DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

March 16, 2017

SIEMENS HEALTHCARE DIAGNOSTICS
KATHLEEN DRAY-LYONS
REGULATORY AND CLINICAL AFFAIRS SPECIALIST
500 GBC DRIVE
P.O. BOX 6101
NEWARK DE 19714

Re: K162298
Trade/Device Name: LOCI Vitamin D Total Assay
LOCI VITD CAL
Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D test system
Regulatory Class: II
Product Code: MRG, JIT
Dated: February 3, 2017
Received: February 6, 2017

Dear Kathleen Dray-Lyons:

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 Parts 801 and 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.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kellie B. Kelm -S

for Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology 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)*
K162298

Device Name

LOCI Vitamin D Total Assay

Indications for Use *(Describe)*

The LOCI Vitamin D Total assay is an in vitro diagnostic test for the quantitative measurement of total 25(OH)vitamin D in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of vitamin D are used in the assessment of vitamin D sufficiency.

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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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)*
K162298

Device Name

LOCI VITD CAL

Indications for Use *(Describe)*

The LOCI VITD CAL is an in vitro diagnostic product for the calibration of the Vitamin D (VITD) Total assay on the Dimension® EXL™ integrated chemistry system with LOCI® module.

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

The assigned 510(k) number is: K162298

1. Manufacturer's Name, Address, Telephone, and Contact Person, Date of Preparation

Applicant:
Siemens Healthcare Diagnostics Inc.
500 GBC Drive
M/S 514
P.O. Box 6101
Newark, DE 19714

Contact Information:
Siemens Healthcare Diagnostics Inc.
500 GBC Drive
P.O. Box 6101
Newark, DE 19714

Attn: Kathleen Dray-Lyons
Tel: 781-826-4551
Email: kathleen.a.dray-lyons@siemens.com

Date of Preparation: March 15, 2017

2. Device Names:

- LOCI Vitamin D Total Assay
- LOCI VITD CAL

Classification:

- 21 CFR §862.1825; Vitamin D test system, Class II
- 21 CFR §862.1150; Calibrator Secondary, Class II

Product Code:

- MRG
- JIT

Panel:

- Clinical Chemistry
- Clinical Chemistry

3. Identification of the Predicate Devices:

ADVIA Centaur Vitamin D Total (VitD) Assay - K110586

ADVIA Centaur Vitamin D Total (VitD) Calibrators - K110586

4. Device Description:

LOCI Vitamin D Total assay:
The LOCI Vitamin D Total assay is a homogeneous competitive chemiluminescent immunoassay based on LOCI technology. The assay measures the total 25(OH)vitamin D concentration [comprising both 25(OH)vitamin D_2 and 25(OH)vitamin D_3] in both serum and plasma. LOCI Vitamin D Total reagents include a releasing reagent, biotinylated monoclonal antibody, and two synthetic bead reagents. Patient sample is incubated with the releasing reagent to release 25(OH)vitamin D molecules from the vitamin D-binding proteins. The reaction mixture is then incubated with biotinylated antibody to form a 25(OH)vitamin D/biotinylated antibody complex.

Chemibeads containing 25(OH)vitamin D_3 analog and chemiluminescent dye are added to remove the excess free biotinylated antibody. Streptavidin-coated Sensibeads containing a photosensitive dye are added to bind the biotinylated antibody. Aggregates of the Chemibead analog/biotinylated antibody/streptavidin Sensibeads are formed as a result. Illumination of the reaction mixture by light at 680 nm generates singlet oxygen from the Sensibeads, which diffuses into the Chemibeads and triggers a chemiluminescent reaction. The resulting chemiluminescent signal is measured at 612 nm and is inversely proportional to the concentration of total 25(OH)vitamin D in the sample.

LOCI VITD CAL:
The LOCI VITD CAL is a five level, liquid, single analyte, frozen product, which is stored at -15 ºC to -25 ºC. The calibrator matrix consists of processed human serum with preservatives and stabilizers. Level 1 is a zero level, while levels 2 3, 4, and 5 contain approximately 12, 30, 75, and 165 ng/mL respectively. Each lot of calibrators will have lot specific assigned values assigned from master pool levels that are traceable by method correlation to Ghent University's ID-LC/MS/MS 25(OH)vitamin D Reference Method Procedure (RMP). The ID-LC/MS/MS RMP is traceable to the NIST SRM 2972.

5. Device Intended Use:

LOCI Vitamin D Total ssay:
The LOCI Vitamin D Total assay is an *in vitro* diagnostic test for the quantitative measurement of total 25(OH)vitamin D in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of vitamin D are used in the assessment of vitamin D sufficiency.

LOCI VITD CAL:
The LOCI VITD CAL is an *in vitro* diagnostic product for the calibration of the total Vitamin D (VITD) assay on the Dimension® EXL™ integrated chemistry system with LOCI® module.

6. Medical device to which equivalence is claimed:

Substantial Equivalence:
The LOCI Vitamin D Total assay is substantially equivalent to the ADVIA Centaur Vitamin D Total (VitD) assay cleared under K110586. The LOCI VITD CAL is substantially equivalent to the ADVIA Centaur Vitamin DTotal (VitD) Calibrators (K110586).

Comparison to the predicate:

LOCI Vitamin D Total Assay:
A comparison of the similarities and differences between the currently marketed ADVIA Centaur Vitamin D Assay (predicate) versus the proposed LOCI VITD Total assay is provided in the table below.

Similarities and Differences
LOCI Vitamin D Total Assay versus
ADVIA Centaur Vitamin D Total Assay

Attributes	Proposed LOCI VITD Total Assay	Predicate ADVIA Centaur Vitamin D Total Assay (K110586)
Intended Use	The LOCI Vitamin D Total assay is an *in vitro* diagnostic test for the quantitative measurement of total 25-hydroxyvitamin D (25-OH-D) in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of vitamin D are used in the assessment of vitamin D sufficiency.	The ADVIA Centaur® Vitamin D Total (VitD) assay is for *in vitro* diagnostic use in the quantitative determination of total 25(OH)vitamin D in human serum and plasma (EDTA, lithium-heparin, sodium heparin) using the ADVIA Centaur systems. The ADVIA Centaur VitD assay is intended as an aid in the determination of vitamin D sufficiency.
Assay format	Competitive Immunoassay	Same
Detection	Direct Chemiluminescent Technology	Same
Antibody	Sheep Monoclonal	Mouse Monoclonal
Sample size	8 µL	20 µL
Analyzers	Dimension EXL with LM, Dimension EXL with LM-PMT and Dimension EXL 200 systems	ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems
Sample type	Serum, EDTA plasma, and litium heparin plasma	Serum Plasma (EDTA, lithium heparin and sodium heparin)
Measuring Range	5.0 - 150.0 ng/mL	4.2 to 150 ng/mL

LOCI VITD CAL:
A comparison of the similarities and differences between the currently marketed ADVIA Centaur Vit D Calibrator (predicate) versus the proposed LOCI VITD CAL is provided in the table below.

Similarities and Differences
LOCI VITD CAL versus
ADVIA Centaur VitD Calibrators

Feature	Proposed LOCI VITD CAL	Predicate ADVIA Centaur VitD Calibrators (K110586)
Intended Use	The LOCI VITD CAL is an *in vitro* diagnostic product for the calibration of the total Vitamin D (VITD) assay on the Dimension® EXL™ integrated chemistry system with LOCI® module.	The ADVIA Centaur Vitamin D Total (VitD) Calibrators is for *in vitro* diagnostic use in calibrating ADVIA Centaur® systems Vitamin D Total (VitD) assay.
Calibrator base	Human serum	Human plasma
Calibrator form	Liquid	Lyophilized
Traceable to:	Standardized using internal standards traceable by method correlation to Ghent University's ID-LC-MS/MS 25 OH vitamin D Reference Method Procedure (RMP) which is traceable to NIST SRM 2972.	Internal standards which are traceable to the LC-MS/MS 25(OH)vitamin D.
Number of levels	Five	Two
Packaging Content	2 vials: Level 1 (1.5 mL), Level 2 (2.0 mL), Level 3, 4, 5, (1.5 mL) per vial	2 vials Low - 2 mL per vial 2 vials High -2 mL per vial
Storage	-25 to -15°C	2° to 8°C

7. Performance Characteristics

Method Comparison versus the ID-LC-MS/MS:
LOCI Vitamin D Total assay on the Dimension EXL™ with LM system was compared to vitamin D values obtained from the University of Ghent using the ID-LC-MS/MS 25(OH) vitamin D Reference Measurement Procedure (RMP), which is traceable to the NIST Standard SRM2972. A split sample method comparison between the LOCI Vitamin D Total assay versus ID-LC-MS/MS was performed with 163 remnant de-identified human serum samples across the assay range (5.0 - 150.0 ng/mL). Analysis of the results using standard Passing Bablok regression yielded the following:

Passing Bablok regression:

Method	N	ID-LC-MS/MS Sample Range Analyzed (ng/mL)	Slope (95% CI)	Intercept ng/mL (95% CI)	r – Value*
LOCI Vitamin D Total versus ID-LC-MS/MS	163	5.2 – 126.1	1.06 (1.01 to 1.12)	0.44 (-0.54 to 1.42)	0.977

***** Correlation coefficient (r) was obtained from ordinary least squares regression.

Repeatability and Within Lab Precision:

Testing was performed over twenty (20) days, two (2) runs per day, a single test from two (2) independent cups were analyzed for each test material using one lot of LOCI Vitamin D Total assay on the Dimension® EXL™ with LM analyzer . Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of CLSI EP05-A3. Typical precision observed is summarized below.

Repeatability and Within-Lab Results

Material	Mean	Repeatability		Within-Lab Precision	
	ng/mL	SD	%CV	SD	%CV
Tri-Level Vitamin D Plus					
QC (Low)	18.9	0.58	3.1	1.01	5.4
QC (Level 1)	38.7	1.02	2.6	2.02	5.2
QC (Level 2)	89.6	1.72	1.9	3.67	4.1
Serum 1	8.2	0.46	5.6	0.71	8.7
Serum 2	29.4	0.76	2.6	1.46	5.0
Serum 3	76.5	1.63	2.1	3.11	4.1
Plasma 2	25.2	0.44	1.8	0.78	3.1

Linearity

Linearity across the assay range, 5.0 – 150.0 ng/mL [12.5 – 375.0 nmol/L] was confirmed by testing a sample with a high concentration of vitamin D and serially diluting with a sample of low concentration vitamin D. Each dilution was assayed in replicates of n=5. Linear regression of observed (y) vs. expected values(x) yielded a slope of 1.02, an intercept of 1.4 ng/mL and a correlation coefficient (r) of 0.998. Percent bias between observed and predicted values was within the allowable 10% deviation from the linear fit.

Recovery

Known amounts of 25(OH)vitamin D_2 (30 ng/mL [75.0 nmol/L]) and 25(OH)vitamin-D_3 (30 ng/mL [75.0 nmol/L]) were added to separate serum samples containing vitamin D at 28.3 ng/dL [70.8 nmol/L] and 54.7 ng/mL [136.8 nmol/L].

The calculated percent recoveries are listed below:

Vitamin D at 28.3 ng/mL [70.8 nmol/L]		
Added	**Amount added ng/mL [nmol/L]**	**% Recovery**
25(OH)vitamin D_2	30.0 [75.0]	95
25(OH)vitamin D_3	30.0 [75.0]	89
Vitamin D at 54.7 ng/mL [136.8 nmol/L]		
Added	**Amount added ng/mL [nmol/L]**	**% Recovery**
25(OH)vitamin D_2	30.0 [75.0]	94
25(OH)vitamin D_3	30.0 [75.0]	90

Detection Capability

The Limit of Detection (LoD) for the VITD assay is 1.3 ng/mL [3.3 nmol/L], determined consistent with CLSI guideline EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures and with proportions of false positives (α) less than 5% and false negatives (β) less than 5%; based on 120 determinations, with 60 blank and 60 low level replicates. The Limit of Blank (LoB) is 0.8 ng/mL [2.0 nmol/L].

Limit of Quantitation

The limit of quantitation (LoQ) was determined consistent with the CLSI Guideline EP17-A2. TheLoQ for the VITD assay is 5.0 ng/mL [12.5 nmol/L] at a total precision of ≤20% CV. LoQ is defined as the lowest concentration of 25(OH)vitamin D that can be detected at total precision CV of ≤20%.

Interference Testing

Interference testing was performed according to CLSI EP07-A2: Interference Testing in Clinical Chemistry to determine the effect of various endogenous and exogenous substances on the LOCI Vitamin D Total assay. For all interferents, the percent bias was determined by testing a control sample without the interferent and comparing it to the value obtained from a test sample to which the potential interferent had been added. Interferents were tested at three levels of vitamin D concentrations: 13.9-16.9 ng/mL, 28.4-32.0 ng/mL and 70.2-77.3 ng/mL. For each spiked sample, the % recovery was determined. Using 10% as the allowable clinically acceptable threshold for interference, the data below summarizes the concentration of interfering substance tested where there is no interference and the concentration of the interfering substance where interference is first observed.

Hemolysis, Icterus, Lipemia (HIL) Interference

Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference.

Substance Tested	Substance Concentration	Vitamin D ng/mL	Bias* %
Hemoglobin (hemolysate)	Hemoglobin (monomer) 250 mg/dL [0.155 mmol/L]	15.0	5
		31.7	9
		75.1	8
	500 mg/dL [0.31 mmol/L]	15.0	11
		31.7	19
		75.1	13
Bilirubin (unconjugated)	40 mg/dL [684.5 µmol/L]	13.5	7
		27.3	7
		66.7	8
	80 mg/dL [1368 µmol/L]	13.5	13
		27.3	12
		66.7	6
Bilirubin (conjugated)	20 mg/dL [342 µmol/L]	14.9	7
		31.7	4
		75.3	3
	40 mg/dL [684 µmol/L]	14.9	17
		31.7	12
		75.3	11
Lipemia (Intralipid)	300 mg/dL [3 g/L]	14.9	-5
		32.3	-6
		75.9	-5
	500 mg/dL [5 g/L]	14.9	-10
		32.3	-11
		75.9	-8

*** Analyte results should not be corrected based on this bias.**

Non-Interfering Substances

The following substances were evaluated for interference using CLSI EP07-A2[18] and found not to interfere with the VITD assay when present in serum at the concentrations indicated. Inaccuracies (biases) due to these substances do not exceed 10% at vitamin D concentrations of 13.9 – 16.9 ng/mL, 28.4 – 32.0 ng/mL and 70.2 – 77.3 ng/mL.

Substance	Test Concentration
Acetaminophen	20 mg/dL
Ascorbic Acid	3 mg/dL
Biotin	200 ng/mL
Cholesterol	300 mg/dL

Dextran 40	6000 mg/dL
Hemoglobin	250 mg/dL
Heparin	3 U/mL
Ibuprofen	30 mg/dL
Lipemia (Intralipid)	300 mg/dL
Protein (Albumin)	5 g/dL
Protein (Total)	15.9 g/dL
Rheumatoid Factor	500 IU/mL
Salicylic Acid	65 mg/dL
Triglycerides	686 mg/dL
Uric Acid	20 mg/dL

Human Anti-Mouse Antibodies (HAMA): Human Anti-Mouse Antibodies (HAMA): 20 samples containing vitamin D at 5.0 ng/mL [12.5 nmol/L] to 87.5 ng/mL [218.7 nmol/L] with varying concentrations of HAMA, from 8 ng/mL to 161,000 ng/mL were tested for HAMA interference. Mean (n=5) percent bias of 2.8% was observed on a sample with a vitamin D concentration of 28.3 ng/mL [70.7 nmol/L] containing 161,000 ng/mL of HAMA. Maximum mean (n=5) percent bias of 10% was observed on a sample with a vitamin D concentration of 5.0 ng/mL [12.5 nmol/L] containing 106 ng/mL of HAMA.

Interfering Substances:

Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. *Bias exceeding 10% is considered interference.

Total Protein at 19 g/dL causes a decrease in the vitamin D concentration by 6% at 14.3 ng/mL, 11% at 30.9 ng/mL and 12% at 77.3 ng/mL.

Hemoglobin at 500 mg/dL causes an increase in the vitamin D concentration by 11% at 15 ng/mL, 19% at 31.7 ng/mL and 13% at 75.1 ng/mL.

Unconjugated bilirubin at 80 mg/dL causes an increase in the vitamin D concentration by 13% at 13.5 ng/mL, 12% at 27.3 ng/mL and 6% at 66.7 ng/mL.

Conjugated bilirubin at 40 mg/dL causes an increase in vitamin D concentration by 17% at 14.9 ng/mL, 12% at 31.7 ng/mL and 11% at 75.3 ng/mL.

Lipemia (Intralipid) at 500 mg/dL causes a decrease in vitamin D concentration by 10% at 14.9 ng/mL, 11% at 32.3 ng/mL and 8% at 75.9 ng/mL.

Cholesterol at 350 mg/dL causes a decrease in vitamin D concentration by 10% at 25.2 ng/mL [63.0 nmol/L] and 12% at 64.0 mg/dL [160.0 nmol/L].

*Analyte results should not be corrected based on observed bias. See additional HIL results under Specificity section.

Serum Plasma Equivalency

Matched lithium heparin plasma, K2 EDTA plasma, serum separator tube (SST) and red top serum samples were collected from 70 patients. Out of the 70 matched serum/plasma sets, 8 were freshly drawn native samples, 62 were frozen and of these eight sets were split and spiked with 25-hydroxyvitamin D3 to cover the upper range of the assay. The results were analyzed by standard Passing Bablok regression and Least Squares (Standard Linear Regression). The correlation coefficient (r) was obtained by linear regression. A summary of the results is presented below.

Sample Comparison	Slope	Intercept ng/mL [nmol/L]	Correlation Coefficient	n	Min ng/mL [nmol/L]	Max ng/mL [nmol/L]
Lithium heparin plasma vs serum (red top)	0.99	0.1 [0.3]	0.992	70	11.5 [28.7]	146.4 [366.0]
EDTA plasma vs serum (red top)	0.98	1.4 [3.4]	0.997	70	11.6 [29.0]	142.5 [356.2]
Serum SST vs serum (red top)	0.99	0.5 [1.2]	0.997	70	11.4 [28.5]	148.6 [371.5]

Cross Reactivity

Cross reactivity testing was performed to determine the effect of potential cross-reactants on the LOCI Vitamin D Total assay using CLSI EP07-A2. Percent cross-reactivity was calculated as follows:

$$\% \text{ Cross-reactivity} = \frac{[\text{measured vitamin D}] - [\text{control vitamin D}]}{[\text{cross-reactant}]} \times 100$$

The following substances were evaluated for cross-reactivity with the VITD assay when present in serum at the vitamin D concentrations listed in the following table.

Cross-reactivity

Cross- Reactant	Cross-Reactant Concentration (ng/mL)	% Cross-reactivity @ Vitamin D Concentration	% Cross-reactivity @ Vitamin D Concentration
Vitamin D_2 (ergocalciferol)	1000	0.1 @ 27.5 ng/mL [68.8 nmol/L]	-0.1 @ 52.0 ng/mL [130.0 nmol/L]
Vitamin D_3 (cholecalciferol)	1000	-0.1 @ 27.5 ng/mL [68.8 nmol/L]	0.1 @ 52.0 ng/mL [130.0 nmol/L]
* 1,25$(OH)_2$vitamin D_2	0.5	151.9 @ 27.5 ng/mL [68.8 nmol/L]	1.3 @ 52.0 ng/mL [130.0 nmol/L]
* 1,25$(OH)_2$vitamin D_3	0.5	1.7 @ 27.5 ng/mL [68.8 nmol/L]	-224.5 @ 52.0 ng/mL [130.0 nmol/L]
3-epi-25(OH)vitamin D_3	100	3.9 @ 27.5 ng/mL [68.8 nmol/L]	2.5 @ 52.0 ng/mL [130.0 nmol/L]
Paricalcitol	24	93.8 @ 28.8 ng/mL [72.0 nmol/L]	70.8 @ 54.7 ng/mL [136.8 nmol/L]

1αOH Vitamin D_3 (alfacalcidol)	3000	0.1 @ 26.5 ng/mL [66.3 nmol/L]	0.0 @ 51.6 ng/mL [129.0 nmol/L]
24, 25$(OH)_2$vitamin D_3	60	2.5 @ 26.5 ng/mL [66.3 nmol/L]	1.2 @ 51.6 ng/mL [129.0 nmol/L]
25(OH)vitamin D_2	30	95.1 @ 28.3 ng/mL [70.8 nmol/L]	94.1 @ 54.7 ng/mL [136.8 nmol/L]
25(OH)vitamin D_3	30	88.6 @ 28.3 ng/mL [70.8 nmol/L]	90.1 @ 54.7 ng/mL [136.8 nmol/L]

*1,25$(OH)_2$ vitamin D_2 and 1,25$(OH)_2$ vitamin D_3 were tested at supra-physiological concentrations.

Expected Values:

30.0 – 100.0 ng/mL [75.0 – 250.0 nmol/L]
Vitamin D levels may vary according to factors such as geography, season, or the patient's health, diet, age, ethnic origin, use of vitamin D supplementation or environment. To assure proper representation of specific populations, each laboratory should establish its own reference intervals.

Health Based Reference Values:
Health-based reference values based on Clinical Guidelines Subcommittee of the Endocrine Society Task Force are recommended to replace population based reference values. A review of the available literature suggests that the recommendations for 25(OH)vitamin D levels are summarized in the table below. Consult the listed references for discussion of vitamin D toxicity levels.

Vitamin D Status	**Range, Adult 25(OH)vitamin D ng/mL[nmol/L]**
Deficient	< 20 [<50]
Insufficient	20 – < 30 [50 – <75]
Sufficient	30 – 100 [75 – 250]

Observed Values in an Apparently Healthy Population:
Data using the LOCI Vitamin D Total assay were obtained on serum samples collected from 252 adults: 246 adults not taking supplements containing vitamin D, and 6 adults taking supplements containing vitamin D. To represent a broad spectrum of UV light exposure in intended use population, the blood samples tested were collected during different seasons and from subjects residing in diverse U.S. geographical locations. Samples with abnormal values for PTH, calcium, magnesium, phosphorus, and TSH were excluded from this study.

Based on the 95% confidence interval, the following values were established following CLSI guideline EP28-A3c.
The following 25(OH)vitamin D values were obtained:

Median	28.3 ng/mL [70.8 nmol/L]
Observed 95% interval (2.5^{th} and 97.5^{th} percentiles)	13.9 – 61.0 ng/mL [34.8 – 152.5 nmol/L]

Calibrator Traceability:
The LOCI Vitamin D Total assay is standardized using internal standards which are traceable to the ID-LC/MS/MS 25(OH)vitamin D Reference Method Procedure (RMP). The ID-LC/MS/MS is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 2972.

8. Conclusion:

The LOCI Vitamin D Total assay and LOCI VITD CAL are substantially equivalent to the predicate devices based on intended use, principle and the performance characteristics above.