October 4, 2018

Diazyme Laboratories Inc.
Abhijit Datta
VP of Operations
12889 Gregg Court
Poway, CA 92130

Re: K180209
Trade/Device Name: Diazyme 1,5-AG Assay
Regulation Number: 21 CFR 864.7470
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: Class II
Product Code: NOZ
Dated: August 23, 2018
Received: August 24, 2018

Dear Abhijit 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. 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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/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 -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

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)*
k180209

Device Name
Diazyme 1,5-AG Assay

Indications for Use *(Describe)*
Diazyme 1,5-anhydroglucitol (1,5-AG) Assay is an enzymatic method intended for the quantitative determination of 1,5-anhydroglucitol (1,5-AG) in serum or plasma. The 1,5-AG Assay is for the intermediate term (preceding 1-2 weeks) monitoring of glycemic control in people with diabetes. 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)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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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 The assigned 510(k) number is k180209.

Submitter's name:	Diazyme Laboratories Inc.
Submitter's address:	12889 Gregg Court Poway, CA 92064
Name of Contact Person:	Dr. Abhijit Datta Diazyme Laboratories Inc. 12889 Gregg Court Poway, CA 92064 Phone: 858-455-4762
Date the Summary was Prepared:	September 28, 2013
Name of the Device	Diazyme 1,5-AG Assay
Trade Name:	Diazyme 1,5-AG Assay
Common/Usual Name	1,5-anhydroglucitol(1,5-AG) Assay
Device Classification	Assay, Glycosylated Hemoglobin; 21 CFR 864.7470
Product code:	NOZ
Panel:	Hematology (81)
Submission Type	510k
Regulation Number	21 CFR 864.7470
Device Class	II
Predicate Device:	GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604).
Manufacturing Address	Diazyme Laboratories Inc. 12889 Gregg Court Poway, CA 92064 USA
Establishment Registration	2032900

DESCRIPTION OF THE DEVICE

Diazyme's 1,5-AG assay is an enzymatic method intended for the quantitative determination of 1,5-anhydroglucitol (1,5-AG) in serum or plasma. The assay uses the enzyme pyranose oxidase (PROD) to oxidize the 2nd position hydroxyl group of 1,5-AG and to detect the generated hydrogen peroxide by colorimetry using peroxidase (POD). To eliminate reactive glucose in sample, it is pretreated by enzymatic reactions using hexokinase and pyruvate kinase (PK). Hexokinase uses adenosine triphosphate (ATP) to convert glucose into non-reactive glucose-6-phosphate (G-6-P), generating adenosine diphosphate (ADP). The reaction is driven to completion with PK, as ADP is phosphoralated to ATP during the conversion of phosphoenolpyruvate (PEP) into pyruvate.

INDICATIONS FOR USE

Diazyme 1,5-anhydroglucitol (1,5-AG) Assay is an enzymatic method intended for the quantitative determination of 1,5-anhydroglucitol (1,5-AG) in serum or plasma. The 1,5-AG Assay is for the intermediate term (preceding 1-2 weeks) monitoring of glycemic control in people with diabetes. For *in vitro* diagnostic use only.

Substantial Equivalence Information

Predicate device name(s): GlycoMark™ 1,5-anhydroglucitol (1,5-AG) k031604

Comparison of new device to predicate: The tables below identify similarities and differences between the predicate device and the Diazyme 1,5-AG Assay (k180209).

Indications for Use

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209	Equivalency
The GlycoMark™ test provides quantitative measurement of 1,5-anhydroglucitol (15AG) in serum or plasma. The test is for professional use, and is indicated for the intermediate term monitoring of glycemic control in people with diabetes.	Diazyme 1,5-AG Assay is an enzymatic method intended for the quantitative determination of 1,5-anhydroglucitol (1,5-AG) in serum or plasma. The 1,5-AG Assay is for the intermediate term (preceding 1-2 weeks) monitoring of glycemic control in people with diabetes. For *in vitro* diagnostic use only.	Same

Assay Principle

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209	Equivalency
The method uses the enzyme pyranose oxidase (PROD) to oxidize the 2nd posi-	Diazyme's 1,5-AG assay uses the enzyme pyranose oxidase (PROD) to oxidize the 2nd position hydroxyl group of 1,5-AG	same

tion hydroxyl group of 15AG and to detect the generated hydrogen peroxide by colorimetry using peroxidase (POD). As PROD reacts with glucose, the sample is pretreated by enzyme reaction using glucokinase (GK). Glucose is converted into glucose-6-phosphate (G-6-P), a species non-reactive with PROD. To drive the reaction to completion, an adenosine triphosphate (ATP)-regenerating system consisting of pyruvate kinase (PK) and phosphoenol pyruvate (PEP) is utilized. As ATP is converted to adenosine diphosphate (ADP), PK, in the presence of PEP, catalyzes the phosphorylation of ADP back to ATP. Following the conversion of glucose to G-6-P, the assay is rendered specific for 15AG.	and to detect the generated hydrogen peroxide by colorimetry using peroxidase (POD). To eliminate reactive glucose in sample, it is pretreated by enzymatic reactions using hexokinase and pyruvate kinase (PK). Hexokinase uses adenosine triphosphate (ATP) to convert glucose into non-reactive glucose-6-phosphate (G-6-P), generating adenosine diphosphate (ADP). The reaction is driven to completion with PK, as ADP is phosphoralated to ATP during the conversion of phosphoenolpyruvate (PEP) into pyruvate.	

Test Objective

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209	Equivalency
For the *in vitro* quantitative determination of 1,5-AG in human serum or plasma.	For the *in vitro* quantitative determination of 1,5-AG in human serum or plasma.	Same

Type of Test

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209	Equivalency
Quantitative	Quantitative	Same

Specimen Type

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209	Equivalency
Human serum or plasma.	Human serum or plasma.	Same

Product Type

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209	Equivalency

Assay reagent kit: liquid stable two reagent system	Assay reagent kit: liquid stable two reagent system	Same

Performance

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604)	Diazyme 1,5-AG Assay k180209
Linearity: up to 110 μg/mL Precision: CV% of 0.8 – 3.8% (2 controls and 2 serum samples) Method comparison (vs Roche Tina-Quant A1c): 89.6% concordance	Linearity: up to 110 μg/mL Precision: CV% of less than 5% Accuracy (vs. GlycoMark™ 1,5-AG): Correlation Coefficient (R^2) = 0.9995, slope = 1.0164, and y intercept = -0.2042.

Rationale for Considering the Device Substantially Equivalent to Devices Approved for Inter State Commerce

GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604) was selected for method comparison with Diazyme 1,5-AG Assay. The method comparison study between the subject and predicate using clinical patient samples showed excellent correlation. The similarities and differences between the predicate reagent and the Diazyme 1,5-AG Assay are given in the table above. Detailed performance characteristics and comparison analysis are given in the filing and demonstrate substantial equivalence to predicate device. The performance characteristics of the Diazyme 1,5-AG Assay are substantially similar to that of the approved predicate test. Performance data and risk analysis indicates that differences should not affect the safety and effectiveness of the Diazyme 1,5-AG Assay and offers users an *in vitro* diagnostic device system to measure 1,5-AG in human serum and plasma.

Conclusion

Detailed method comparison analysis (accuracy studies) presented in this 510k submission, together with linearity, precision and interference studies, demonstrates that the Diazyme 1,5-AG Assay performance is acceptable, safe and effective. There is no significant deviation between the results obtained by Diazyme 1,5-AG Assay and the legally marketed predicate device GlycoMark™ 1,5-anhydroglucitol (1,5-AG) (k031604) when testing clinical patient samples and is thus substantially similar.

PERFORMANCE SUMMARY

Precision Study

In the study, six serum samples were tested following CLSI EP5-A2 protocol.

Result:

Sample	Mean µg/mL (N=240)	Within-Run SD CV%	Between-Run SD CV%	Between-Day SD CV%	Between-Lot SD CV%	Total SD CV%
S1	3.07	0.07 2.3%	0.07 2.3%	0.11 3.5%	0.14 4.7%	0.15 4.8%
S2	5.70	0.07 1.3%	0.08 1.4%	0.07 1.2%	0.13 2.2%	0.13 2.2%
S3	11.56	0.09 0.8%	0.11 1.0%	0.05 0.5%	0.15 1.3%	0.15 1.3%
S4	23.17	0.14 0.6%	0.15 0.6%	0.07 0.3%	0.22 0.9%	0.22 0.9%
S5	61.84	0.32 0.5%	0.36 0.6%	0.42 0.7%	0.63 1.0%	0.64 1.0%
S6	97.26	0.48 0.5%	0.51 0.5%	0.62 0.6%	0.93 1.0%	0.94 1.0%

Linearity/Reportable Range

To establish the linearity of the Diazyme 1,5-AG 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.

Result:

Dilution	**Recovery Triplicate**			**Recovery Mean (µg/ mL)**	**Expected Recovery (µg/ mL)**	**Error**	**%Recovery**
Level 0	0.2	0.2	0.2	0.20	0.20	0%	100%
Level 1	10.9	10.9	11.0	10.93	11.85	-8%	92%
Level 2	21.8	22.2	22.4	22.13	23.49	-6%	94%
Level 3	34.4	34.2	34.5	34.37	35.14	-2%	98%
Level 4	45.3	45.6	45.0	45.30	46.79	-3%	97%
Level 5	58.4	58.7	58.5	58.53	58.43	0%	100%
Level 6	68.6	68.2	68.9	68.57	70.08	-2%	98%
Level 7	80.7	81.5	81.2	81.13	81.73	-1%	99%
Level 8	92.5	92.7	92.9	92.70	93.37	-1%	99%
Level 9	103.9	103.5	104.5	103.97	105.02	-1%	99%
Level 10	116.7	116.7	116.6	116.67	116.67	0%	100%

Dilution	Recovery Triplicate			Recovery Mean (µg/ mL)	Expected Recovery (µg/ mL)	Error	%Recovery
Level 0	0.1	0.1	0.3	0.17	0.17	0%	100%
Level 1	1.4	1.3	1.4	1.37	1.37	0%	100%
Level 2	2.3	2.4	2.5	2.40	2.57	-6%	94%
Level 3	3.5	3.6	3.4	3.50	3.77	-7%	93%
Level 4	4.7	4.6	4.8	4.70	4.97	-5%	95%
Level 5	5.7	5.8	5.8	5.77	6.17	-6%	94%
Level 6	7.0	7.1	7.0	7.03	7.37	-5%	95%
Level 7	8.3	8.2	8.2	8.23	8.57	-4%	96%
Level 8	9.4	9.5	9.6	9.50	9.77	-3%	97%
Level 9	10.9	10.9	10.8	10.87	10.97	-1%	99%
Level 10	12.2	12.2	12.1	12.17	12.17	0%	100%

The Diazyme 1,5-AG Assay is linear up to 116.7 µg/mL, and also in the clinically relevant range of 0.6- 10.0 µg/mL 1.5-AG.

LoB/LoD/LoQ

The Limit of Blank (LoB), the Limit of Detection (LoD) and the Limit of Quantitation (LoQ) of the Diazyme 1,5-AG assay were determined according to CLSI EP17-A2: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline using three lots of the reagents on Beckman AU680. The LOB was determined to be 0.3 µg/mL; the LOD was determined to be 0.5 µg/mL; the LOQ was determined to be 0.6 µg/mL.

Analytical specificity

To determine the level of interference from the substances normally present in the patient samples, Diazyme 1,5-AG Assay was used to test low (5.0 µg/mL), medium (23.0 µg/mL), and high (50 µg/mL) 1,5-AG samples with various concentrations of substances following CLSI EP7-A2.

The following substances normally present in the samples produced less than 10% deviation when tested at levels equal to the concentrations listed below.

Interference Substances	Concentration
Free Bilirubin	5 mg/dL
Bilirubin Conjugated	5 mg/dL
Hemoglobin	125 mg/dL
Ascorbic Acid	37.5 mg/dL
Triglyceride	1000 mg/dL
Glucose	1000 mg/dL
Maltose	500 mg/dL
Uric Acid	20 mg/dL
Creatinine	10 mg/dL
Urea	20 mg/dL

Comparison Studies

Protocol: Clinical and Laboratory Standards Institute EP9-A2 - Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline-Second Edition (2002). For method comparison, the 1,5- AG Assay was evaluated by testing individual serum samples with comparison to predicate legally marketed 1,5- AG device. A total of 102 patient samples covering the AMR were tested by both 1,5- AG Assay and Predicate 1,5- AG Assay.

Result:

Parameter	Results
Slope	1.0164
95% CI	1.012 to 1.021
Intercept	-0.21
95% CI	-0.35 to -0.07
Standard Error of Estimate	0.51
Correlation Coefficient(R)	0.9997
R^2	0.9995

Reference Range Study

To determine the reference interval of the normal population, serum samples from 140 apparently healthy males and 140 apparently healthy females were tested using the 1,5- AG Assay according to CLSI C28-A3 guideline.

Using non-parametric 5^{th}-95^{th} percentiles, the reference interval for males was established to be 8.19 to 32.19 µg/mL and 6.00 to 29.10 µg/mL for females.