May 29, 2020

Siemens Healthcare Diagnostics Inc.
Paul DaSilva
Regulatory Affairs Specialist
511 Benedict Avenue
Tarrytown, NY 10591

Re: K200509
Trade/Device Name: ADVIA Centaur® Vitamin D Total (VitD)
Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D Test System
Regulatory Class: Class II
Product Code: MRG
Dated: February 28, 2020
Received: March 2, 2020

Dear Paul DaSilva:

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,

Marianela Perez-Torres, Ph.D.
Acting Deputy 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)*
K200509

Device Name
ADVIA Centaur® Vitamin D Total (VitD)

Indications for Use *(Describe)*

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.

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

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Device Act of 1990.

The assigned 510(k) Number is: K200509

1. Date Prepared

May 29, 2020

2. Applicant Information

Contact: Paul DaSilva
Regulatory Affairs Specialist

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3. Regulatory Information

Trade Name	ADVIA Centaur® Vitamin D Total (VitD)
Classification Name	Vitamin D test system
FDA Classification	Class II
Review Panel	Clinical Chemistry
Product Code	MRG
Regulation Number	862.1825

4. Predicate Device Information

Predicate Device Name: ADVIA Centaur® Vitamin D Total (VitD) assay

510(k) Number: K133156

5. Intended Use / Indications for Use

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® system. The ADVIA Centaur® VitD assay is intended as an aid in the determination of vitamin D sufficiency.

510(k) Summary

6. Device Description

The ADVIA Centaur® Vitamin D reagent kit comes in two configurations (100 or 500 test kit) and each kit contains the following:

- ReadyPack® primary reagent pack containing ADVIA Centaur VitD Lite Reagent, Solid Phase Reagent, and Ancillary Well Reagent
- ReadyPack ancillary pack containing ADVIA Centaur VitD Ancillary Reagent
- ADVIA Centaur VitD Low Calibrator
- ADVIA Centaur VitD High Calibrator
- ADVIA Centaur systems VitD Master Curve card
- ADVIA Centaur systems VitD Calibrator Assigned Value Card

The VitD Reagents consists of the following:

Lite Reagent 5.0 mL/reagent pack:
The reagent contains anti-VitD (monoclonal mouse) antibody labeled with acridinium ester (~0.8 µg/mL) in buffer with bovine serum albumin, mouse IgG, and sodium azide (< 0.1%)

Solid Phase Reagent 10.0 mL/reagent pack:
The Solid Phase Reagent contains anti-fluorescein (monoclonal mouse)-coated paramagnetic particles (PMP) (~0.60 mg/mL) in buffer with bovine serum albumin, surfactant, and sodium azide (< 0.1%)

Ancillary Well Reagent 5.0 mL/reagent pack:
The Ancillary Well Reagent contains vitamin D-analog conjugated to fluorescein (~0.2 µg/mL) and 1-anilinonaphthalene-8-sulfonic acid in buffer with bovine serum albumin and sodium azide (< 0.1%)

Ancillary Reagent Pack 25.0 mL/reagent pack:
The Ancillary Reagent Pack contains releasing agent in buffered saline with sodium azide (<0.1%) and stabilizers

The VitD Calibrators 2 x 2.0 mL/vial:
After reconstitution, low or high levels of 25(OH)vitamin D in buffered, defibrinated human plasma with bovine serum albumin, cholesterol, preservatives, and sodium azide (<0.1%).

Material Required but Not Provided

- ADVIA Centaur Wash 1

Optional Materials

- ADVIA Centaur VitD Quality Control Material
- ADVIA Centaur VitD Diluent
- ADVIA Centaur VitD Master Curve Material (MCM)

7. Comparison of Technological Characteristics with the Predicate Device

Similarities:

Item	Modified ADVIA Centaur® Vitamin D Total (VitD) assay (Candidate Device)	ADVIA Centaur® Vitamin D Total (VitD) assay (Predicate Device – K133156)
Intended Use	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.	same
Measurement	Quantitative	same
Assay Principle	Competitive immunoassay	Same
Methodology	Chemiluminescence	Same
Detection Antibody	Monoclonal mouse antibody labeled with acridinium ester (AE)	Same
Capture Antibody	Anti-fluorescein monoclonal mouse antibody covalently bound to paramagnetic particles (PMP)	Same
Assay Range	4.2 – 150 ng/mL	Same
Expected Values (adult)	7.4–44.0 ng/dL	Same
Expected Values (pediatric)	11.4 – 45.8 ng/mL	Same
Sample Volume	20 µL	Same
Traceability/ Standardization	ID-LC-MS/MS 25(OH)vitamin D (RMP)	Same
Calibration	2-point	Same
Calibrators	ADVIA Centaur VitD Calibrators	Same
Number of calibrators	Two (2) levels	Same
Use of Controls	Yes (recommended)	Same
Number of controls	Two levels	Same

Differences:

Item	Modified ADVIA Centaur® Vitamin D Total (VitD) assay (Candidate Device)	ADVIA Centaur® Vitamin D Total (VitD) assay (Predicate Device – K133156)
Ancillary Reagent Pack	Buffering agent (high molarity) and enhanced releasing agent (low molecular weight)	Buffering agent (low molarity) and enhanced releasing agent (high molecular weight)

8. Performance Characteristics: Modified ADVIA Centaur Vitamin D

8.1 Detection Limit

The limit of blank (LoB), limit of detection (LoD), and the limit of quantitation (LoQ) were determined as described in CLSI Document EP17-A2.[31] The ADVIA Centaur VitD assay had an LoB of 1.7 ng/mL (4.3 nmol/L), an LoD of 3.20 ng/mL (8.0 nmol/L), and an LoQ of 4.2 ng/mL (10.5 nmol/L). The LoD is defined as the lowest concentration of 25(OH)vitamin D that can be detected with 95% probability. The LoQ is defined as the lowest concentration of 25(OH)vitamin D that can be detected at a total CV of 20%.

8.2 Linearity

Linearity was evaluated according to the CLSI protocol EP6-A.35 A sample containing high levels of total 25(OH)vitamin D was mixed in various proportions with a sample containing low levels of total 25(OH)vitamin D. The resulting sample mixtures were assayed for total vitamin D. On the ADVIA Centaur systems, the VitD assay is linear from 4.2 to 150 ng/mL.

8.3 Precision

The ADVIA Centaur VitD assay is designed to have a Within-Run precision CV of ≤ 8%, and a Total CV of ≤ 12%, with samples > 20 ng/mL.

510(k) Summary

Precision was evaluated according to the CLSI protocol EP5-A2.[32] Six samples were assayed twice a day in replicates of 2, over 20 days (n = 80 replicates per sample) using the ADVIA Centaur VitD assay. The following results were obtained:

Mean	Within-Run Repeatability		Total Precision (Within-Lab)	
(ng/mL)	SD	%CV	SD	%CV
21.29	1.36	6.4	2.04	9.6
26.10	1.56	6.0	2.37	9.1
32.16	1.71	5.3	2.38	7.4
65.47	2.52	3.8	3.60	5.5
84.12	1.90	2.3	3.34	4.0
132.32	3.13	2.4	4.76	3.6

8.4 Method Comparison

For 126 samples (118 native, 8 contrived) in the range of 5.9 - 130.8 ng/mL (14.8 - 327.0 nmol/L), the relationship between the ADVIA Centaur VitD (y) and a comparable assay (x) is described using Deming regression:
ADVIA Centaur VitD (y) = 1.03 (x) + 0.85 ng/mL, r = 0.99

8.5 Specimen Equivalence

Specimen equivalency was determined using a Weighted-Deming regression analysis in accordance with CLSI Document EP9-A2.

Sixty-six (66) native and 8 contrived matched set samples (serum, SST, Lithium Heparin, Sodium Heparin, K2 EDTA, K3 EDTA) for a total n=74 matched set samples. Weighted-Deming fit was used for regression analysis comparing all tube types to serum. The following results were obtained:

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Gel-barrier tube (serum)	y = 0.97x + 0.87 (y = 2.43x + 2.18)	13.03–142.85 ng/mL (32.58–357.13 nmol/L)	74	0.99
dipotassium EDTA (plasma)	y = 0.97x + 0.64 (y = 2.43x + 1.60)	13.03–142.85 ng/mL (32.58–357.13 nmol/L)	74	0.99
tripotassium EDTA (plasma)	y = 0.96x + 0.68 (y = 2.40x + 1.70)	13.03–142.85 ng/mL (32.58–357.13 nmol/L)	74	0.99
lithium heparin (plasma)	y = 0.99x - 0.18 (y = 2.48x - 0.45)	13.03–142.85 ng/mL (32.58–357.13 nmol/L)	74	0.99
sodium heparin (plasma)	y = 1.02x - 1.13 (y = 2.55x - 2.83)	13.03–142.85 ng/mL (32.58–357.13 nmol/L)	74	0.99

[a] Number of samples tested.
[b] Correlation coefficient

8.6 Dilution Recovery

Five serum samples in the range of (186.0-211.0 ng/mL (465.0-527.5 nmol/L) of total 25(OH)vitamin D were diluted 1:2 with ADVIA Centaur VitD diluent and assayed for recovery and parallelism. The recoveries ranged from 97.0 to 109.0% with a mean of 101.0%.

Sample	Dilution	Observed ng/mL	Expected ng/mL	Recovery %
1	1:2	96.0	97.5	98.0
2	1:2	96.3	93.0	103.0
3	1:2	102.6	103.5	99.0
4	1:2	102.5	105.5	97.0
5	1:2	102.1	93.5	109.0
Mean				101.0

8.7 Reference Interval

A study was performed referencing CLSI EP28-A3c confirming that the previously established Reference Interval could be transferred to the modified VitD assay.

Observed reference values were obtained for the ADVIA Centaur VitD assay using serum samples collected from adult and pediatric populations. The adult population consisted of 291 apparently healthy male and female subjects of light and dark skin types ranging in age from 21–93 years. The pediatric population consisted of 237 male and female subjects of light and dark skin types: 32 subjects between the ages of 1–3 years, 114 subjects between 3–12 years, and 91 subjects between 12 and up to 21 years.

The samples were collected in different seasons and from different geographical regions of the United States. Adult samples from subjects not taking supplements containing vitamin D >2000 IU per day, and with normal values for PTH, calcium, and TSH were included in this study.

Pediatric samples with normal values for PTH and TSH were included in this study. Based on the 95% confidence interval, the following values were established following CLSI guideline C28-A2.30

	Observed Values, Adult ng/mL (nmol/L)	**Observed Values, Pediatric (12 months up to 21 years)**
Median 25(OH)vitamin D	22.5 ng/mL (56.3 nmol/L)	23.8 ng/mL (59.5 nmol/L)
Observed Range 2.5th to 97.5th Percentile	7.4–44.0 ng/mL (18.5–110.0 nmol/L)	11.4–45.8 ng/mL (28.5–114.5 nmol/L)

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient samples.[30] Consider these values as guidelines only.

510(k) Summary

9. Conclusions

Based on the results of comparative testing, the Modified ADVIA Centaur® Vitamin D Total (VitD) is substantially equivalent to the currently marketed predicate device, the ADVIA Centaur® Vitamin D Total (VitD) assay (k133156).