510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k160762

B. Purpose for Submission:

New device

C. Measurand:

Whole Blood Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative, enzymatic

E. Applicant:

Diazyme Laboratories

F. Proprietary and Established Names:

Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis)
Diazyme Direct HbA1c Assay Calibrator Set
Diazyme Direct HbA1c Assay Control Set

G. Regulatory Information:

Classification Name	Regulation Section	Device Class	Product Code	Panel
Glycosylated Hemoglobin Assay	21 CFR 864.7470	II	LCP	Hematology (81)
Calibrator	21 CFR 862.1150	II	JIT	Chemistry (75)
Quality Control Material (assayed and unassayed)	21 CFR 862.1660	I, reserved	JJX	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use below.

2. Indication(s) for use:

   Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis) test kit is intended for use in the quantitative determination of stable HbA1c in venous whole blood samples with on board blood lysis application in a clinical laboratory. This test is not to be used to diagnose or screen for diabetes. The measurement of HbA1c concentration is for use in monitoring long-term glucose control of persons with diabetes. For *in-vitro* diagnostic use only.

   Diazyme Direct HbA1c Assay Calibrator Set is intended to be used for calibration of Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis). For *in-vitro* diagnostic use only.

   Diazyme Direct HbA1c Assay Control Set is intended to be used for quality control by monitoring accuracy and precision of Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis). For *in-vitro* diagnostic use only.

3. Special conditions for use statement(s):

   For prescription use only

   This test is not for screening or diagnosis of diabetes

   For in-vitro diagnostic use only

   This test should not be used in monitoring daily glucose control

   Should not be used to replace daily home testing of urine and blood glucose levels

   Should not be used for analyzing samples from patients with conditions causing shortened red blood cell survival, such as hemolytic diseases, pregnancy, and significant acute or chronic blood loss

   Hemoglobinopathies may interfere with glycated hemoglobin analysis. Hemoglobin variant interference study results indicate that there is no significant interference for Hemoglobin C (≤38.2%), Hemoglobin D (≤43.1%), Hemoglobin E (≤21.1%), and Hemoglobin S (≤37.3%).

   High HbF (> 10%) may result in inaccurate HbA1c values.

The linearity of the assay is up to 12% HbA1c. Samples with values above 12% should not be diluted and retested. Instead, the values should be reported as higher than 12% (> 12%).

The assay is formulated for use with K2-EDTA whole blood samples.

Total hemoglobin in the sample should be in the range 8 – 21 g/dL.

4. Special instrument requirements:

All validation studies were performed on the Roche Modular P automated analyzer.

I. Device Description:

The Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis) contains the following:

- Lysis Buffer (>100mM Tris, pH >8.0; 1% Triton X 100, >1.5% nonionic and ionic detergents; >4KU/mL proteases)
- Reagent 1 (5mM MES,pH > 6.0; <3mM redox agent)
- Reagent 2 (>5mM bis-Tris, pH >7.0; >10U/mL fructosyl valine oxidase (FVO) enzyme; 90U/mL POD; >50μM chromagen)

The Diazyme Direct HbA1c Assay Calibrator Set consists of two levels of lyophilized hemolyzed human whole blood with chemical additives. The target HbA1c concentration of Level 1 calibrator is 6.0% and Level 2 is 11%.

The Diazyme Direct HbA1c Assay Control Set consists of two levels of lyophilized human whole blood with chemical additives. The target HbA1c concentration of the Level 1 control is 6.2% HbA1c and Level 2 is 9.5% HbA1c.

The Diazyme Direct HbA1c Assay Calibrator Set (Level 1, Level 2) and the Diazyme Direct HbA1c Assay Control Set (Level 1, Level 2) must be purchased separately.

Each donor unit of human whole blood used in the preparation of the Control Set and Calibrator Set was tested by FDA-approved methods and found negative for the Human Immunodeficiency Virus Antibody (HIV I/II Ab), Hepatitis B Surface Antigen (HBsAg), and Hepatitis C Virus Antibody (HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):

Diazyme Direct HbA1c Enzymatic Assay
Diazyme Direct HbA1c Assay Calibrator Set
Diazyme Direct HbA1c Assay Control Set

2. Predicate 510(k) number(s):

   k070734

3. Comparison with predicate:

Similarities/Differences Assay		
Item	Device Direct HbA1c Assay (Enzymatic, On-Board Lysis)	Predicate Direct HbA1c Enzymatic Assay (k070734)
Intended Use	Quantitative determination of stable HbA1c in human whole blood samples. Measurement of hemoglobin A1c is a valuable indicator for long-term diabetic control. For *in-vitro* diagnostic use only.	Same
Test principle	Enzymatic	Same
Sample Type	K2-EDTA whole blood	Same
Sample Lysis	Samples are lysed on-board the analyzer	Samples are lysed manually
Reagents	Lysis Buffer, Reagent 1, Reagent 2	Lysis Buffer, Reagent 1a, Reagent 1b, Reagent 2
Blood Sample Volume	150µL (10µL on-board)	20µL
Measuring range	4.0 – 12.0 % HbA1c	Same
Hematocrit range	8 – 21 g/dL	9 – 21 g/dL
Storage conditions	2 – 8°C	Same
Use Lifetime (on-board)	4 weeks	Same

Similarities/Differences Calibrator		
Item	Device Direct HbA1c Assay Calibrator Set	Predicate Direct Enzymatic HbA1c Calibrator Set (k070734)
Intended Use	Intended to be used for calibration of Diazyme Direct HbA1c Assay. For in vitro diagnostic use only.	Same
Format (Material)	Lyophilized whole blood based	Same
Levels	Two (Level 1, Level 2)	Same
Storage conditions	2 – 8°C	Same
Use Lifetime (reconstituted)	14 days	Same

Similarities/Differences Control		
Item	Device Direct HbA1c Assay Control Set	Predicate Direct Enzymatic HbA1c Control Set (k070734)
Intended Use	Intended to be used for quality control by monitoring accuracy and precision of the HbA1c Assay. For in vitro diagnostic use only.	Same
Format (Material)	Lyophilized whole blood based	Same
Levels	Two (Level 1, Level 2)	Same
Storage conditions	2 – 8°C	Same
Use Lifetime (reconstituted)	14 days	Same

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP05-A2, Evaluation of Precision of Clinical Chemistry Devices, Approved Guideline, Second Edition

CLSI EP06-A, Evaluation of the Linearity of Quantitative Analytical Measurement Procedure: A Statistical Approach, Approved Guideline

CLSI EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition

CLSI: EP09-A2, Measurement Procedure Comparison and Bias Estimation Using Patient Samples, Approved Guideline, Second Edition

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, Approved Guideline, Second Edition

L. Test Principle:

The Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis) is an enzymatic assay in which lysed whole blood samples are subjected to extensive protease digestion with Bacillus sp protease. This process releases amino acids including glycated valines from the hemoglobin beta chains. Glycated valines then serve as substrates for specific recombinant fructosyl valine oxidase (FVO) enzyme. The recombinant FVO specifically cleaves N-terminal valines and produces hydrogen peroxide. This, in turn, is measured using a horseradish peroxidase (POD) catalyzed reaction and a suitable chromogen. No separate

measurement for total Hemoglobin (Hb) is needed in this Direct HbA1c Assay.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Internal Precision Study

   Precision studies were performed according to CLSI EP5-A2 guideline. Within-run precision, between-run precision, between-day precision, and total precision were determined using the Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis). The study included five unaltered, K2- EDTA whole blood samples (4.6%, 5.4%, 7.5%, 9.7% and 11.9% HbA1c) as well as three lots of Diazyme Direct HbA1c Assay calibrators and three lots of Diazyme Direct HbA1c Assay controls (Level 1, Level 2). Samples were analyzed in duplicate twice a day for 20 days with three lots of reagent on the Roche Modular P analyzer. Results are shown below:

Sample	Mean (N=240)	Within-Run		Between-Run		Between-day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	4.64	0.04	0.8%	0.07	1.5%	0.00	0.0%	0.08	1.7%
Sample 2	5.36	0.05	0.9%	0.05	0.9%	0.00	0.0%	0.07	1.2%
Sample 3	7.51	0.05	0.6%	0.05	0.7%	0.00	0.0%	0.07	0.9%
Sample 4	9.61	0.06	0.6%	0.05	0.5%	0.03	0.3%	0.08	0.9%
Sample 5	11.89	0.09	0.7%	0.08	0.6%	0.04	0.4%	0.12	1.0%
Cntrl 1 Lot 1	6.22	0.05	0.8%	0.03	0.5%	0.01	0.1%	0.06	1.0%
Cntrl 2 Lot 1	9.47	0.06	0.6%	0.04	0.4%	0.02	0.2%	0.07	0.8%
Cntrl 1 Lot 2	5.70	0.04	0.8%	0.04	0.7%	0.02	0.4%	0.06	1.1%
Cntrl 2 Lot 2	9.11	0.05	0.5%	0.04	0.4%	0.03	0.3%	0.07	0.7%
Cntrl 1 Lot 3	6.04	0.05	0.7%	0.05	0.9%	0.00	0.0%	0.07	1.2%
Cntrl 2 Lot 3	9.68	0.05	0.6%	0.04	0.4%	0.00	0.0%	0.07	0.7%

Cal 1 Lot 1	6.22	0.04	0.6%	0.04	0.6%	0.00	0.0%	0.05	0.9%
Cal 2 Lot 1	12.30	0.07	0.6%	0.04	0.3%	0.03	0.2%	0.09	0.7%
Cal 1 Lot 2	5.68	0.05	0.9%	0.04	0.7%	0.02	0.4%	0.07	1.2%
Cal 2 Lot 2	9.70	0.06	0.6%	0.04	0.4%	0.02	0.2%	0.07	0.8%
Cal 1 Lot 3	6.04	0.05	0.8%	0.04	0.7%	0.00	0.0%	0.06	1.1%
Cal 2 Lot 3	11.30	0.06	0.5%	0.04	0.3%	0.01	0.1%	0.07	0.6%

External Precision Study

An external precision study using five EDTA whole blood samples (4.6%, 5.4%, 7.5%, 9.7% and 11.9% HbA1c) as well as three lots of Diazyme Direct HbA1c Assay calibrators and three lots of Diazyme Direct HbA1c Assay controls (Level 1, Level 2) was performed at two external sites and one internal site. Samples were tested in duplicate, 2 runs per day for 5 working days with one lot of reagent by three different operators on three different Modular P instruments. Results for all sites combined are shown below:

Sample	**Mean (n=60)**	**Within-Run**		**Between-Run**		**Between-day**		**Between-Site**		**Total**	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	4.67	0.05	1.0%	0.04	0.8%	0.02	0.5%	0.07	1.4%	0.07	1.4%
Sample 2	5.37	0.04	0.8%	0.05	1.0%	0.00	0.0%	0.06	1.2%	0.07	1.2%
Sample 3	7.52	0.05	0.7%	0.06	0.8%	0.00	0.0%	0.07	0.9%	0.08	1.0%
Sample 4	9.67	0.07	0.8%	0.11	1.1%	0.00	0.0%	0.12	1.3%	0.13	1.4%
Sample 5	11.92	0.09	0.8%	0.09	0.8%	0.06	0.5%	0.14	1.2%	0.14	1.2%
Cntrl 1 Lot1	6.21	0.03	0.6%	0.00	0.0%	0.00	0.0%	0.03	0.5%	0.03	0.6%
Cntrl 2 Lot1	9.48	0.05	0.6%	0.05	0.6%	0.03	0.3%	0.08	0.9%	0.08	0.9%
Cntrl 1 Lot2	5.63	0.04	0.7%	0.02	0.4%	0.03	0.6%	0.06	1.0%	0.06	1.0%
Control 2 Lot2	9.11	0.05	0.5%	0.04	0.4%	0.03	0.3%	0.07	0.7%	0.07	0.7%
Cntrl 1 Lot3	6.01	0.05	0.8%	0.01	0.2%	0.02	0.3%	0.06	0.9%	0.06	0.9%

Cntrl 2 Lot3	9.65	0.06	0.7%	0.05	0.5%	0.04	0.4%	0.09	0.9%	0.09	1.0%
Cal 1 Lot1	6.21	0.04	0.7%	0.03	0.5%	0.00	0.0%	0.05	0.8%	0.06	0.9%
Cal 2 Lot1	12.32	0.07	0.6%	0.05	0.4%	0.05	0.4%	0.10	0.8%	0.10	0.8%
Cal 1 Lot2	5.63	0.06	1.0%	0.00	0.0%	0.02	0.3%	0.05	1.0%	0.06	1.1%
Cal 2 Lot2	9.74	0.06	0.6%	0.06	0.7%	0.03	0.4%	0.10	1.0%	0.10	1.0%
Cal 1 Lot3	6.02	0.05	0.8%	0.03	0.4%	0.01	0.1%	0.05	0.9%	0.05	0.9%
Cal 2 Lot3	11.36	0.06	0.6%	0.08	0.7%	0.05	0.5%	0.12	1.0%	0.12	1.0%

b. *Linearity/assay reportable range:*

Linearity was evaluated according to CLSI-06A. The linearity of the Direct HbA1c Assay (Enzymatic, On-Board Lysis) was verified using two K2-EDTA whole blood samples, including a normal sample with HbA1c concentration of 3.8% and an elevated HbA1c level sample with HbA1c concentration at 12.3%. The normal and high samples were inter-mixed to make a total of 11 samples with concentrations covering the assay range (3.8, 4.7, 5.5, 6.4, 7.2, 8.1, 8.9, 9.8, 10.6, 11.5 and 12.3%). The samples were analyzed in replicates of three on the Roche Modular P analyzer. % recovery was calculated by comparing the mean observed %HbA1c to the expected % HbA1c. Recovery for all 11 levels ranged from 97-100%. The linear regression is as follows:

$y = 0.9859x – 0.0588$, $r^2 = 0.999$

The study supports the sponsors claimed linearity range of 4.0-12.0% HbA1c.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability:

The Direct HbA1c Assay (Enzymatic, On-Board Lysis) is certified with the National Glycohemoglobin Standardization Program (NGSP). The NGSP certification expires in one year. See NGSP website for current certification at http://www.ngsp.org.

Test results are reported in the NGSP format. The relationship between HbA1c results from the NGSP network (%HbA1c) and the IFCC network (mmol/mol) has been evaluated and a master equation has been developed: NGSP = [0.09148 × IFCC] + 2.152. The IFCC results (mmol/mol) can be obtained by calculation on-board the analyzer.

Value Assignment:

Controls:

With a reference lot of Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis) reagents and calibrator set, the bi-level control materials are value assigned by testing the two levels of control materials in replicates of nine using 3 lot of Diazyme Direct HbA1c reagent to obtain mean values and a range for each level of control. The mean values are assigned as the target values of the controls. Values are given in NGSP/DCCT value system. The control mean and range for each of the two control levels are shown below:

Level 1: Mean 6.2% Range: 5.0 to 7.4%

Level 2: Mean 9.5% Range: 7.6-11.4%

Calibration:

The master calibrators are traceable to an NGSP certified reference method.

Stability:

Real-time stability shelf life studies are ongoing. Accelerated (shelf life) and real-time (reconstituted, on-board) stability protocols were reviewed and considered acceptable to support the following claims:

Stability claim	**Reagent**	**Calibrators**	**Controls**
Shelf life	18 months at 2-8°C	18 months at 2-8°C	18 months at 2-8°C
Reconstituted	N/A	14 days at 2-8°C	14 days at 2-8°C
On-board	4 weeks	N/A	N/A

d. Detection limit:

Detection limit studies were performed according to the CLSI EP17-A2 guideline.

Limit of Blank (LoB)

To determine the LoB, 60 replicates of a true blank solution were tested with the Direct HbA1c Assay (Enzymatic, On-Board Lysis) reagents on the Roche Modular P analyzer using three lots of reagents. The LoB was defined as the highest mean of the 57^{th} and 58^{th} replicate values.

Limit of Detection (LoD)

To determine the LoD, five low level whole blood samples were tested with the Direct HbA1c Assay (Enzymatic, On-Board Lysis) reagents on the Roche Modular P

analyzer. 12 replicates of each sample were tested in three runs, with four replicates per run, and three lots of reagents. The LoD was calculated as follows:
$LoD = LoB + (1.645 * SD_{LoD\ samples})$.

Limit of Quantitation (LoQ)

To determine the LoQ, five whole blood samples from a commercial source were diluted with true blank solution to a target concentration range of 0.5% to 4.0%. The diluted whole blood samples were tested with three lots of the Direct HbA1c Assay (Enzymatic, On-Board Lysis) reagents on the Roche Modular P analyzer (n = 120). LoQ was defined as the lowest concentration at which %CV ≤ 20%.

Results are as follows:

LoB = 0.2%

LoD = 0.5%

LoQ = 0.8%

e. Analytical specificity:

Endogenous substances:

To determine the level of interference from substances present in whole blood samples, the Direct HbA1c Assay (Enzymatic, On-Board Lysis) was used to test three whole blood samples containing low (5.5%), medium (8%), and high (11%) HbA1c concentrations according to the CLSI EP7-A2 guideline. To evaluate interference, each whole blood sample was spiked with potential endogenous interference substances and tested in triplicate on the Roche Modular P analyzer. The sponsor defined non-significant interference as ≤ ±10% bias in recovery for spiked samples compared to control samples. Results are shown below:

Substance	**Highest Concentration tested at which no interference was observed**
Ascorbic Acid	12mg/dL
Bilirubin	15 mg/dL
Bilirubin Conjugated	13 mg/dL
Triglycerides	4000 mg/dL
Glucose	4000 mg/dL
Uric Acid	30 mg/dL
Urea	80 mg/dL
Acetaminophen	20 mg/dL
Acetysalicylic Acid	65.2 mg/dL
Metformin	4 mg/dL
Ibuprofen	50 mg/dL

Substance	Highest Concentration tested at which no interference was observed
Glyburide	0.19 mg/dL
Total Protein	21 g/dL
Vitamin E	13.6 mg/dL
Rheumatoid factor	375 IU/mL

Hemoglobin interference:
Hemoglobin interference testing was performed by evaluating 102 K2-EDTA whole blood patient samples in which the % HbA1c value was determined by the Tosoh G8 HPLC method and the hemoglobin value was determined by a legally marketed device (Roche TinaQuant II Hemoglobin reagent). The HbA1c values ranged from 4.6% to 10% and hemoglobin ranged from 8 g/dL to 21 g/dL. The samples were tested with the Diazyme Direct HbA1c Assay (Enzymatic, On-Board Lysis) and the % deviation from the expected HPLC value was calculated. The sponsor defined non-significant interference as ≤ ± 10% difference from the reference method. The results support the claimed hematocrit range of 8 – 21 g/dL.

Hemoglobin variant interference:
A hemoglobin variant study was performed using 56 whole blood samples (5.0 – 14. 4% HbA1c) containing known levels of hemoglobin variants C, D, E, F and S. The samples were tested for % HbA1c in singlicate using the Direct HbA1c Assay (Enzymatic, On-Board Lysis) and results were reported as % difference compared to results obtained on the reference method (Primus HPLC method, k891235). Non-significant interference was defined as ≤ ± 10% difference between the candidate and reference methods.

The testing results indicate that there is no significant interference for Hemoglobin C (≤ 38.2%), Hemoglobin D (≤ 43.1%), Hemoglobin E (≤ 21.1%), and Hemoglobin S (≤ 37.3%).

The labeling contains the following limitation statements:

"Hemoglobinopathies may interfere with glycated hemoglobin analysis. Testing results indicate that there is no significant interference for Hemoglobin C (≤38.2%), Hemoglobin D (≤43.1%), Hemoglobin E (≤21.1%), and Hemoglobin S (≤37.3%).

"High HbF (> 10%) may result in inaccurate HbA1c values."

Labile A1c interference:

Three whole blood samples containing 0, 500, and 1000 mg/dL glucose were incubated for five hours at 37°C to facilitate the formation of labile A1c. The samples were tested in triplicate using the Direct HbA1c Assay (Enzymatic, On-Board Lysis). The sponsor defined non-significant interference as ≤ ± 10% difference between samples containing glucose and the control sample. The results support the sponsor's

claim that labile HbA1c does not interfere with the Direct HbA1c Assay (Enzymatic, On-Board Lysis).

Carbamylated hemoglobin interference:

Three whole blood samples containing 0, 150, and 300 mg/dL urea were incubated for five hours at 37°C to facilitate the formation of carbamylated hemoglobin. The samples were tested in triplicate using the Direct HbA1c Assay (Enzymatic, On-Board Lysis). The sponsor defined non-significant interference as ≤ ± 10% difference between samples containing urea and the control sample. The results support the sponsor's claim that carbamylated hemoglobin does not interfere with the Direct HbA1c Assay (Enzymatic, On-Board Lysis).

Acetylated hemoglobin interference:

Three whole blood samples containing 0, 400, and 800 mg/dL acetylsalicylic acid were incubated for five hours at 37°C to facilitate the formation of acetylated hemoglobin. The samples were tested in triplicate using the Direct HbA1c Assay (Enzymatic, On-Board Lysis). The sponsor defined non-significant interference as ≤ ± 10% difference between samples containing acetylsalicylic acid and the control sample. The results support the sponsor's claim that acetylated hemoglobin does not interfere with the Direct HbA1c Assay (Enzymatic, On-Board Lysis).

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted by testing a total of 376 K2- EDTA whole blood patient samples at 3 external sites (124 at site 1, 132 at site 2, and 120 at site 3). The samples tested ranged from 4.2 to 12.0% HbA1c. Samples were analyzed in singlicate on three Roche Modular P analyzers by three operators. Samples were tested with one lot of the Direct HbA1c Assay (Enzymatic, On-Board Lysis) and compared to the Tosoh Bioscience G8 HPLC method.

Linear regression results are as follows:

Site	N	Slope (95%CI)	Intercept (95% CI)	R^2
1	124	1.006 (0.983-1.030)	0.04 (-0.13 to 0.21)	0.9918
2	132	1.033 (1.015-1.051)	-0.126 (-0.27 to 0.015)	0.9950
3	120	1.026 (1.005-1.047)	-0.18 (-0.34 to -0..01)	0.9938
Combined	376	1.023 (1.011-1.035)	-0.090 (-0.18 to 0.00)	0.9937

Deming regression results are as follows:

Site	N	Slope (95%CI)	Intercept (95% CI)	R^2
1	124	1.015 (0.992-1.038)	-0.02 (-0.19 to -0.15)	0.9918
2	132	1.039 (1.021-1.057)	-0.167 (-0.31 to -0.03)	0.9950
3	120	1.033 (1.012-1.054)	-0.23 (-0.40 to -0.06)	0.9938
Combined	376	1.030 (1.018-1.042)	-0.14 (-0.23 to -.050)	0.9937

b. Matrix comparison:

Not applicable. The Direct HbA1c Assay (Enzymatic, On-Board Lysis) is for use with K2-EDTA whole blood samples only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The sponsor states the following:

The American Diabetes Association (ADA) criteria for testing HbA1c to diagnose diabetes[1] is listed in the following table:

Category	HbA1c Range (NGSP/DCCT)
Normal	< 5.7%
Prediabetes (increased risk for diabetes)	5.7% - 6.4%
Diabetes	≥ 6.5%

The HbA1c value can be found at as low as 4.0% in healthy population.[2,3] The American Diabetes Association recommends that a reasonable diabetes treatment goal for many

nonpregnant adults is < 7.0% HbA1c.[1] However, each laboratory should establish its own reference range and HbA1c goal in their country of business taking into account sex, age, ethnicity and individual patient situation.

References:

1. American Diabetes Association. Standards of medical care in diabetes — 2015. Diabetes Care 2015; 38 (suppl 1): S1-S93
2. Sacks DB (ed). Global harmonization of hemoglobin A1c. Clinical Chemistry 2005; 51(4): 681-683
3. Steffes M, *et al*. Hemoglobin A1c measurements over nearly two decades: sustaining comparable values throughout the diabetes control and complications trial and the epidemiology of diabetes interventions and complications study. Clinical Chemistry 2005; 51(4): 753-758

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.