July 13, 2018

Siemens Healthcare Diagnostics Inc.
Alan Haley
Regulatory and Clinical Affairs Specialist
500 GBC Drive
Newark, DE 19702

Re: K173909
Trade/Device Name: Dimension Hemoglobin A1c Assay
Regulation Number: 21 CFR 862.1373
Regulation Name: Hemoglobin A1c test system
Regulatory Class: Class II
Product Code: PDJ
Dated: June 11, 2018
Received: June 12, 2018

Dear Alan Haley:

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 Part 801 and Part 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.

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

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)*
k173909

Device Name
Dimension® Hemoglobin A1c Assay

Indications for Use *(Describe)*
The Dimension® Hemoglobin A1c assay is an in vitro diagnostic assay for the quantitative determination of %HbA1c (DCCT/NGSP) and mmol/mol HbA1c (IFCC) in human anticoagulated venous whole blood for use on the Dimension® clinical chemistry system. Measurement of Hemoglobin A1c is used as an aid in diagnosis and monitoring of long-term blood glucose control in patients with diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.

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 – K173909

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

1. Submitter

Company	Siemens Healthcare Diagnostics Inc.
Address	500 GBC Drive Newark, DE 19702
Contact	Alan Haley
Telephone	302.631.9883
Fax	302.631.6299
Date of Preparation	July 12, 2018

2. Device Information

Trade Name	Dimension® Hemoglobin A1C Assay
Common Name	Hemoglobin A1c Test System
Classification Name	Hemoglobin A1c Test System
Regulation	21 CFR 862.1373
Device Class	Class II
Product Code	PDJ
Panel	Clinical Chemistry

3. Identification of Predicate

Trade Name	Roche Diagnostics Operations (RDO)
510(k) Submitter	Cobas C13 Tina-Quant HbA1cDx Gen.3 Assay
510(k) Number	K160571
Clearance Date	December 19, 2016

4. Device Description

The Dimension® Hemoglobin A1C assay is an *in vitro* diagnostic device intended to measure the concentration of hemoglobin A1c in venous human anticoagulated whole blood. The assay consists of three reagents packaged in Dimension® Flex® cartridges. The reagents are liquid and ready to use.

5. Intended Use Statement

The Dimension® Hemoglobin A1C assay is an *in vitro* diagnostic assay for the quantitative determination of %HbA1c (DCCT/NGSP) and mmol/mol HbA1c (IFCC) in human anticoagulated venous whole blood for use on the Dimension® clinical chemistry system. Measurement of Hemoglobin A1c is used as an aid in diagnosis and monitoring of long-term blood glucose control in patients with diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.

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6. Technological Characteristics

(a) Similarities and Differences

Device Characteristic	Predicate Device Cobas C13 Tina-Quant HbA1cDx Gen.3 Assay (K160571)	Proposed Device Dimension® Hemoglobin A1C Assay
Intended Use	This test is intended for use as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. It is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche/Hitachi cobas c 513 clinical chemistry analyzer. HbA1c determinations are useful for monitoring of long-term blood glucose control in individuals with diabetes mellitus.	The Dimension® Hemoglobin A1C assay is an *in vitro* diagnostic assay for the quantitative determination of %HbA1c (DCCT/NGSP) and mmol/mol HbA1c (IFCC) in human anticoagulated venous whole blood for use on the Dimension® clinical chemistry system. Measurement of Hemoglobin A1c is used as an aid in diagnosis and monitoring of long-term blood glucose control in patients with diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.
Type of Test	Quantitative turbidimetric inhibition immunoassay	Same
Measurand	Whole blood Glycosylated Hemoglobin (HbA1c)	Same
Reporting Units	% HbA1c NGSP/DCCT and mmol/mol IFCC	Same
Measuring Ranges	*Hemoglobin* 4 to 35 g/dL (2.48 to 21.7 mmol/L) *HbA1c* 0.3 to 3.4 g/dL (0.186 to 2.11 mmol/L) *%HbA1c* 4.2 to 15.5% (23 to 146 mmol/mol)	*Hemoglobin* 5.0 to 25.0 g/dL (3.1 to 15.5 mmol/L) *HbA1c* 0.25 to 2.90 g/dL (0.16 to 1.80 mmol/L) *%HbA1c* 3.8 to 14.0% (18 to 130 mmol/mol)
Instrument Platform	Cobas c 513 (absorbance spectroscopy)	Dimension® RxL clinical chemistry system (absorbance spectroscopy)
Anticoagulants	Li-Heparin K2-EDTA K3-EDTA EDTA/Fluoride	K2-EDTA K3-EDTA Na Fluoride/Na2-EDTA Lithium Heparin Na Fluoride/ K-Oxalate

Device Characteristic	Predicate Device Cobas C13 Tina-Quant HbA1cDx Gen.3 Assay (K160571)	Proposed Device Dimension® Hemoglobin A1C Assay
Calibration Frequency	Each lot, every 29 days, and as required following quality control procedures	Each lot, every 30 days, and as required following quality control procedures
Reagent Stability	*Unopened* 2 – 8ºC until expiration date *On-board in use* 2 – 8ºC for 28 days	*Unopened* 2 – 8ºC until expiration date *On-board sealed* 2 – 8ºC for 30 days
Antibody	Polyclonal anti-HbA1c, ovine	Same

(b) Non-Clinical Performance Evaluation

(i) Method Comparison

Method comparison testing was performed in accordance with CLSI EP09-A3, *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition*. 147 human whole blood samples with values spanning the assay range were tested using the Dimension® Hemoglobin A1C Assay on the Dimension® RxL clinical chemistry system. Assay results were compared to NGSP reference method results from testing performed at an NGSP reference laboratory. Sample distribution is shown in Table A. Slope and Y-intercept results were generated with both Passing-Bablok and Deming regressions. Results are presented in Tables B, C, D, and E.

Table A. Method Comparison Sample Distribution

Range of Results (%HbA1c)	Percentage of Samples	Number of Samples
< 5	4.8%	7
5 to 6	12.2%	18
6 to 6.5	20.4%	30
6.5 to 7	21.8%	32
7 to 8	14.3%	21
8 to 9	8.2%	12
> 9	18.4%	27
Total	**100%**	**147**

Table B. Method Comparison, Passing-Bablok

Units	N	Slope [95% CI]	y-int. [95% CI]
NGSP (%HbA1c)	147	0.983 [0.966 to 1.001]	0.030 [-0.095 to 0.144]
IFCC (mmol/mol HbA1c)	147	0.973 [0.955 to 0.992]	0.437 [-0.474 to 1.450]

Table C. Bias Estimations, Passing-Bablok

%HbA1c	Bias	% Bias
5.0	-0.05	-1.10
6.5	-0.08	-1.24
8.0	-0.11	-1.33
12.0	-0.17	-1.45

Table D. Method Comparison, Deming

Units	N	Slope [95% CI]	y-int. [95% CI]
NGSP (%HbA1c)	147	0.978 [0.957 to 1.000]	0.052 [-0.094 to 0.198]
IFCC (mmol/mol HbA1c)	147	0.970 [0.948 to 0.992]	0.532 [-0.603 to 1.666]

Table E. Bias Estimations, Deming

%HbA1c	Bias	% Bias
5.0	-0.06	-1.16
6.5	-0.09	-1.40
8.0	-0.12	-1.55
12.0	-0.21	-1.77

(ii) Precision

Precision testing was performed in accordance with CLSI EP05-A3, *Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline – Third Edition.* Samples consisted of two (2) commercial quality controls and four (4) whole blood patient pools with target values of 5.0%, 6.5%, 8.0%, and 12.0% HbA1c. Testing was performed over twenty (20) testing days by two (2) operators using three (3) instruments and three (3) reagent lots on each instrument. One (1) calibration was performed over the duration of the study. Each testing day, two (2) runs were performed (with a minimum of 2 hours in between) for a total of 80 results for each sample. Data were analyzed using Analysis of Variance (ANOVA), consistent with the recommendations of CLSI EP05-A3. Results are presented in Tables F and G.

Table F. Precision, All Instruments, NGSP Units (%HbA1c)

SAMPLE	Mean	Repeat-ability		Between Run		Between Day		Between Instrument		Between Lot		Total	
		SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
MDP1	5.3	0.05	0.9	0.04	0.7	0.01	0.1	0.07	1.4	0.09	1.6	0.13	2.4
MDP2	6.4	0.05	0.7	0.03	0.5	0.03	0.4	0.09	1.4	0.00	0.0	0.11	1.7
MDP3	7.8	0.06	0.8	0.04	0.5	0.03	0.3	0.10	1.3	0.00	0.0	0.13	1.6
MDP4	11.9	0.09	0.8	0.05	0.4	0.05	0.4	0.06	0.5	0.18	1.5	0.22	1.8
QC 1	5.2	0.05	1.0	0.04	0.8	0.02	0.4	0.03	0.5	0.11	2.1	0.13	2.6
QC 2	9.5	0.08	0.8	0.06	0.7	0.03	0.3	0.12	1.2	0.03	0.3	0.16	1.7

Units: SD = % HbA1c, CV = %

Table G. Precision, All Instruments, IFCC Units (mmol/mol HbA1c)

SAMPLE	Mean	Repeat-ability		Between Run		Between Day		Between Instrument		Between Lot		Total	
		SD	CV	SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
MDP1	35	0.54	1.5	0.40	1.2	0.08	0.2	0.81	2.3	0.95	2.7	1.42	4.1
MDP2	47	0.52	1.1	0.33	0.7	0.28	0.6	0.95	2.0	0.00	0.0	1.17	2.5
MDP3	62	0.68	1.1	0.44	0.7	0.28	0.5	1.13	1.8	0.00	0.0	1.41	2.3
MDP4	107	0.99	0.9	0.57	0.5	0.56	0.5	0.60	0.6	1.96	1.8	2.41	2.3
QC 1	34	0.56	1.7	0.48	1.4	0.24	0.7	0.31	0.9	1.19	3.5	1.47	4.4
QC 2	81	0.87	1.1	0.68	0.8	0.36	0.4	1.26	1.6	0.27	0.3	1.73	2.2

Units: SD = mmol/mol HbA1c, CV = %

(iii) Total Error at Decision Levels

The bias estimation values determined in the method comparison study and precision estimates determined in the precision study were used to determine the total error at each of the levels listed in Tables H and I. Total error was calculated as follows:

$$\%TE = |\%Bias| + 1.96 \times \%CV \times \left(1 + \frac{\%Bias}{100}\right)$$

Table H. Total Error Summary, Passing-Bablok

%HbA1c Decision Level	% Bias	% CV	%TE
5.0	-1.10	2.4	5.8
6.5	-1.24	1.7	4.5
8.0	-1.33	1.6	4.4
12.0	-1.45	1.8	4.9

Table I. Total Error Summary, Deming

%HbA1c Decision Level	% Bias	% CV	%TE
5.0	-1.16	2.4	5.8
6.5	-1.40	1.7	4.7
8.0	-1.55	1.6	4.6
12.0	-1.77	1.8	5.2

(iv) Endogenous and Exogenous Interference

Testing to determine the interference bias of various endogenous interferents on the Dimension® Hemoglobin A1C Assay was performed according to CLSI EP07-A2, *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition.* The effect of each interferent was evaluated using a paired difference analysis. Four replicates were tested at each of two HbA1c levels: 6.5% ± 1.0% and 8.0% ± 1.0%. No significant interference (i.e., greater than ± 5.0%) was observed for the potential interferents at the concentrations listed in Table J.

Table J. Endogenous and Exogenous Interference

Interferent	Concentration
Acetaminophen	20 mg/dL
Ampicillin	100 mg/dL
Acetylsalicylic acid	100 mg/dL
Ascorbic acid	30 mg/dL
Calcium dobesilate	20 mg/dL
Bilirubin (Conjugated)	66 mg/dL
Bilirubin (Unconjugated)	66 mg/dL
Cefoxin sodium	250 mg/dL
Cholesterol	503 mg/dL
Cyclosporin	1.66 mg/dL
Doxycycline hyclate	5 mg/dL
Glucose	2000 mg/dL
Heparin	5 U/mL
Ibuprofen	50 mg/dL
Insulin	593 µU/mL
Intralipid	1000 mg/dL
Levodopa	2 mg/dL
Metformin	4 mg/dL
Methyldopa	2 mg/dL
Metronidazole	20 mg/dL
N-acetylcysteine	166.3 mg/dL
Phenylbutazone	40 mg/dL
Protein: Total	22 g/dL
Rheumatoid Factor	750 IU/mL
Rifampicin	6 mg/dL
Rosiglitazone	0.8mg/dL
Salicylic acid	60 mg/dL
Theophylline	10 mg/dL
Triglycerides	600 mg/dL

(v) Hemoglobin Variant Interference

Interference testing to determine the effect of hemoglobin variants on the Dimension® Hemoglobin A1C Assay was performed according to CLSI EP07-A2, *Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition*. Anticoagulated human blood samples with known concentrations of hemoglobin variant and HbA1c were analyzed. The effect of each hemoglobin variant on assay performance was evaluated comparing the *mean observed %HbA1c* values to the *mean expected %HbA1c* values. Four (4) replicates were tested for each sample. No significant interference bias (i.e., greater than ± 5.0%) was observed for HbC, HbD, HbE, and HbA2. Significant interference bias was observed for HbF. Results are presented in Tables K and L.

Table K. Hemoglobin Variant Samples

Hb Variant	n	Range (% Variant)	Range (%HbA1c)
HbC	37	26.1 to 40.0	4.4 to 15.7
HbD	20	24.8 to 38.4	5.0 to 13.0
HbE	22	19.7 to 30.4	4.7 to 11.0
HbS	22	27.2 to 36.3	5.3 to 14.0
HbA2	23	4.3 to 6.2	5.1 to 8.4
HbF	20	4.3 to 29.3	4.3 to 10.1

Table L. Hemoglobin Variant Interference

Hb Variant	Relative %Bias [Range of %Bias] Observed to Reference Method	
	HbA1c ~6%	HbA1c ~8%
HbC	-1.0% [-5.0% to 4.9%]	-0.9% [-4.6% to 4.4%]
HbD	-2.2% [-4.9% to 4.4%]	-2.5% [-4.4% to -1.3%]
HbE	-2.1% [-4.9% to 3.1%]	-2.5% [-4.3% to -1.0%]
HbS	-1.3% [-4.7% to 4.9%]	-2.0% [-4.9% to 3.5%]
HbA2	0.1% [-4.8% to 3.6%]	-2.0% [-3.0% to -1.1%]
HbF	-23.2% [-30.3% to 1.2%]	-24.7% [-25.8% to -23.3%]

(vi) Hemoglobin Derivatives

Interference testing to determine the effect of hemoglobin derivatives, including acetylated hemoglobin, carbamylated hemoglobin, labile hemoglobin, and hemoglobin fractions on the Dimension® A1C assay was performed in accordance with CLSI document EP07-A2. Inaccuracies (biases) due to these substances are less than or equal to 5 % at Hemoglobin A1c concentrations of 5.0% ± 1.0% , 6.5% ± 1.0%, and 8.0% ± 1.0%.

- Acetylated Hemoglobin with ≥ 50 mg/dL of acetylsalicylic acid
- Carbamylated Hemoglobin with ≥ 10 mmol/L of Cyanate
- Labile Hemoglobin with ≥ 1500 mg/dL of Glucose

(vii) Linearity

Linearity testing was conducted CLSI EP06-A, *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.* Nine (9) samples with HbA1c levels across the assay range were prepared and tested. Four (4) replicates were tested at each level. No deviations from linearity were observed for results from 3.6 to 15.9% HbA1c.

(viii) Limit of Blank (LoB) and Limit of Detection (LoD)

Limit of Blank (LoB) and Limit of Detection (LoD) testing was conducted in accordance with CLSI EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures*. The LoB was determined using 60 determinations with 5 blank samples each for tHb and 75 determinations with 5 blank samples each for % HbA1c/HbA1c. The LoD was determined using 60 determinations, with 5 low level samples each for tHb and 75 determinations with 5 low samples each for % HbA1c/HbA1c. Results are presented in Table M.

Table M. Limit of Blank / Limit of Detection

	HbA1c (%)	tHb (g/dL)	HbA1c (g/dL)
LoB	3.6	0.0	0.21
LoD	3.7	0.5	0.23

(ix) Anticoagulant Comparison

Testing was performed to demonstrate equivalence between five different anticoagulants in accordance with CLSI EP09-A2, *Method Comparison and Bias Estimation Using Patient Samples*. Testing was performed to demonstrate equivalence between K_2 EDTA, K_3 EDTA, Na Fluoride/Na_2 EDTA, Lithium Heparin and Na Fluoride/K-Oxalate collection tubes. HbA1c values were measured for each sample using the Dimension® Hemoglobin A1C Assay on the Dimension® RxL clinical chemistry system. Regression analysis was used to analyze the measured values using the K_2 EDTA samples as the comparator. The slope and y-intercept values were determined by Passing-Bablok and Deming regression. HbA1c values for the samples ranged from 4.7 to 12.8%. Results are presented in Tables N and O.

Table N. Anticoagulant Equivalence Summary, Passing-Bablok

Anticoagulant (y axis)	Comparator (x axis)	N	Slope [95% CI]	y-intercept [95% CI]
K_3-EDTA	K_2-EDTA	79	0.994 [0.982 to 1.007]	0.030 [-0.055 to 0.102]
Na Fluoride/ Na_2-EDTA	K_2-EDTA	79	0.997 [0.986 to 1.011]	0.006 [-0.080 to 0.074]
Lithium Heparin	K_2-EDTA	79	1.006 [0.995 to 1.019]	-0.038 [-0.120 to 0.041]
Na Fluoride/ K-Oxalate	K_2-EDTA	79	1.010 [0.994 to 1.023]	-0.037 [-0.113 to 0.059]

Table O. Anticoagulant Equivalence Summary, Deming

Anticoagulant (y axis)	Comparator (x axis)	N	Slope [95% CI]	y-intercept [95% CI]
K_3-EDTA	K_2-EDTA	79	0.997 [0.978 to 1.015]	0.011 [-0.102 to 0.124]
Na Fluoride/ Na_2-EDTA	K_2-EDTA	79	1.003 [0.985 to 1.020]	-0.033 [-0.135 to 0.069]
Lithium Heparin	K_2-EDTA	79	1.008 [0.990 to 1.027]	-0.042 [-0.152 to 0.068]
Na Fluoride/ K-Oxalate	K_2-EDTA	79	1.007 [0.989 to 1.025]	-0.018 [-0.127 to 0.091]

(x) Conclusion

The proposed Dimension® Hemoglobin A1C assay is substantially equivalent to the legally marketed predicate based on the similarities in intended use, technological characteristics, and performance testing presented above.