MAR 1 4 2014

k133410

510(k) SUMMARY

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

Submitter's name:	Diazyme Laboratories
Submitter's address:	12889 Gregg Court Poway, CA 92064
Name of Contact Person:	Dr. Abhijit Datta Director, Technical Operations Diazyme Laboratories 12889 Gregg Court Poway, CA 92064 Email: abhijit.datta@diazyme.com Phone: 858-455-4762 Fax: 858-455-2120
Date the Summary was Prepared:	November 04, 2013
Name of the Device	Diazyme 25-OH Vitamin D Assay Kit Diazyme 25-OH Vitamin D Control Set
Trade Name:	Diazyme 25-OH Vitamin D Assay Diazyme 25-OH Vitamin D Control Set
Common/Usual Name	Vitamin D Assay
Device Classification Name	Vitamin D Test System
Product code:	MRG – Vitamin D Test System JJX – Single (specified) Analyte Controls (Assayed and Unassayed)
Panel:	Chemistry (75)
Submission Type	510k

Regulation Number	21 CFR 862.1825 – Vitamin D Test System 21 CFR 862.1660 – Quality Control material (Assayed and Un-assayed)
Device Class	II (Assay) I (Control)
Predicate Device:	The Diazyme 25-OH Vitamin D Assay Kit and Control Set is substantially equivalent to the currently marketed LIAISON® 25-OH Vitamin D TOTAL Assay (k112725, k071480).
Manufacturing Address	Diazyme Laboratories 12889 Gregg Court Poway, CA 92064 USA
Establishment Registration	2032900

DESCRIPTION OF THE DEVICE

The Diazyme 25-OH Vitamin D Assay is a direct competitive colorimetric immunoassay for the quantitative determination of total 25-OH vitamin D in serum and plasma. The assay is based on the principle of α–complementation of the enzyme β-galactosidase and the competition between an enzyme donor-25-OH Vitamin D conjugate, an anti-Vitamin D antibody and the 25-OH Vitamin D content of a serum sample. Samples with higher 25-OH Vitamin D concentrations produce higher β-galactosidase activities and *vice versa*. A nitro-phenyl-ß-galactoside derivative (NPG) is used as the enzyme substrate. The reaction's product has maximum absorbance at 415 nm. The 25-OH Vitamin D concentration of a specimen is proportional to the measured β-galactosidase activity. Five calibration levels are needed for each run. Calibrators are treated exactly the same as patient samples.

The Diazyme 25-OH Vitamin D Control Set (2 levels) is intended for use with the Diazyme 25-OH Vitamin D Assay kit only. Controls are treated exactly the same as patient samples. The quality controls assist laboratory users in verification steps ensuring that the assay reagents are functioning correctly. Users are instructed to verify the calibration curve with the controls.

INDICATIONS FOR USE

The Diazyme 25-OH Vitamin D Assay is intended for use in clinical laboratories for the quantitative determination of total 25-OH Vitamin D in human serum and plasma on automated chemistry analyzer. Measurement of 25-hydroxyvitamin D (25-OH-D) is for the assessment of vitamin D sufficiency. For in vitro diagnostic use only.

The Diazyme 25-OH Vitamin D Control Set is intended for use as quality controls for the Diazyme 25-OH Vitamin D Assay Kit only. For *in vitro* diagnostic use only.

Table 1 Summary of Assay Kit Components

LIAISON® 25-OH Vitamin D TOTAL Assay (predicate k112725)	**Diazyme 25-OH Vitamin D Assay**
Kit can be only used for the 25-OH Vitamin D quantification on the Diasorin Liaison® analyzer.	Kit can be used for the 25-OH Vitamin D quantification on the Roche Modular P Chemistry Analyzer and similar chemistry analyzer systems.
Magnetic Particles: Magnetic particles coated with antibody against 25-OH Vitamin D, protein, phosphate buffer, < 0.1% sodium azide.	**Dilution buffer:** Sheep Antibody against 25-OH Vitamin D, proteins, phosphate buffer, < 0.1% sodium azide.
Assay Buffer: Buffer with 10% ethanol, surfactants and preservatives.	**Reagent R1:** Proprietary dissociation solution with surfactants and preservatives.
Conjugate: 25-OH Vitamin D conjugated to an isoluminol derivative, in phosphate buffer with 10% ethanol, EDTA, surfactant and preservatives.	**Reagent R2:** Enzyme Donor-Vitamin D conjugate, proteins, surfactants and preservatives.
LIAISON Starter 1: Catalyst in 4% NaOH.	**Reagent R3:** Enzyme Acceptor, proteins, surfactants and preservatives.
LIAISON Starter 2: 0.12% peroxide solution.	N/A
LIAISON Wash/System Liquid: Phosphate buffer solution (10x concentrate). Preservative: sodium azide.	N/A
LIAISON 25 OH Vitamin D diluent: Human serum with buffer salts and <0.1% sodium azide.	N/A
Calibrator Set (k071480)	Calibrator set
1 x 1.0 mL Calibrator 1 1 x 1.0 mL Calibrator 2	1 x 1.0 mL Calibrator 1 1 x 1.0 mL Calibrator 2 1 x 1.0 mL Calibrator 3 1 x 1.0 mL Calibrator 4 1 x 1.0 mL Calibrator 5

Control set (k071480)	Diazyme Control set
1 x 1.0mL Control 1 1 x 1.0mL Control 2	1 x 1.0mL Control 1 1 x 1.0mL Control 2
Serum-based controls	Serum-based controls
Liquid form	Liquid form
Stable for at least 12 months at 2-8C.	Stable for at least 12 months at 2-8C.
Assigned range is mean +/- 25%.	Assigned range is mean +/- 25%.

PERFORMANCE TESTING SUMMARIES ON THE ROCHE MODULAR-P CHEMISTRY ANALYZER

Precision Study

The precision of the Diazyme 25-OH Vitamin D Assay was evaluated according to the Clinical and Laboratory Standards Institute (CLSI) EP5-A guideline. A total of 11 precision levels were used in the study:

- Two serum controls (containing 23.1 ng/mL and 45.7 ng/mL).
- Nine serum samples distributed across the dynamic range of the assay.

Controls and samples were measured daily over the span of 20 days, using three lots of reagents and one chemistry analyzer. A total of 40 independents run were performed on each specimen. Each run produced two measurements. A total of 80 data points were obtained per specimen.

The mean value (Mean), standard deviation, within-run imprecision and total imprecision are calculated and summarized in the following tables:

25-OH Vitamin D (ng/mL)			Within-run		Between-run		Total	
Specimen	n	Mean (ng/mL)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)
Control #1	80	23.1	1.47	6.4	1.04	4.5	1.68	7.3
Control #2	80	45.7	2.06	4.5	1.67	3.7	2.12	4.6
Sample #1	80	22.6	1.19	5.3	1.11	4.9	1.45	6.4
Sample #2	80	31.7	1.42	4.5	1.59	5.0	1.81	5.7
Sample #3	80	40.6	1.42	3.5	1.59	3.9	1.66	4.1
Sample #4	80	48.6	2.32	4.8	1.71	3.5	2.41	4.9
Sample #5	80	55.8	2.14	3.8	1.73	3.1	2.34	4.2
Sample #6	80	65.4	2.03	3.1	1.79	2.7	2.42	3.7
Sample #7	80	69.7	2.02	2.9	1.99	2.9	2.55	3.7
Sample #8	80	92.8	2.52	2.7	2.02	2.2	3.40	3.7
Sample #9	80	134.6	2.97	2.2	2.69	2.0	3.87	2.9
Very low Sample #1	80	9.4	1.22	13.0	0.98	10.4	1.31	14.0
Very low Sample #2	80	11.2	1.58	14.2	0.88	7.9	1.55	13.9

Linearity/Reportable Range

To establish the linearity of the 25-OH Vitamin D assay, a study design was used based on the CLSI protocol EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach: Approved Guideline.

Eleven levels of linearity were prepared by diluting a high serum sample containing 147.8 ng/mL of 25-OH Vitamin D with Vitamin D-depleted serum (0 ng/mL, Seracare Life Sciences). These samples were tested with the Diazyme 25-OH Vitamin D assay, in triplicates. The results were processed using the EP Evaluator Software (Version 8.0) parameterized to an allowable systematic error of 8.9%. The assay was found to be linear between 7.6 ng/mL and 147.8 ng/mL.

LoB/LoD/LoQ

The Limit of Blank (LoB), the Limit of Detection (LoD) and the Limit of Quantitation (LoQ) of the Diazyme 25-OH Vitamin D assay on microplate were determined according to CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation. The following are the limits determined with the Diazyme 25-OH Vitamin D Assay:

LoB = 2.0 ng/mL

LoD = 3.5 ng/mL

LoQ = 7.6 ng/mL

Analytical specificity

Interference Study

The Diazyme 25-OH Vitamin D Assay was subjected to an interference study according the CLSI EP7-A2 protocol. The following substances normally present in the blood produced less than 10% deviation when tested at levels equal to the concentrations listed below:

Interference	Concentration
Conjugated Bilirubin	40 mg/dL
Free Bilirubin	40 mg/dL
Hemoglobin	100 mg/dL
Ascorbic Acid	176 mg/dL
Triglycerides	750 mg/dL
Uric Acid	20 mg/dL
Biotin	2 mg/dL
Human Serum Albumin	9 g/dL
N-Acetyl Cysteine Amide	1663 ng/mL
Ampicillin	1000 ng/mL
Cyclosporine C	105 ng/mL
Cefoxitin	660 ng/mL
Acetylsalicylic Acid	1000 ng/mL

Rifampicin	64 ng/mL
Acetaminophen	200 ng/mL
Ibuprofen	500 ng/mL
Theophylline	100 ng/mL

Cross Reactivity

Cross-reactivity of the Diazyme 25-OH Vitamin D Assay was determined by adding Vitamin D metabolites to serum pool samples. Based on the results in the table below, the assay did not cross react with Vitamin D2 and Vitamin D3 and the assay recovers both 25-OH Vitamin D2 and 25-OH Vitamin D3 similarly. Cross-reactivity with various Vitamin D metabolites is summarized in the table below:

Compound	Concentration tested (ng/mL)	Cross-reactivity
25-OH Vitamin D3	44.0	100%
25-OH Vitamin D2	44.0	92.3%
Vitamin D3	44.0	1.0%
Vitamin D2	44.0	2.9%
1,25-(OH)2 Vitamin D3	2.9	2.5%
1,25-(OH)2 Vitamin D2	2.9	-1.5%
24R,25-(OH)2 Vitamin D3	41.0	5.1%
3-epi-25-OH Vitamin D3	42.0	61.7%
3-epi-25-OH Vitamin D2	42.0	55.1%

*% Cross-reactivity = (Corrected Assay Value /Concentration Spiked)*100

No significant cross-reactivity (4.1%) was found for Paricalcitol (Zemplar®) up to 25ng/mL.

Comparison Studies

Method Comparison

Human serum samples were tested with the Diazyme 25-OH Vitamin D Assay and the obtained results were compared to the predicate method. A total of 98 unaltered serum samples were used in this experiment. Using this study, we found that the Diazyme 25-OH Vitamin D Assay correlated with the predicate method with the following results:

Deming Regression Analysis	95% Confidence Interval
Slope	1.005 (0.969 to 1.041)
Intercept	-0.21 (-2.15 to 1.73)
Correlation Coefficient	0.984 (0.976 to 0.989)
Range	9.5-140.9

Matrix Comparison

To evaluate the effect of anticoagulants, the Diazyme 25-OH Vitamin D Assay was used to measure the 25-OH Vitamin D concentrations of matched sets of serum, K_3-EDTA plasma and Li-Heparin plasma. The reported values for each sample and for each matrix were obtained from single measurements. The total number of matched sets tested was 66. In order to cover the claimed measuring range for each matrix, seven spiked patient samples were included in the study.

Linear regression of the "Li-Heparin plasma versus Serum" data yielded the following results: $y = 0.9657 x - 0.6596$ and $R^2 = 0.9736$.
Linear regression of the "K3-EDTA plasma versus Serum" data yielded the following results: $y = 0.9948x - 0.7057$ and $R^2 = 0.9866$.

Reference Range Study

To determine a reference range for the Diazyme 25-OH Vitamin D Assay, the 25-OH Vitamin D serum concentrations of a US population of 157 apparently healthy individuals were measured with the Diazyme method. The individual patient serum samples used in this study were obtained from certified commercial sources. Forty seven (47) samples from Pennsylvania (Northern U.S.) were collected from an FDA Licensed Donor Center with informed consent. Fifty six (56) samples from Tennessee (Central U.S.) and Fifty four (54) samples from Texas (Southern U.S.) were collected according to an IRB approved protocol.

All participating individuals met the following inclusion conditions:

- The age of all individuals was within the 21-80 years old range.
- Individuals were from three different geographical locations: 47 from Pennsylvania (Northern US), 56 from Tennessee (Central US) and 54 from Texas (Southern US).
- All samples were collected during the months of October and November (fall season).
- The studied population consisted of 72 light skin individuals (46%) and 85 dark skin individuals (54%).
- 155 individuals (98.7%) did not take any artificial Vitamin D supplements. Two individuals (1.3%) did take some Vitamin D supplements but did not exceed the daily dose of 2000 IU.
- All 157 individuals did not have any family history of parathyroid or calcium regulatory disease.
- All 157 individuals did not have any history of kidney disease, GI disease, liver disease, calcium-levels related disease, thyroid disease, parathyroid disease, calcium related disease, seizures, chronic disease or bariatric surgery.
- All 157 individuals were not currently taking any medications that are known to affect absorption or catabolism of Vitamin D (including cholesterol absorption inhibitors such as Vytorin®, Inegy™ or Zetia; anticonvulsants such as Neurontin, Depakine® and Trileptal; glucocorticoids such as Cortisol, Prednisone and Dexamethasone; HAART (AIDS treatment) or antirejection medications.

Analysis of the reference range study data yielded the following results:

- Lowest 25-OH Vitamin D concentration: 12.6 ng/mL.
- Highest 25-OH Vitamin D concentration: 51.4 ng/mL.
- Median 25-OH Vitamin D concentration: 25.6 ng/mL
- Observed range (2.5th to 97.5th percentile): 15.0 to 45.9 ng/mL.

Conclusion

The Diazyme 25-OH Vitamin D assay has a linear range of 7.6 – 147.8 ng/mL for serum samples. For samples with Vitamin D levels ranging from 23.1 ng/mL to 134.6 ng/mL; within-run CVs were 1.8 to 8.8% and total CVs were 2.1 to 8.8%. For 98 tested serum samples, Deming regression yielded a correlation coefficient between the Diazyme 25-OH Vitamin D assay and the Diasorin Liaison® 25-OH Vitamin D Total assay was 0.984, the slope was 1.005, and the y intercept was -0.21. Interference studies demonstrated that this assay was not significantly affected by triglycerides (up to 750 mg/dL), ascorbic acid (up to 176mg/dL), free bilirubin (up to 40 mg/dL), conjugated bilirubin (up to 40 mg/dL) and hemoglobin (up to 100 mg/dL).

The Diazyme 25-OH Vitamin D Assay and the Diazyme 25-OH Vitamin D Control data presented and provided is complete and supports the basis for substantial equivalence to the predicate device.

References

1. Wacker M, Holick MF. Sunlight and Vitamin D: A global perspective for health. Dermatoendocrinol. 2013, 5, 51-108.
2. National Osteoporosis Foundation. Prevention – Vitamin D. http://www.nof.org/aboutosteoporosis/prevention/vitamind

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 14, 2014

DIAZYME LABORATORIES
ABHIJIT DATTA
DIRECTOR, TECHNICAL OPERATIONS
12889 GREGG COURT
POWAY CA 92064

Re: K133410
Trade/Device Name: Diazyme 25-OH Vitamin D Assay;
Diazyme 25-OH Vitamin D Control Set
Regulation Number: 21 CFR 862.1825
Regulation Name: Vitamin D test system
Regulatory Class: II
Product Code: MRG, JJX
Dated: February 10, 2014
Received: February 12, 2014

Dear Dr. Datta:

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 Small Manufacturers, International and Consumer Assistance 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" (21CFR 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 Small Manufacturers, International and Consumer Assistance 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,

Courtney H. Lias -S

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 on last page.

510(k) Number *(if known)*
k133410

Device Name
Diazyme 25-OH Vitamin D Assay and Diazyme 25-OH Vitamin D Control set

Indications for Use *(Describe)*

The Diazyme 25-OH Vitamin D Assay is intended for use in clinical laboratories for the quantitative determination of 25-hydroxyvitamin D (25-OH-D) in human serum and plasma on automated chemistry analyzer. Measurement of 25-hydroxyvitamin D (25-OH-D) is for assessment of vitamin D sufficiency. For in vitro diagnostic use only.
The 25-OH Vitamin D Control Set is intended for use as quality controls for Diazyme 25-OH Vitamin D Assay Kit only. For in vitro diagnostic use only.

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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yung W. Chan -S