

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k063209

B. Purpose for Submission:

New Device

C. Measurand:

Hemoglobin A1c (HbA1c)

D. Type of Test:

Quantitative immunoturbidimetric assay, calibrators, and controls

E. Applicant:

ThermoFisher Scientific

F. Proprietary and Established Names:

HbA1c Test System, HbA1c Calibrators, HbA1c Control Normal, HbA1c Control Abnormal.

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7470 Assay, glycosylated hemoglobin

21 CFR 864.8165 Calibrator for hemoglobin or hematocrit measurement

21 CFR 862.1660 Quality control material (assayed and unassayed)

2. Classification:

Assay -Class II

Calibrator – Class II

Control – Class I, reserved

3. Product code:

LCP, KRZ, JJX

4. Panel:

Assay and Calibrators - Hematology (71), Controls –Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

The DPC T60 hemoglobin A1c (HbA1c) test system with associated calibrators and controls is intended for quantitative in-vitro diagnostic determination of the hemoglobin A1c (HbA1c) concentration as a percentage of total hemoglobin in human whole blood using T60 Clinical Chemistry Analyzers. Measurement of percent HbA1c is effective in monitoring long-term glucose control in individuals with diabetes mellitus.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

DPC T60 Clinical Chemistry Analyzers

I. Device Description:

The device consists of three reagents, four calibrators, and two controls. Reagent A contains sheep anti-HbA1c antibodies buffers and stabilizers, reagent B contains HbA1c-polyhapten buffers and stabilizers, and reagent C contains phosphate buffer and stabilizers. The lyophilized calibrators and controls are human and sheep blood based hemolysate and reconstituted with water.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Bio-Rad Laboratories VARIANT II Hemoglobin A1c Program.

Boehringer Mannheim Precinorm HbA1c and Precipath HbA1c

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

k984268, k934070

3. Comparison with predicate:

Similarities		
Item	k063209 Device	K984268 Predicate
Traceability	Standardized to IFCC reference method and transferable to DCCT/NGSP by calculation.	Standardized to IFCC reference method and transferable to DCCT/NGSP by calculation.
Results	HbA1c is automatically calculated as a percent of total hemoglobin	HbA1c is automatically calculated as a percent of total hemoglobin
Calibrator	Lyophilized blood based	Lyophilized blood based
Reagents	Liquid ready to use	Liquid ready to use

Differences		
Item	k063209 Device	K984268 Predicate
Sample type	EDTA-whole blood	EDTA, sodium heparin, or sodium citrate whole blood.
Sample pretreatment	Manual pretreatment with Hemolyzing reagent	No manual pretreatment required
Measuring range	4% to 17% HbA1c	1.3% to 18.9% HbA1c
Detection Method	Turbidimetric inhibition immunoassay for hemolyzed whole blood.	Chromatographic separation of HbA1c on a cation exchange cartridge
Similarities		
Item	k063209 Device	K934070 Predicate
Form	Lyophilized blood based	Lyophilized blood based
Storage	Unopened at 2-8°C	Unopened at 2-8°C

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

CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures:
A Statistical Approach

CLSI EP7-A: Interference Testing in Clinical Chemistry

CLSI EP9-A: Method Comparison and Bias Estimation Using Patient Samples

L. Test Principle:

The HbA1c concentration is determined by turbidimetric inhibition immunoassay using hemolyzed whole blood samples. Glycohemoglobin (HbA1c) in the sample reacts with anti-HbA1c antibody in Reagent A to form a soluble antigen-antibody complex. The polyhapten in Reagent B react with excess anti-HbA1c antibodies to form an insoluble antibody-polyhapten complex, which is determined turbidimetrically. HbA1c results are expressed as a percentage of total hemoglobin.

Liberated hemoglobin in the hemolyzed sample is converted to a derivative having a characteristic absorption spectrum which is measured bichromatically.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision was performed using CLSI EP5-A as a guideline with normal and elevated whole blood patient samples and Control Normal and Control Abnormal with one T60 analyzer and one reagent lot for 20 days, (n = 80). Results are summarized below.

HbA1c%	Whole Blood Mean 5.4%		Control Normal Mean 6.6%		Control Abnormal Mean 10.7%		Whole Blood Mean 11.4%	
	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Within run	0.05	0.9	0.08	1.2	0.12	1.2	0.10	0.9
Between run	0.11	2.1	0.10	1.6	0.14	1.3	0.08	0.7
Total	0.12	2.3	0.17	2.5	0.24	2.3	0.18	1.6

b

b. Linearity/assay reportable range:

The reportable range of the assay is 4% to 17% HbA1c. Linearity across much of the reportable range was demonstrated by mixing a high HbA1c

sample (15.55% HbA1c) and a low HbA1c sample (4.35% HbA1c) in 10% increments. Each sample was measured in duplicate and the mean measured values were within $\pm 3.5\%$ of the expected values. A linear regression plot produced a slope of 1.03 and a y-intercept of 0.00.

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

Traceability

The calibrator values are traceable to the IFCC and NGSP reference methods. HbA1c and Hb values are assigned to each calibrator with the HbA1c IFCC Reference Method and the Hb Cyanmethemoglobin Reference method, respectively.

The IFCC HbA1c% results are calculated straight from HbA1c (g/dl) and total Hb (g/dL):

$$\text{HbA1c\% (IFCC)} = \text{HbA1c (g/dL)} / \text{Hb (g/dL)} \times 100$$

The DCCT/NGSP HbA1c% values are calculated via the Master equation, by the analyzer:

$$\text{HbA1c\% (DCCT/NGSP)} = 0.915 \times \text{HbA1c \% (IFCC)} + 2.15$$

The control HbA1c (g/dL) target values are traceable to the HbA1c IFCC Reference Method, and Hb (g/L) target values are traceable to Hb Cyanmethemoglobin Reference method via the calibrators. The final product control values for HbA1c Control Normal and HbA1c Control Abnormal are confirmed by calibrating Hb (g/dl) and HbA1c (g/dl) with the calibration set included in the HbA1c reagent kit, which is traceable to IFCC reference method. Multiple runs and calibrations are performed with several instruments to arrive at the final product control values.

Stability

Calibrators and controls are stable until the expiration date printed on the label when stored unopened at 2-8°C. Once opened calibrators are stable for 8 hours at 15-25°C, 2 days at 2-8°C, and 3 months at -20°C. Once opened controls are stable for 8 hours at 15-25°C, 7 days at 2-8°C, and 3 months at -20°C.

d. *Detection limit:*

The analytical sensitivity, or detection limit, was determined with 24 replicates of 0.9 % NaCl solution within one run. The analytical sensitivity (Limit of Blank) was defined as the concentration corresponding to three standard deviations above the average concentration. Based on the above procedure, the following results were obtained:

- Hb - 0.3 g/dl.

- HbA1c - 0.1 g/dL

The sponsor is claiming 4% HbA1c as the low end of the reportable range of this assay.

e. Analytical specificity:

Interferents were added to a normal HbA1c sample at multiple concentrations and tested in one run. The results showed no interference at levels up to 30 mg/dL ascorbic acid, 58 mg/dL bilirubin, and 1000 mg/dL Intralipid.

HbA0, HbA1a, HbA1b, acetylated hemoglobin, carbamylated hemoglobin, glycated albumin, and labile HbA1c showed no cross reactivity when tested. Cross reactivity to HbA1d was not evaluated.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A comparison study to the predicate method was performed using CLSI EP9-A as a guideline. 61 EDTA whole blood samples from diabetics were evaluated with the following results.

Linear regression (Deming) (HbA1c %, DCCT/NGSP)

$$y = 0.93x + 0.2$$

$$r = 0.994$$

The sample concentrations ranged from 4.7 to 17.0% by the predicate method and 5.0 to 16.2% by the ThermoFisher HbA1c test system.

b. Matrix comparison:

Not Applicable.

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:

Metabolically healthy patients: 4.8 - 6.0%

Diabetes patients with HbA1c levels below 7% meet the goal of the American Diabetes Association. The ADA suggests therapeutic action at HbA1c levels above 8%.

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.