September 1, 2021

Roche Diagnostics
Jamie Ferguson, Regulatory Affairs Principal
9115 Hague Road
PO Box 50416
Indianapolis, IN 46250

Re: K210901
Trade/Device Name: Elecsys Vitamin D total III
Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D Test System
Regulatory Class: Class II
Product Code: MRG
Dated: March 25, 2021
Received: March 26, 2021

Dear Jamie Ferguson:

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.
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: 06/30/2023
See PRA Statement below.

Submission Number *(if known)*

k210901

Device Name

Elecsys Vitamin D total III

Indications for Use *(Describe)*

Binding assay for the in vitro quantitative determination of total 25-hydroxyvitamin D in human serum and plasma. This assay is to be used as an aid in the assessment of vitamin D sufficiency in adults.

The electrochemiluminescence binding assay is intended for use on cobas e immunoassay analyzers.

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

Contact Details

k210901

21 CFR 807.92(a)(1)

Applicant Name	Roche Diagnostics
Applicant Address	9115 Hague Road, PO Box 50416, Indianapolis, IN, 46250, United States of America
Applicant Contact Telephone	317-270-7402
Applicant Contact	Mrs. Jamie Ferguson
Applicant Contact Email	jamie.ferguson@roche.com

Device Name

21 CFR 807.92(a)(2)

Device Trade Name	Elecsys Vitamin D total III (09038078160)
Common Name	Vitamin D test system
Classification Name	System, Test, Vitamin D
Regulation Number	862.1825
Product Code	MRG

Legally Marketed Predicate Devices

21 CFR 807.92(a)(3)

Predicate #	Predicate Trade Name (Primary Predicate is listed first)	Product Code
K162840	Elecsys Vitamin D total II	MRG

Device Description Summary

21 CFR 807.92(a)(4)

Elecsys Vitamin D total III is a binding assay for the in vitro quantitative determination of total 25-hydroxyvitamin D in human serum and plasma. The assay is to be used as an aid in the assessment of vitamin D sufficiency in adults. The assay is intended for use on the cobas e immunassay analyzers. The cobas e family of analyzers employ the electrochemiluminescence "ECLIA" technology.

Elecsys Vitamin D total III utilizes a competition test principle and has a total test duration of 27 minutes:

- 1st incubation: By incubating the sample (15 µL) with pretreatment reagent 1 and 2, bound 25-hydroxyvitamin D is released from the vitamin D binding protein (VDBP).
- 2nd incubation: By incubating the pretreated sample with the ruthenium labeled VDBP, a complex between the 25-hydroxyvitamin D and the ruthenylated VDBP is formed. A specific unlabeled antibody binds to 24,25-dihydroxyvitamin D present in the sample and inhibits cross-reactivity to this vitamin D metabolite.
- 3rd incubation: After addition of streptavidin-coated microparticles and 25-hydroxyvitamin D labeled with biotin, unbound ruthenylated labeled VDBP become occupied. A complex consisting of
the ruthenylated VDBP and the biotinylated 25-hydroxyvitamin D is formed and becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by a 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

The reagent working solutions include the reagent rackpack (M, R1, R2) and the pretreatment reagents (PT1, PT2):

PT1 Pretreatment reagent 1 (white cap), 1 bottle, 4 mL: Dithiothreitol 1 g/L, pH 5.5
PT2 Pretreatment reagent 2 (gray cap), 1 bottle, 4 mL: Sodium hydroxide 57.5 g/L
M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative
R1 Vitamin D binding protein-Ru/(bpy) (gray cap), 1 bottle, 9 mL: Ruthenium labeled vitamin D binding protein 150 µg/L; bis-tris propane buffer 200 mmol/L; albumin (human) 25 g/L; pH 7.5; preservative
R2 25-hydroxyvitamin D~biotin (black cap), 1 bottle, 8.5 mL: Biotinylated 25-hydroxyvitamin D 20 µg/L; bis-tris propane buffer 200 mmol/L; pH 8.6; preservative

Intended Use/Indications for Use 21 CFR 807.92(a)(5)

Binding assay for the in vitro quantitative determination of total 25-hydroxyvitamin D in human serum and plasma. This assay is to be used as an aid in the assessment of vitamin D sufficiency in adults.

The electrochemiluminescence binding assay is intended for use on cobas e immunoassay analyzers.

Indications for Use Comparison 21 CFR 807.92(a)(5)

Elecsys Vitamin D total III is substantially equivalent to Elecsys Vitamin D total II, cleared under K162840.

The intended use of Elecsys Vitamin D total III was updated to specify it is a binding assay and to remove analyzers that are no longer supported for use with Roche assays. The indications for use of Elecsys Vitamin D total III did not change from the predicate device.

Technological Comparison 21 CFR 807.92(a)(6)

Roche Diagnostics has updated the current Elecsys Vitamin D total II assay in order to improve biotin tolerance. A technical solution was implemented by adding an anti-biotin antibody to one of the reagents, which allows depletion of biotin in a patient sample by binding free biotin. Roche also increased robustness for pre-analytical sample qualities by optimizing the ratio of chemical components. In addition, the measuring range was expanded to meet customer needs. No other technological characteristics were changed. The submitted information in this premarket notification supports a substantial equivalence decision.

Non-Clinical and/or Clinical Tests Summary & Conclusions 21 CFR 807.92(b)

Precision measurements were conducted for both 21 days and 5 days with the Elecsys Vitamin D total III assay to evaluate repeatability (within-run precision) and intermediate precision (within-laboratory precision) according the CLSI guideline EP05-A3. All predefined acceptance criteria was met for the precision experiments.

Lot-to-lot reproducibility was performed for the Elecsys Vitamin D total III assay using three reagent lots. All predefined acceptance criteria was met for the lot-to-lot reproducibility experiment.

The Limit of Blank (LoB) was determined according to CLSI EP17-A2. The LoB claim in the labeling will be set to 2.0 ng/mL.

The Limit of Detection (LoD) was determined according to CLSI EP17-A2. The LoD claim in the labeling will be set to 3.0 ng/mL.

The Limit of Quantitation (LoQ) was determined according to CLSI EP17-A2. The LoQ claim in the labeling will be set to 6.0 ng/mL.

Linearity was evaluated according to CLSI EP06-A with the Elecsys Vitamin D total III assay on one cobas e 601 analyzer. Linearity was confirmed in the range of 2.04 - 129 ng/mL, and a measuring range of 6.00 - 120 ng/mL will be claimed in the labeling.

The high-dose hook effect (HDHE) of the Elecsys Vitamin D total III assay was assessed on one cobas e 601 analyzer in two-fold determination. No hook effect was seen up to 10,000 ng/mL for both samples.

The effect of the presence of human anti-mouse antibodies (HAMA) on the Elecsys Vitamin D total III assay was assessed on one cobas e 601 analyzer. No HAMA interference was observed.

Ten endogenous substances were evaluated for potential interference with the Elecsys Vitamin D total III assay on the cobas e 601 analyzer. All predefined acceptance criteria was met, and the proposed labeling claims for each endogenous substance can be found below:

Biotin ≤ 600 ng/mL
Lipemia (Intralipid) ≤ 300 mg/dL

Hemoglobin ≤ 600 mg/dL
Bilirubin ≤ 66 mg/dL
Rheumatoid Factor ≤ 1200 IU/mL
Serum Albumin ≤ 7 g/dL
IgG ≤ 7 g/dL
IgA ≤ 1.3 g/dL
IgM ≤ 1 g/dL
Triglyceride ≤ 300 mg/dL

A cross-reactivity study was conducted with Elecsys Vitamin D total III on the cobas e 601 analyzer to evaluate the potential cross-reactivity of the assay with other vitamin D metabolites that occur in the human body during anabolism and catabolism. The percent cross-reactivity was calculated and normalized to the cross-reactivity of 25-hydroxyvitamin D3. The mean results are summarized below:

Cross-reactant / Mean cross-reactivity (%)
25-hydroxyvitamin D3 (50 ng/mL) / 100
25-hydroxyvitamin D2 (50 ng/mL) / 103.3
24,25-dihydroxyvitamin D3 (100 ng/mL) / 8.1
3-epi-25-hydroxyvitamin D3 (50 ng/mL) / 121.6
3-epi-25-hydroxyvitamin D2 (50 ng/mL) / 102.7
1,25-dihydroxyvitamin D3 (100 ng/mL) / not determined
1,25-dihydroxyvitamin D2 (100 ng/mL) / 0.9
Vitamin D3 (1000 ng/mL) / 0.9
Vitamin D2 (1000 ng/mL) / 0.7

An exogenous interference study was conducted to evaluate 17 commonly and three specially used pharmaceutical compounds for potential interference with the Elecsys Vitamin D total III assay on the cobas e 601 analyzer. The predefined acceptance criteria was met for all drugs tested, and no interference was observed.

A method comparison was performed with the LC-MS/MS reference method and the Elecsys Vitamin D total III assay, using a total of 157 single donor serum samples (CDC Verification Samples provided by the Vitamin D Standardization and Certification Program with assigned values by the candidate Reference Method Procedure: ID-LCMS/MS at the CDC Vitamin D Reference Laborabory). The sample concentrations were between 5.64 ng/mL (14.1 nmol/L) and 118 ng/mL (295 nmol/L). The results can be found below:

Deming
$y = 0.981x + 0.795$
$r = 0.982$
Passing Bablok
$y = 0.979x + 0.675$
$\tau = 0.908$

A method comparison was performed with the predicate device, Elecsys Vitamin D total II, and the Elecsys Vitamin D total III assay, using a total of 151 human serum samples. The results can be found below:

Passing Bablok
$y = 0.896x + 2.63$
$\tau = 0.913$

The effect on quantitation of analyte in the presence of anticoagulants with Elecsys Vitamin D total III was determined by comparing values obtained from single-donor samples drawn into serum, Serum Separation Tubes (SST), and Li-Heparin, K2-EDTA, and K3-EDTA plasma primary tubes. All predefined acceptance criteria was met, supporting the labeling claim that serum, SSTs, and Li-Heparin, K2-EDTA and K3-EDTA plasma primary tubes are acceptable sample types.

The effect on quantitation of analyte with the use of plasma separation tubes (PSTs) with Elecsys Vitamin D total III was determined by comparing values obtained from single-donor samples drawn into PSTs from 3 separate manufacturers. The predefined acceptance criteria was met, supporting the labeling claim PSTs are an acceptable sample type.

Reagent stability after first opening for the Elecsys Vitamin D total III assay was tested on one cobas e 601 analyzer. Elecsys Vitamin D total III reagent kits can be used after first opening for up to 8 weeks (56 days) when stored at 2-8°C.

On-board reagent stability for the Elecsys Vitamin D total III assay was tested on one cobas e 601 analyzer. Elecsys Vitamin D total III reagent kits can be stored on-board the analyzers for up to 28 days (4 weeks). A new calibration of the kit kept on-board is recommended every 7 days.

Lot calibration frequency for the Elecsys Vitamin D total III assay was tested on one cobas e 601 analyzer. Calibrations of an Elecsys Vitamin D total III reagent lot is recommended every 12 weeks (3 months). During that time period, fresh reagent kits of the same lot can be used without calibration using the calibration curve of the day 0 reagent kit.

Reagent on-board calibration frequency for Elecsys Vitamin D total III assay was tested on one cobas e 601 analyzer. Elecsys Vitamin D total III reagent kits can be stored on board of the analyzers for up to 7 days without a new calibration.

A Reference Range study for the Elecsys Vitamin D total III assay on the cobas e 601 analyzer was performed in order to determine reference range values under routine laboratory conditions. Serum samples were collected from adult subjects during summer and winter months from three geographically diverse locations in the U.S. (Northern, Mid and Southern regions). One clinical laboratory was contracted to measure samples with Elecsys Vitamin D total III on the cobas e 601 analyzer and a variety of characterization assays on either the cobas e 601 or cobas c 501 analyzer. Characterization testing was used to determine whether the sample met the stated inclusion/exclusion criteria. Subjects that were not within the respective reference ranges of any of the eight characterization testing assays were not included in the final Elecsys Vitamin D total III reference range determination.

A total of 827 subjects were enrolled and had characterization testing preformed. Of the 827 subjects enrolled and tested, 361 were excluded as they did not pass all eight characterization tests and two were excluded after testing was complete due to concomitant medication use. One subject did not have serum available for vitamin D testing. A total of 463 eligible subjects were included in the final Elecsys Vitamin D total III reference range determination.

The calculated 95% reference range for the total enrolled population of Elecsys Vitamin D total III is 10.2 – 49.4 ng/mL (25.4 – 123 nmol/L).

The information provided in this 510(k) Premarket Notification support the determination that Elecsys Vitamin D total III is substantially equivalent to the predicate device, Elecsys Vitamin D total II.