 days
Calibrators	5 levels	2 levels
Sample size	500 µL	75 µL
Reference range	25.1- 66.1 pg/mL	19.9-79.3 pg/mL

Controls:

Similarities and Differences		
Item	Predicate device LIAISON N-TACT PTH GEN II Control Set (k132515)	Candidate device LIAISON XL 1,25 Dihydroxyvitamin D Control Set
Intended Use	Intended for use as assayed quality control samples to monitor the accuracy and precision of the assay.	Same
Number of levels	2 levels: low and high	Same
Matrix	Lyophilized serum	Same
Storage temperature	2-8°C	Same
Analyte	PTH	1,25 dihydroxyvitamin D

Calibration Verifiers

Similarities and Differences		
Item	Predicate device LIAISON N-TACT PTH GEN II Calibration Verifiers (k132515)	Candidate device LIAISON XL 1,25 Dihydroxyvitamin D Calibration verifiers
Intended Use	Assayed quality control samples intended for the quantitative verification of calibration and reportable range of the assay.	Same

Similarities and Differences		
Item	Predicate device LIAISON N-TACT PTH GEN II Calibration Verifiers (k132515)	Candidate device LIAISON XL 1,25 Dihydroxyvitamin D Calibration verifiers
Number of levels	4	Same
Volume	2.0 mLs	Same
Packaging	Provided separately	Same
Storage temperature	2-8°C	Same
Analyte	PTH	1,25 dihydroxyvitamin D

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline

CLSI EP17-A2: Evaluation of Determination of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline

CLSI EP9-A3: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline

CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

L. Test Principle:

The LIAISON[®] XL 1,25 Dihydroxyvitamin D assay is a modified three-step sandwich assay that uses a recombinant fusion protein for capture of the 1,25 (OH)₂ D molecule and a murine monoclonal antibody which specifically recognizes the complex formed by the recombinant fusion protein with the 1,25(OH)₂ D molecule. Results are determined by a two-point calibration conversion of the master curve to a working curve. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of 1,25dihydroxyvitamin D present in the calibrators, controls or patient samples.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision study was performed in accordance with CLSI EP5 A2. A panel

comprised of six frozen serum samples (2 spiked and 4 native), 2 levels of LIAISON XL 1, 25 Dihydroxyvitamin D controls, and 4 levels of LIAISON XL 1, 25 Dihydroxyvitamin D Calibration Verifiers were tested using 2 lots of reagent on 2 analyzers, in 2 replicates per run, 2 runs per day for 20 days for a total of 160 replicate results per sample. The two lots of reagents demonstrated similar precision results and precision result of one representative lot is summarized in the table below. For the combined precision study, the between lot and across lots precision results are summarized in the table below.

LIAISON XL 1, 25 Dihydroxyvitamin D Combined Lot Precision

Sample	n	Between-Lot			Total	
		Mean (ng/mL)	SD	CV%	SD	CV%
Control1	160	30.9	0.84	2.7%	1.16	3.8%
Control 2	160	122.9	6.09	5.0%	4.36	3.6%
Serum 1	160	23.3	0.05	0.2%	1.53	6.6%
Serum 2	160	38.9	0.63	1.6%	2.20	5.7%
Serum 3	160	52.7	0.64	1.2%	2.65	5.0%
Serum 4	160	76.0	1.33	1.7%	3.13	4.1%
Serum 5	160	137.4	1.91	1.4%	6.55	4.8%
Serum 6	160	193.4	5.53	2.9%	11.34	5.9%
Cal Ver A	160	13.4	0.36	2.7%	0.76	5.7%
Cal Ver B	160	38.9	2.76	7.1%	1.36	3.5%
Cal Ver C	160	78.4	3.37	4.3%	2.82	3.6%
Cal Ver D	160	153.0	1.35	0.9%	5.61	3.7%

LIAISON XL 1, 25 Dihydroxyvitamin D Lot 1 Precision

Sample ID	n	mean (pg/mL)	Intra-Run		Run-to-Run		Day-to-Day		Total (Within-lot)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Control 1	80	30.3	0.75	2.5%	0.08	0.3%	1.06	3.5%	1.30	4.3%
Control 2	80	119	3.78	3.2%	0.00	0.0%	1.73	1.5%	4.15	3.5%
Serum 1	80	23.3	0.91	3.9%	0.93	4.0%	1.26	5.4%	1.81	7.8%
Serum 2	80	38.4	1.27	3.3%	0.83	2.2%	2.08	5.4%	2.58	6.7%
Serum 3	80	52.2	1.35	2.6%	1.27	2.4%	2.09	4.0%	2.79	5.3%
Serum 4	80	75.1	2.08	2.8%	1.40	1.9%	2.30	3.1%	3.40	4.5%
Serum 5	80	136	3.26	2.4%	3.72	2.7%	4.83	3.5%	6.91	5.1%
Serum 6	80	190	5.14	2.7%	6.07	3.2%	7.73	4.1%	11.1	5.9%
Cal Ver A	80	13.6	0.43	3.2%	0.27	2.0%	0.84	6.1%	0.98	7.2%
Cal Ver B	80	40.9	0.95	2.3%	0.71	1.7%	0.98	2.4%	1.54	3.8%
Cal Ver C	80	76.1	2.09	2.7%	1.79	2.3%	1.98	2.6%	3.38	4.4%
Cal Ver D	80	152	4.62	3.0%	2.08	1.4%	2.43	1.6%	5.61	3.7%

b. *Linearity/assay reportable range:*

Linearity was evaluated based on CLSI EP-6A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. One serum sample pool was spiked in order to obtain a concentration above the assay measuring range. The sample was then diluted with specimen diluent to yield 13 sample concentrations spanning the measuring range of the assay (5-200 pg/mL). Each dilution point was tested in singlicate on one LIAISON XL Analyzer. The 1-25 dihydroxyvitamin D values of the samples were compared to their expected concentrations to determine the linear regression equations for each sample type shown below:

Linear Regression	R ²	Sample range (pg/mL)
$y=0.97x - 2.67$	0.993	0.015 to 222.0

The linearity results support the claimed measuring range of this device (5- 200 pg/mL).

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability:

The LIAISON XL 1, 25 Dihydroxyvitamin D calibrators, LIAISON XL 1, 25 Dihydroxyvitamin D Calibration Verifiers, and LIAISON XL 1, 25 Dihydroxyvitamin D Controls are traceable to in-house standards prepared from 1 α , 25 dihydroxyvitamin D₃ certified primary reference material from a commercial source which is traceable to NIST. The process is comprised of the following steps:

The intermediate stock solution is prepared from the certified reference material. The stock solution is diluted to generate 10 master standards which are used to generate the master curve. The master standards are tested using multiple lots of reagents with a minimum of ten separate runs. The 2 point master calibrators are value assigned by testing 3 different assays against the master standards. The kit calibrators are prepared and value assigned against the master calibrators. The working calibration curve is obtained by assigning a curve to the two point calibrators based upon the master curve.

Value Assignment:

The LIAISON XL 1, 25 Dihydroxyvitamin D calibrators are value assigned using an internal procedure. A minimum of 5 vials of each level of calibrator are tested on a minimum of 3 LIAISON XL Analyzers, in a minimum of 5 assay runs with six replicates per vial resulting in a minimum of 30 individual replicate results per calibrator level for final value assignment. The LIAISON XL 1, 25 Dihydroxyvitamin D kit calibrators have the following 1,25 dihydroxyvitamin D target values:

Calibrator Level 1: 25 pg/mL
Calibrator Level 2: 100 pg/mL

The LIAISON XL 1,25 Dihydroxyvitamin D controls are value assigned by testing a minimum of 10 vials of each level of control on a minimum of 3 different LIAISON XL Analyzers, in a minimum of 5 assay runs with 4 replicates per vial resulting in a minimum of 40 individual replicate results per control level for final value assignment. The LIAISON XL 1,25 Dihydroxyvitamin D controls have the following 1,25 dihydroxyvitamin D target values and ranges:

Control Level 1: 35 pg/mL
Control Level 2: 120 pg/mL
Final control ranges are established based on ± 2 standard deviations.

The LIAISON XL 1,25 Dihydroxyvitamin D Calibration Verifiers are value assigned by testing a minimum of 10 vials of each level of calibration verifier on 2 different LIAISON XL 1,25 Dihydroxyvitamin D assay kit lots on a minimum of 3 LIAISON XL Analyzers, in a minimum of 5 assay runs with 4 replicates per vial, resulting in a minimum of 40 individual replicate results per level for final value assignment. The LIAISON XL 1, 25 Dihydroxyvitamin D Calibration Verifiers have the following 1,25 dihydroxyvitamin D target values and ranges:

Cal verifier A: 15 pg/mL
Cal verifier B: 40 pg/mL
Cal verifier C: 80 pg/mL
Cal verifier D: 150 pg/mL
Final calibration verifier ranges are established based on ± 2 standard deviations.

Stability:

Calibrator: An accelerated stability study determined the shelf life of the LIAISON XL 1,25 Dihydroxyvitamin D kit calibrators to be six months when stored at 2-8°C. A real-time study to determine shelf-life is ongoing. Stability studies demonstrated that the open-vial stability of the reconstituted LIAISON XL 1.25 Dihydroxyvitamin D calibrators is 6 hours at room temperature and on the analyzer; and 14 days at 2-8°C. The stability study protocol and the acceptance criteria have been found acceptable.

Calibration Verifiers: An accelerated stability study determined the shelf life of the LIAISON XL 1,25 Dihydroxyvitamin D Calibration Verifiers to be six months when stored at 2-8°C. A real-time study to determine shelf-life is ongoing. Open-vial stability of the reconstituted LIAISON XL 1.25 Dihydroxyvitamin D calibration verifiers is 6 hours at room temperature and on the analyzer; and 28 days at 2-8°C. The stability study protocol and acceptance criteria were reviewed and found to be acceptable.

Control: An accelerated stability study determined the shelf life of the LIAISON XL 1,25 Dihydroxyvitamin D Control Set to be six months when stored at 2-8°C. A real-time study to determine shelf-life is ongoing. Stability studies demonstrated that the open-vial stability of the reconstituted LIAISON XL 1.25 Dihydroxyvitamin D Control Set is 28 days when stored at 2-8°C. The stability study protocol and the acceptance criteria have been found acceptable.

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantification (LoQ) studies were performed according to CLSI EP-17A2.

To establish the Limit of Blank (LoB), five blank samples consisting of vitamin D stripped human serum were assayed in duplicate on two analyzers, with two reagent lots over six runs for a total of 60 test results per reagent lot. The Limit of Blank was determined by the following equation:

$$\text{LoB} = \mu (\text{Blank Dose}) + 1.653 * \sigma (\text{Blank Dose})$$

The LoB was determined to be 0.35 pg/mL.

To establish the Limit of Detection (LoD), four samples consisting of human serum diluted with vitamin D stripped human serum in the range of approximately 0 to 9 pg/mL were tested in duplicate on two analyzers with two reagent lots over six runs over three days for a total of 96 results. LoD was calculated for each of the 2 reagent lots using the following equation:

$$\text{LoD} = \mu (\text{Blank Dose}) + 1.653 * \sigma (\text{Blank Dose}) + 1.655 * \sigma_s (\text{Sample Dose})$$

The LoD was determined to be 0.70 pg/mL

The Limit of Quantification (LoQ) was determined by measuring 9 samples consisting of human serum diluted with vitamin D stripped human serum in a concentration range of 0 to 20 pg/mL in duplicate on two analyzers with two reagent lots over six runs and three days yielding 144 results. LoQ was defined as the lowest concentration at which the interassay precision is $\leq 20\%$. Of the 3 reagent lots tested, the highest LoQ was found to be 3.96 pg/mL. The sponsor defines the LoQ as 5.0 pg/mL.

Detection limits results

Limit of Blank	Limit of Detection	Limit of Quantitation
0.35 pg/mL	0.70 pg/mL	5.0 pg/mL

The claimed measuring range of the assay is 5.0-200 pg/mL.

e. Analytical specificity:

An interference study was performed based on CLSI EP7-A2 guideline to assess common or known substances that could interfere with the measurement of 1,25 dihydroxyvitamin D. The potential interferents listed below were spiked into human

serum samples with 1,25 dihydroxyvitamin D levels of 20 pg/mL and 60 pg/mL. The two sets of matched spiked and unspiked samples were tested in 9 to 12 replicates with one lot of reagent. Significant interference was defined as greater or equal to $\pm 10\%$ difference from the expected concentration. The interference study results are summarized in the following table:

Potential Interferent	Highest Tested Concentration at which no significant interference ($\leq \pm 10\%$) was observed
Bilirubin, conjugated	40 mg/dL
Bilirubin, unconjugated	40 mg/dL
Hemoglobin	300 mg/dL
Triglycerides	3000 mg/dL
Cholesterol	400 mg/dL
HAMA	3774 ng/mL
Rheumatoid factor	7310 IU/mL
Albumin	12 g/dL
Uric Acid	20 mg/dL
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	65 mg/dL
Salicylic Acid	60 mg/dL
Ibuprofen	50 mg/dL
Biotin	0.1 mg/dL
Ascorbic Acid	6 mg/dL
Metoprolol	1.2 mg/dL
Propranolol Hydrochloride	0.23 mg/dL
Hydrochlorothiazide	0.6 mg/dL
Furosemide	6 mg/dL
Valproic Acid	57.5 mg/dL
Spinolactone	0.6 μ g/mL
Nifedipine	43 μ g/dL
Verapamil	216 μ g/dL
Losartan Potassium	2.25 μ g/mL
Tetracycline	15.1 μ g/mL
Enalapril	42.4 μ g/dL
Doxycycline	34.6 μ g/mL
Lisinopril	32.7 μ g/dL

Cross reactivity study: Substances similar in chemical structure to 1,25 Dihydroxy vitamin D were assessed for cross reactivity. All cross reactants were tested with two serum samples with target 1, 25 Dihydroxyvitamin D concentrations of 20 pg/mL and 60 pg/mL. Two sets of matched spiked and unspiked samples were tested in triplicate

with one reagent lot. The equation used to calculate % cross reactivity is as follows:

$$\frac{\text{Mean conc. of spiked sample} - \text{Mean conc. of the original sample}}{\text{Spiked Concentration}} \times 100$$

The following table summarizes the specificity of the LIAISON XL 1,25 Dihydroxyvitamin D Assay:

Analyte	Cross-Reactivity
25-hydroxyvitamin D3	<0.1%
Cholecalciferol (D3)	<0.1%
Ergocalciferol (D2)	<0.1%
3-epi-25(OH)D3	<0.1%
24,25-(OH) ₂ D3	<0.1%
1,25-(OH) ₂ D3	103.4%
1,25-(OH) ₂ D2	104.8%
3-epi-25(OH)D2	<0.1%
25,26-(OH)D3	<0.1%
Sensipar	<0.1%
Zemplar	113%

The sponsor states the following limitation in the labeling:

“The LIAISON XL 1,25 Dihydroxyvitamin D has been shown to cross-react with Zemplar (paricalcitol) an active form of Vitamin D.”

Sponsor has the following limitation stated in the labeling: The LIAISON® XL 1,25 Dihydroxyvitamin D has been shown to cross-react with Zemplar (paricalcitol) an active form of Vitamin D.

Hook Effect Study: High Dose Hook Effect testing was performed with 1 kit lot of LIAISON XL 1,25 Dihydroxyvitamin D. A zero sample was spiked with 1,25 dihydroxyvitamin D to equal several concentrations above the assay measuring range of 200 pg/mL. The spiked samples were measured in triplicate. The study demonstrated that no high dose hook was observed for 1,25 Dihydroxyvitamin D concentrations up to 5000 pg/mL.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The sponsor performed a method comparison study on 141 serum samples following CLSI EP09-A3. Mean results for the 1,25-Dihydroxyvitamin D ¹²⁵I RIA assay and singlicate results for the LIAISON® XL 1,25 Dihydroxyvitamin D were plotted using a

Deming regression analysis on the results across the measuring range (5 – 200 pg/mL) for both assays. The sample results ranged from 5.45 pg/mL to 184.3 pg/mL. There were 8 diluted samples and 15 spiked samples used in order to span the measuring range. The results are summarized in the table below.

1,25 Dihydroxyvitamin D: DiaSorin LIAISON compared to DiaSorin ¹²⁵I RIA

N	Slope	95% CI	Intercept	95% CI	R
141	0.973	0.855 to 1.092	-1.614	-7.475 to 4.248	0.918

b. *Matrix comparison:*

Fifty-two (52) matched human sample sets SST serum, EDTA plasma, and Lithium Heparin plasma samples with values that spanned the range of the assay of serum were tested to determine if these sample types provide equivalent results on the LIAISON[®] XL 1,25 Dihydroxyvitamin D assay. The following results were obtained:

Serum vs	Slope	95% CI	Intercept	95% CI	R ²
SST Serum	1.001	0.99 to 1.03	-0.285	-1.08 to 0.83	0.9908
EDTA Plasma	1.010	0.98 to 1.04	0.321	-1.15 to 1.64	0.9975
Li Heparin Plasma	1.000	0.97 to 1.04	0.1000	-1.24 to 1.31	0.9957

The resulting data support the package insert claim that human serum, SST serum, Li-Heparin plasma, and EDTA plasma, are acceptable sample types for use with the LIAISON[®] XL 1,25 Dihydroxyvitamin D assay.

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:

To determine the expected reference range for the LIAISON[®] XL 1,25 Dihydroxyvitamin D assay, a study was performed with serum samples from 123 apparently healthy adults aged 21 -75 years of age from mixed ethnic backgrounds (48% dark skinned and 52% light skinned). Samples were collected in the winter (48.8%) and summer (51.2%) from subjects with normal Total Calcium, TSH, and PTH values from the northern, central and southern regions of the U.S. Based on the 95% Reference Interval, the following values were established following CLSI guideline C28-A3.

LIAISON[®] XL 1,25 Dihydroxyvitamin D Observed Reference Range

US Subjects	Median	Observed Range 2.5 th to 97.5 th percentile
123	47.8 pg/mL	19.9 to 79.3 pg/mL

The sponsor states in the labeling that it is recommended that each laboratory establish its own range of expected values.

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.