

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

A. 510(k) Number:

k130255

B. Purpose for Submission:

New device

C. Measurand:

Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative, enzymatic

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Hemoglobin A1c

Hemoglobin A1c Calibrators

Hemoglobin A1c Controls

G. Regulatory Information:

Regulation Description	Product Code	Device Class	Regulation	Panel
Hemoglobin A1c Test System	PDJ	II	21 CFR § 862.1373	Chemistry, 75
Glycosylated Hemoglobin Assay	LCP	II	21 CFR 864.7470	Hematology, 81
Calibrator	JIT	II	21 CFR §862.1150	Chemistry, 75
Quality Control Material	JJX	II	21 CFR §862.1660	Chemistry, 75

H. Intended Use:

1. Intended use(s): See Indications for use below.
2. Indication(s) for use:

The Hemoglobin A_{1c} assay is used in clinical laboratories for the quantitative *in vitro* measurement of percent hemoglobin A_{1c} (NGSP) or HbA_{1c} fraction mmol/mol (IFCC) in human whole blood and hemolysate on the ARCHITECT c 8000 System.

Hemoglobin A_{1c} measurements are used as an aid in the diagnosis of diabetes mellitus, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.

The Hemoglobin A_{1c} Calibrators are for use in the calibration of the Hemoglobin A_{1c} assay on the ARCHITECT c 8000 System.

The Hemoglobin A_{1c} Controls are for the estimation of test precision and the detection of systematic analytical deviations of Hemoglobin A_{1c} assay on the ARCHITECT c 8000 System.

3. Special conditions for use statement(s):

- For prescription use only
- This device has significant negative interference with fetal hemoglobin (HbF). HbA_{1c} results are invalid for patients with abnormal amounts of HbF including those with known Hereditary Persistence of Fetal Hemoglobin.
- Glycated HbF is not detected by the assay as it does not contain the β-chain that characterizes HbA_{1c}. However, HbF is measured in the total Hb assay and as a consequence, specimens containing high amounts of HbF (>5%) may result in lower than expected mmol/mol HbA_{1c} values (IFCC) and % HbA_{1c} values (DCCT/NGSP).
- The Hemoglobin A_{1c} assay should not be used to diagnose diabetes during pregnancy. Hemoglobin A_{1c} reflects the average blood glucose levels over the preceding 3 months (*i.e.*, the average life span of a red blood cell) and therefore may be falsely low during pregnancy or any other condition associated with recent onset of hyperglycemia and/or decreased red blood cell survival.
- The Hemoglobin A_{1c} assay should not be used to diagnose or monitor diabetes in patients with the following conditions:
 - hemoglobinopathies except as demonstrated to produce acceptable performance (e.g., sickle cell trait)
 - abnormal red blood cell turnover. (e.g., anemias from hemolysis and iron deficiency)
 - malignancies, and severe chronic hepatic and renal disease
- In cases of rapidly evolving Type 1 diabetes, the increase of HbA_{1c} values might be delayed compared to the acute increase in glucose concentrations. In these conditions, diabetes mellitus must be diagnosed based on plasma glucose concentrations and/or the typical clinical symptoms.
- This test should not replace glucose testing for patients with Type 1 diabetes, pediatric patients or pregnant women.

4. Special instrument requirements:

For use on the ARCHITECT c8000 System

I. Device Description:

The Hemoglobin A1c Reagent Kit contains two working reagents, Reagent 1 and Reagent 2 and a hemolyzing reagent (Diluent) with the following constituents:

Reagent	Reactive Ingredients	Concentration
Reagent 1	10-(carboxymethylaminocarbonyl)-3,7-bis(dimethylamino)phenothiazine sodium salt	0.000817%
	Protease (bacterial)	< 1 mU/dL
Reagent 2	Peroxidase (horseradish)	5 to 15 kU/dL
	Fructosyl-peptide-oxidase (<i>E. coli</i> , recombinant)	300 to 900 U/dL
Diluent	Sodium nitrite	> 0.05 to < 0.3%

Inactive Ingredients: Reagent 1 contains sodium azide as a stabilizer and preservative. Reagent 1 and Diluent contain ProClin 300 as a preservative. Reagent 2 contains ofloxacin as a preservative.

The Hemoglobin A1c assay consists of two application types: The Whole Blood application used an automated on-board pretreatment with hemolyzing reagent, (Diluent). The Hemolysate application consists of a manual pretreatment step which is performed using the hemolyzing reagent before the sample is placed on the analyzer.

The Hemoglobin A1c Calibrators

The Hemoglobin A1c Calibrators are for use in the calibration of the Hemoglobin A1c assay on the ARCHITECT c 8000 System.

The Hemoglobin A1c Calibrator Kit contains two levels of calibrator material, Calibrator 1 (Cal 1) and Calibrator 2 (Cal 2). A1c Calibrators (lyophilized) contain hemoglobin and glycated hemoglobin from human whole blood. Prior to lyophilization, the calibrator matrix is an MES-buffered solution. Preservative: Ofloxacin.

The value-assigned A1c Calibrator values are within the following hemoglobin A1c ranges:

Calibrator 1: 4.59% to 6.02% HbA1c

Calibrator 2: 10.52% to 13.37% HbA1c

Actual analyte concentrations for each lot of calibrators are listed in the Hemoglobin A1c Calibrator Value Sheet, packaged with the calibrator.

The Hemoglobin A1C Controls

The Hemoglobin A_{1c} Control Kit contains: a low control (Control L) and a high control (Control H)A_{1c} Controls (lyophilized) contain hemoglobin and glycated hemoglobin from human whole blood. Prior to lyophilization, the control matrix is an MES-buffered solution. Preservative: Ofloxacin.

The value-assigned A_{1c} Control values are within the following hemoglobin A_{1c} ranges:

Control L: 4.59% to 6.02% HbA_{1c}

Control H: 9.42% to 11.07 % HbA_{1c}.

Actual analyte concentrations for each lot of controls are listed in the Hemoglobin A_{1c} Control Value Sheet, packaged with the controls.

All human source materials were tested by FDA approved methods and found to be negative for the presence of HBs Ag and antibody to HIV1/HIV2, and HCV

J. Substantial Equivalence Information:

Predicate Device Name	Predicate Device 510(k) number
COBAS INTEGRA 800 Tina –quant HbA _{1c} Dx Gen.2 assay	k121291
Roche C.f.a.s (Calibrator for Automated Systems) HbA _{1c}	k052101
Roche Precicontrol HbA _{1c} norm and Precicontrol HbA _{1c} path	k103099

Comparison with predicate:

Reagent		
Similarities and Differences		
Characteristics	Candidate HbA1c k130255	Predicate COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 k121291
Intended Use	Same	The assay is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol HbA1c (IFCC) and % HbA1c (DCCT/NGSP).
Platform	ARCHITECT c 8000 System (clinical chemistry analyzer)	Roche COBAS INTEGRA 800 (Clinical chemistry analyzer)
Methodology	Enzymatic	Immunoassay
Specimen Type	Whole blood and Hemolysate: Dipotassium EDTA Lithium Heparin Sodium Heparin Sodium Fluoride/Disodium EDTA Tripotassium EDTA	Whole Blood and Hemolysate: Lithium Heparin K2-EDTA K3-EDTA KF/Na ₂ -EDTA Sodium Fluoride/K-oxalate Sodium Heparin NaF/ Na ₂ -EDTA
Measuring Interval	4.0 to 14.0% HbA1c (DCCT/NGSP) 20.22-129.51 mmol/mol HbA1c (IFCC)	4.2 to 20.1% HbA1c (DCCT/NGSP) 23 to 196 mmol/mol HbA1c (IFCC)

Calibrator Similarities and Differences		
Characteristics	Candidate HbA1c Calibrators k130255	Predicate Roche C.f.a.s HbA1c k052101
Intended Use	Same	For use in the calibration of the Hemoglobin A1c assay
Levels	<p>2 levels (Calibrator 1 and 2)</p> <p>Each lot of calibrators is value-assigned and values are reported in both NGSP and IFCC units. Actual analyte concentrations for each lot of calibrators are listed in the Hemoglobin A1c Calibrator Value Sheet, packaged with the calibrator. The value assigned HbA1c concentration falls within the following HbA1c ranges: Calibrator 1: 4.59% to 6.02% HbA1c Calibrator 2: 10.52% to 13.37% HbA1c</p>	<p>1 level</p> <p>The C.f.a.s. HbA1c calibrator is automatically diluted by the system.</p>
Standardization/Traceability	Calibrators are prepared gravimetrically, lyophilized, and then value assigned using secondary calibrators that are traceable to the IFCC reference method.	This method has been standardized against the approved IFCC reference method for the measurement of HbA1c in human blood and can be transferred to results traceable to DCCT/NGSP by calculation.

Control Similarities and Differences		
Characteristics	Candidate HbA1c Controls k130255	Predicate Roche PreciControl HbA1c norm and PreciControl HbA1c path k103099
Intended Use	Same	For use in quality control by monitoring accuracy and precision for the quantitative methods.
Levels	2 levels (Low and High Control)	PreciControl HbA1c norm: 1 level PreciControl HbA1c path:1 level
Value Assignment	Assignment of values is specific for each lot. The value-assigned A1c Control values are within the following hemoglobin A1c ranges: Control L: 4.59% to 6.02% HbA1c Control H: 9.42% to 11.07 % HbA1c	Assignment values are specific for each lot.
Material	Controls are prepared using hemoglobin and glycated hemoglobin from human whole blood. Prior to lyophilization, the matrix used is MES buffered solution.	PreciControl HbA1c norm is a liquid control based on hemolyzed human blood. The adjusted concentrations of the control components are usually in the normal range or at the normal/pathological threshold. PreciControl HbA1c path is a lyophilized control based on hemolyzed sheep blood.

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

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measuring Procedures: A Statistical Approach; Approved Guideline

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition

CLSI EP7-A: Interference Testing in Clinical Chemistry, Approved Guideline

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantification; Approved Guideline

L. Test Principle:

The Hemoglobin A1c assay consists of two separate concentration measurements: glycated hemoglobin (HbA1c) and total hemoglobin (THb). The two concentrations are used to determine the percent HbA1c (NGSP units) or the hemoglobin fraction in mmol/mol (IFCC units). The individual concentration values of HbA1c and THb generated by the Hemoglobin A1c assay are used only for calculating the percent hemoglobin A1c or HbA1c fraction, and must not be used individually for diagnostic purposes. The anticoagulated whole blood specimen is lysed automatically on the system for the Whole Blood application or may be lysed manually using the Hemoglobin A1c Diluent for the Hemolysate application.

Glycated Hemoglobin (HbA1c)

The Hemoglobin A1c assay utilizes an enzymatic method that specifically measures *N*-terminal fructosyl dipeptides of the β -chain of HbA1c. In the pretreatment process, the erythrocytes are lysed and the hemoglobin is transformed to methemoglobin by reaction with sodium nitrite. With the addition of Reagent 1 to the sample, the glycosylated *N*-terminal dipeptide (fructosyl-VH) of the β -chain of hemoglobin is cleaved by the action of protease. The hemoglobin is transformed to stable methemoglobin azide by the action of sodium azide and the concentration of the hemoglobin is determined by measuring absorbance. Addition of Reagent 2 starts a reaction and fructosyl peptideoxidase (FPOX) is allowed to react with fructosyl-VH. The HbA1c concentration is measured by determining the resultant hydrogen peroxide.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-Laboratory Precision (20-Day)

A 20-day precision study was conducted to evaluate the precision performance of the

Hemoglobin A1c assay based on guidance from the CLSI document EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods. Testing was performed using 3 lots of Hemoglobin A1c Reagents, 3 lots of Hemoglobin A1c Calibrators, 1 lot of Hemoglobin A1c Controls (Low and High), and 1 lot of commercially available human whole blood controls (Control Levels 1, 2, and 3) on 3 ARCHITECT c 8000 analyzers. Three levels of controls made from reconstituted lyophilized anticoagulated human whole blood and three levels of pooled human anticoagulated venous whole blood (panels) were tested a minimum of 2 replicates, twice per day, for a total of 20 testing days. Total number of measurements per sample was 720 (=3 instruments x 3 lots x 20 days x 2 runs x 2 replicates). Results are shown below in NGSP and IFCC units. The HbA1c sample abbreviations are as follows: LC= Hemoglobin A1c Low Control (target value 5.2%), HC= Hemoglobin A1c High Control (target value 10.0%), CL3= commercially available control level 3 (target value 14.6%); PS1 = human whole blood near the lower limit of the measuring interval (target range 4.0-4.6%), PS2=human whole blood near the medical decision point (target range 6.0-7.0%) PS3= human whole blood above the medical decision point (target range 8.0-10.0%).

Hemoglobin A1c Reproducibility

Hemolysate Application NGSP

ARCHITECT c 8000 analyzer # 1

Mean % HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 5.2%	0.01	0.2	0.01	0.1	0.01	0.1	0.02	0.4	0.02	0.4
HC 10.0%	0.02	0.2	0.00	0.0	0.02	0.2	0.05	0.5	0.06	0.6
CL3 14.5%	0.03	0.2	0.03	0.2	0.03	0.2	0.13	0.9	0.14	1.0
PS1 4.4%	0.01	0.3	0.01	0.2	0.01	0.2	0.04	0.8	0.04	0.9
PS2 6.4%	0.01	0.2	0.01	0.1	0.02	0.4	0.05	0.8	0.06	0.9
PS3 8.9%	0.02	0.2	0.01	0.2	0.01	0.2	0.08	0.8	0.08	0.9

ARCHITECT c8000 analyzer #2

Mean % HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 5.3%	0.01	0.2	0.01	0.1	0.00	0.0	0.01	0.2	0.02	0.3
HC 10.1%	0.03	0.3	0.02	0.2	0.02	0.2	0.02	0.2	0.04	0.4
CL3 14.3%	0.07	0.5	0.03	0.2	0.00	0.0	0.20	1.4	0.21	1.5
PS1 4.4%	0.01	0.3	0.01	0.3	0.00	0.1	0.03	0.6	0.03	0.7

PS2 6.4%	0.01	0.2	0.01	0.2	0.01	0.2	0.04	0.7	0.05	0.8
PS3 8.9%	0.03	0.3	0.02	0.2	0.01	0.1	0.07	0.7	0.07	0.8

ARCHITECT c8000 analyzer # 3

Mean % HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 5.2%	0.01	0.3	0.01	0.2	0.01	0.2	0.01	0.3	0.02	0.5
HC 9.9%	0.02	0.2	0.01	0.1	0.02	0.2	0.04	0.4	0.05	0.5
CL3 14.4%	0.03	0.2	0.03	0.2	0.05	0.3	0.14	1.0	0.16	1.1
PS1 4.4%	0.01	0.3	0.01	0.2	0.01	0.3	0.03	0.6	0.03	0.8
PS2 6.4%	0.01	0.2	0.01	0.1	0.02	0.4	0.04	0.6	0.05	0.8
PS3 8.9%	0.02	0.2	0.01	0.1	0.02	0.3	0.06	0.7	0.07	0.8

ARCHITECT c8000 analyzers (combined)

Reproducibility – Hemolysate Application, NGSP												
Mean % HbA _{1c}	Repeatability		Between-run		Between-day		Between-lot		Between-instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 5.2%	0.01	0.2	0.01	0.1	0.01	0.2	0.01	0.3	0.04	0.7	0.04	0.8
HC 10.0%	0.03	0.3	0.02	0.2	0.02	0.2	0.04	0.4	0.08	0.8	0.09	0.9
CL3 14.4%	0.05	0.3	0.03	0.2	0.03	0.2	0.16	1.1	0.11	0.8	0.18	1.3
PS1, 4.4%	0.01	0.3	0.01	0.2	0.01	0.2	0.03	0.7	0.02	0.5	0.04	0.9
PS2 6.4%	0.01	0.2	0.01	0.1	0.02	0.3	0.05	0.7	0.03	0.4	0.06	0.9
PS3 8.9%	0.02	0.2	0.01	0.2	0.02	0.2	0.07	0.8	0.04	0.5	0.09	1.0

Whole Blood Application NGSP

ARCHITECT c8000 analyzer# 1

Mean % HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 4.9%	0.01	0.3	0.02	0.4	0.00	0.0	0.01	0.2	0.03	0.5
HC 9.6%	0.03	0.3	0.02	0.2	0.03	0.3	0.08	0.9	0.09	1.0
CL3 14.5%	0.04	0.3	0.06	0.4	0.03	0.2	0.18	1.2	0.20	1.4
PS1 4.4%	0.01	0.3	0.01	0.3	0.00	0.1	0.03	0.6	0.03	0.7
PS2 6.4%	0.01	0.2	0.01	0.1	0.02	0.2	0.04	0.6	0.05	0.7
PS3 8.9%	0.02	0.2	0.01	0.1	0.01	0.1	0.05	0.6	0.06	0.7

ARCHITECT c8000 analyzer # 2

Mean % HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 4.9%	0.01	0.3	0.01	0.2	0.01	0.2	0.01	0.2	0.02	0.4
HC 9.6%	0.03	0.3	0.01	0.1	0.02	0.2	0.07	0.8	0.08	0.9
CL3 14.5%	0.04	0.3	0.06	0.4	0.00	0.0	0.16	1.1	0.18	1.2
PS1 4.4%	0.01	0.3	0.01	0.2	0.00	0.0	0.02	0.5	0.03	0.7
PS2 6.4%	0.02	0.3	0.01	0.2	0.01	0.2	0.03	0.5	0.04	0.6
PS3 8.9%	0.02	0.3	0.01	0.1	0.01	0.1	0.04	0.5	0.05	0.6

ARCHITECT c8000 analyzer # 3

Mean % HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 4.8%	0.02	0.4	0.02	0.4	0.00	0.0	0.01	0.1	0.03	0.6
HC 9.5%	0.03	0.3	0.02	0.2	0.03	0.3	0.10	1.0	0.11	1.1
CL3 14.3%	0.03	0.2	0.05	0.4	0.06	0.4	0.22	1.5	0.24	1.7
PS1	0.02	0.3	0.01	0.2	0.01	0.3	0.02	0.4	0.03	0.6

4.4%										
PS2 6.4%	0.02	0.2	0.01	0.2	0.02	0.3	0.02	0.4	0.04	0.6
PS3 8.9%	0.02	0.2	0.00	0.1	0.03	0.4	0.04	0.5	0.06	0.6

ARCHITECT c8000 analyzers (combined)

Reproducibility – Whole Blood Application, NGSP												
Mean % HbA _{1c}	Repeatability		Between-run		Between-day		Between-lot		Between-instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 4.9%	0.02	0.3	0.02	0.3	0.00	0.1	0.01	0.2	0.02	0.4	0.03	0.6
HC 9.5%	0.03	0.3	0.02	0.2	0.02	0.2	0.09	0.9	0.05	0.5	0.11	1.1
CL3 14.4%	0.04	0.3	0.06	0.4	0.03	0.2	0.19	1.3	0.10	0.7	0.23	1.6
PS1 4.4%	0.01	0.3	0.01	0.2	0.01	0.2	0.02	0.5	0.01	0.3	0.03	0.7
PS2 6.4%	0.02	0.2	0.01	0.2	0.02	0.3	0.03	0.5	0.02	0.3	0.04	0.7
PS3 8.9%	0.02	0.2	0.01	0.1	0.02	0.2	0.05	0.5	0.04	0.4	0.07	0.7

Hemolysate Application IFCC Units (mmol/mol)

ARCHITECT c8000 analyzer # 1

Mean mmol/mol HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 33.56	0.108	0.3	0.070	0.2	0.064	0.2	0.204	0.6	0.249	0.7
HC 86.04	0.236	0.3	0.063	0.1	0.194	0.2	0.594	0.7	0.671	0.8
CL3 134.94	0.368	0.3	0.344	0.3	0.381	0.3	1.391	1.0	1.527	1.1
PS1 24.71	0.122	0.5	0.082	0.3	0.117	0.5	0.384	1.6	0.428	1.7
PS2 46.58	0.131	0.3	0.094	0.2	0.248	0.5	0.564	1.2	0.637	1.4
PS3 74.15	0.179	0.2	0.162	0.2	0.149	0.2	0.823	1.1	0.871	1.2

ARCHITECT c8000 analyzer # 2

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
HbA _{1c}										
LC 33.94	0.125	0.4	0.066	0.2	0.000	0.0	0.104	0.3	0.176	0.5
HC 86.80	0.315	0.4	0.274	0.3	0.175	0.2	0.194	0.2	0.493	0.6
CL3 133.10	0.735	0.6	0.280	0.2	0.000	0.0	2.133	1.6	2.274	1.7
PS1 24.83	0.144	0.6	0.166	0.7	0.040	0.2	0.271	1.1	0.352	1.4
PS2 46.65	0.150	0.3	0.112	0.2	0.162	0.3	0.479	1.0	0.539	1.2
PS3 74.09	0.280	0.4	0.182	0.2	0.092	0.1	0.715	1.0	0.795	1.1

ARCHITECT c8000 analyzer # 3

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
HbA _{1c}										
LC 33.19	0.153	0.5	0.082	0.2	0.140	0.4	0.149	0.4	0.268	0.8
HC 85.11	0.256	0.3	0.135	0.2	0.222	0.3	0.393	0.5	0.536	0.6
CL3 134.13	0.325	0.2	0.356	0.3	0.493	0.4	1.555	1.2	1.701	1.3
PS1 24.40	0.130	0.5	0.083	0.3	0.140	0.6	0.290	1.2	0.357	1.5
PS2 46.13	0.138	0.3	0.073	0.2	0.275	0.6	0.426	0.9	0.530	1.1
PS3 73.28	0.196	0.3	0.109	0.1	0.272	0.4	0.655	0.9	0.744	1.0

Reproducibility – Hemolysate Application, IFCC												
Mean HbA _{1c} mmol/ mol	Repeatability		Between- run		Between- day		Between- lot		Between- instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 33.56	0.130	0.4	0.074	0.2	0.088	0.3	0.158	0.5	0.396	1.2	0.435	1.3

HC 85.98	0.271	0.3	0.180	0.2	0.198	0.2	0.426	0.5	0.879	1.0	1.005	1.2
CL3 134.06	0.510	0.4	0.332	0.2	0.356	0.3	1.723	1.3	1.222	0.9	1.998	1.5
PS1, 24.65	0.133	0.5	0.117	0.5	0.108	0.4	0.319	1.3	0.236	1.0	0.436	1.8
PS2 46.45	0.140	0.3	0.094	0.2	0.233	0.5	0.493	1.1	0.292	0.6	0.635	1.4
PS3 73.84	0.223	0.3	0.154	0.2	0.187	0.3	0.734	1.0	0.486	0.7	0.937	1.3

Whole Blood Application IFCC Units (mmol/mol)

ARCHITECT c8000 analyzer # 1

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 29.77	0.159	0.5	0.207	0.7	0.000	0.0	0.115	0.4	0.285	1.0
HC 80.98	0.277	0.3	0.176	0.2	0.294	0.4	0.920	1.1	1.020	1.3
CL3 134.86	0.450	0.3	0.671	0.5	0.270	0.2	1.963	1.5	2.140	1.6
PS1 24.61	0.128	0.5	0.128	0.5	0.055	0.2	0.292	1.2	0.348	1.4
PS2 46.61	0.159	0.3	0.100	0.2	0.166	0.4	0.424	0.9	0.493	1.1
PS3 74.29	0.239	0.3	0.148	0.2	0.122	0.2	0.603	0.8	0.677	0.9

ARCHITECT c8000 analyzer # 2

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 29.76	0.160	0.5	0.127	0.4	0.087	0.3	0.078	0.3	0.235	0.8
HC 80.95	0.330	0.4	0.135	0.2	0.173	0.2	0.797	1.0	0.890	1.1
CL3 134.90	0.436	0.3	0.696	0.5	0.000	0.0	1.790	1.3	1.970	1.5
PS1 24.49	0.149	0.6	0.103	0.4	0.000	0.0	0.258	1.1	0.315	1.3
PS2 46.51	0.174	0.4	0.114	0.2	0.111	0.2	0.323	0.7	0.400	0.9
PS3 74.15	0.243	0.3	0.115	0.2	0.082	0.1	0.478	0.6	0.554	0.7

ARCHITECT c8000 analyzer # 3

Mean mmol/mol HbA _{1c}	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 29.43	0.223	0.8	0.187	0.6	0.000	0.0	0.076	0.3	0.301	1.0
HC 80.01	0.282	0.4	0.219	0.3	0.293	0.4	1.072	1.3	1.167	1.5
CL3 133.04	0.355	0.3	0.550	0.4	0.642	0.5	2.416	1.8	2.584	1.9
PS1 24.37	0.162	0.7	0.103	0.4	0.128	0.5	0.183	0.7	0.294	1.2
PS2 46.24	0.167	0.4	0.110	0.2	0.241	0.5	0.264	0.6	0.409	0.9
PS3 73.55	0.236	0.3	0.048	0.1	0.349	0.5	0.444	0.6	0.614	0.8

Reproducibility – Whole Blood Application, IFCC												
Mean mmol/mol HbA _{1c}	Repeatability		Between-run		Between-day		Between-lot		Between-instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
LC 29.65	0.183	0.6	0.180	0.6	0.038	0.1	0.092	0.3	0.207	0.7	0.332	1.1
HC 80.65	0.294	0.4	0.186	0.2	0.260	0.3	0.937	1.2	0.564	0.7	1.169	1.4
CL3 134.27	0.416	0.3	0.657	0.5	0.377	0.3	2.073	1.5	1.101	0.8	2.476	1.8
PS1 24.49	0.147	0.6	0.115	0.5	0.076	0.3	0.248	1.0	0.137	0.6	0.336	1.4
PS2 46.45	0.167	0.4	0.108	0.2	0.181	0.4	0.343	0.7	0.200	0.4	0.473	1.0
PS3 74.00	0.239	0.3	0.112	0.2	0.219	0.3	0.513	0.7	0.395	0.5	0.729	1.0

NGSP Precision Summary:

The between-analyzer and between-lot precision was equal to or less than 1.3% for concentrations in the range of 5.2% and 14.4% HbA_{1c} in the Hemolysate application.

The between-analyzer and between-lot precision was equal to or less than 1.6% for concentrations in the range of 4.9% and 14.4% HbA_{1c} in the Whole Blood application.

IFCC Precision Summary:

The between-analyzer and between-lot precision was equal to or less than 1.8% for concentrations in the range of 24.65 mmol/mol and 134.06 mmol/mol HbA1c in the Hemolysate application.

The between-analyzer and between-lot precision was equal to or less than 1.8% for concentrations in the range of 24.49 mmol/mol and 134.27 mmol/mol HbA1c in the Whole Blood application.

b. Linearity/assay reportable range:

A linearity study was performed based on guidance from the CLSI document EP6-A, Evaluation of the Linearity of Quantitative Measuring Procedures: A Statistical Approach. Commercially available whole-blood HbA1c linearity sets, comprised of Levels 1, 2, 3, and 4, were obtained. Five additional samples were prepared by combining the 4 levels of the commercially available linearity sets in specific ratios. The 9 samples were tested using the Abbott Hemoglobin A_{1c} assay. The mean observed %HbA1c value was determined for each intermediate dilution and plotted versus the relative analyte concentration.

Hemoglobin A_{1c} Linearity Observed vs. Expected Concentration Summary (NGSP)

Expected Concentration (%HbA1c)	N	Observed Mean (%HbA1c)	Predicted Linear fit	Percent deviation
3.3	4	3.5	3.3	5.4
3.8	4	3.9	3.8	2.4
5.1	4	5.0	5.1	-1.6
7.5	4	7.2	7.5	-4.3
9.9	4	9.9	9.9	0.5
12.6	4	12.6	12.6	0.1
14.0	4	14.0	14.0	0.1

NGSP:

The linear regression equation is summarized below:

Correlation Coefficient: 0.9996, Slope: 0.9782, Intercept: -0.59, r²: 0.999

Hemoglobin A_{1c} Linearity Observed vs. Expected

Concentration Summary (IFCC)

Expected Concentration (IFCC)	N	Observed Mean (IFCC)	Predicted Linear fit	Percent deviation
13.12	4	14.48	13.12	10.3
17.88	4	18.82	17.88	5.3
32.16	4	31.16	32.16	-3.1
58.25	4	55.20	58.25	-5.2
84.35	4	85.22	84.35	1.0
114.21	4	114.59	114.21	0.3
129.15	4	129.82	129.15	0.5

IFCC:

The linear regression equation is summarized below:

Correlation Coefficient: 0.9997, Slope: 0.9747, Intercept: -7.23, r^2 : 0.999

The linearity study supports the claimed assay measuring range of 4.0 to 14.0% HbA_{1c} (20.22 to 129.51 mmol/mol HbA_{1c} (IFCC)).

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

Traceability:

The Architect HbA_{1c} assay standardization is traceable to the International Federation of Clinical Chemistry (IFCC) reference calibrators. The Architect HbA_{1c} assay is NGSP certified. The NGSP certification expires in one year. See NGSP website for current certification at <http://www.ngsp.org>. The derived result of (%) from the NGSP correlation is calculated from the individual quantitative results for total hemoglobin and Hemoglobin A_{1c} (HbA_{1c}). The IFCC units of mmol/mol are calculated using the Master Equation $IFCC = (NGSP - 2.15) / 0.092$. Two different units are provided to the users: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol)

Value Assignment

The ARCHITECT HbA_{1c} calibrators are aligned to IFCC reference calibrators through internal value assignment in which calibrator values must meet the sponsor's pre-determined acceptance criteria within a set specification, determined by the manufacturer.

Each lot of calibrators is value-assigned. The concentration of glycated hemoglobin (HbA_{1c}) and total hemoglobin (THb) is provided for each lot. Calibrators are prepared gravimetrically, lyophilized, and then value assigned using secondary calibrators that are traceable to the International Federation of Clinical Chemistry and Laboratory

Medicine (IFCC) reference method.

The value-assigned A1c Calibrator values are within the following hemoglobin A1c ranges:

Calibrator 1: 4.59% to 6.02% HbA1c

Calibrator 2: 10.52% to 13.37% HbA1c

The Hemoglobin A1C Controls, low and high, are value assigned using the secondary calibrators. The values obtained must meet the sponsor's pre-determined acceptance criteria.

The value-assigned A1c Control values are within the following hemoglobin A1c ranges:

Control L: 4.59% to 6.02% HbA1c

Control H: 9.42% to 11.07 % HbA1c.

Stability

Shelf-life claims: Un-opened calibrators and controls can be stored at 2-8°C until the expiration date or for 12 months. The storage and stability study protocols and acceptance criteria provided by the sponsor were reviewed and found acceptable to support the claimed conditions.

Open-vial claims: The recommended storage condition for in-use calibrators and controls is 2-8 °C and is stable for 10 days post-reconstitution. Labeling indicates not to freeze the control and calibrator materials. The storage and stability study protocols and acceptance criteria provided by the sponsor were reviewed and found acceptable to support the claimed conditions.

On-board stability for the ARCHITECT HbA1c was established by real time studies on the ARCHITECT c8000 analyzer and demonstrated on-board reagent stability of 50 days. The unopened ARCHITECT HbA1c reagent is stable until the expiration date printed on the label when stored at 2 to 8°C. The storage and stability study protocols and acceptance criteria provided by the sponsor were reviewed and found acceptable to support the claimed conditions.

d. Detection limit:

Limit of Blank (LoB) and Detection (LoD)

A Limit of Blank (LoB) and Limit of Detection (LoD) study was performed based on guidance from the CLSI document EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantification.

The limit of Blank (LoB) and Limit of Detection (LoD) were determined by assaying two analyte free samples (blank) and five low HbA1c samples. The zero-level samples were tested in a minimum of three replicates and the low-level samples were tested in a minimum of two replicates. Five separate runs were performed over a minimum of three days using two lots of Hemoglobin A_{1c} Reagents, two lots of Hemoglobin A_{1c} Calibrators, and one lot of commercially available controls on two ARCHITECT c 8000 instruments. The detection limits are summarized in the table below.

ARCHITECT c8000 analyzer

Limit of Blank (LoB)	Limit of Detection (LoD)
2.51% (3.89 mmol/mol)	2.52% (4.05 mmol/mol)

The ARCHITECT HbA1c assay has a reportable range of 4.0-14.0%.
(20.22-129.51 mmol/mol HbA1c)

e. Analytical specificity:

i.) An interference study was performed based on CLSI EP7-A2 guideline to assess common or known substances that could interfere with the HbA1c assay. The potential interferents listed below were spiked into human EDTA whole blood samples with different levels of % HbA1c (approximately 6.5 and > 8.0% HbA1c). Each sample was tested in replicates of 14. The % HbA1c values of the spiked samples were compared to the reference samples containing no interferent. Significant interference was defined as greater or equal to $\pm 5\%$ difference from the expected concentration. The interference study results are summarized in the following table:

Potential Interferent	Highest Tested Concentration at which no significant interference ($\geq \pm 5\%$) was observed
Bilirubin, conjugated	15 mg/dL
Bilirubin, unconjugated	10 mg/dL
Total Protein	22g/dL
Triglycerides	3000 mg/dL
Rheumatoid Factor	200 IU/mL
Ascorbic Acid	3.0 mg/dL
Urea	667 mg/dL
Glucose	1000 mg/dL
Vitamin E	8.6 mg/dL

ii.) A hemoglobin variant interference

The hemoglobin variant interference study was performed according to guidance from the CLSI EP7-A2. Interference effects were assessed by comparing the Hemoglobin A1c values to a comparative method for samples containing potentially interfering hemoglobin variants. The samples were tested in duplicate using one lot of HbA1c Reagents on one ARCHITECT c 8000 analyzer. The numbers and concentrations hemoglobin variants tested, and the range of % HbA1c concentrations in which they were tested are shown below:

Hemoglobin Variant	n	Range in % Abnormal Variant	Range in %HbA _{1c} Concentration
HbC	21	33% - 42%	5.2 - 9.3
HbD	20	35% - 41%	5.2 - 10.7
HbE	20	27% - 32%	5.0 - 10.1
HbS	20	33% - 44%	5.1 - 9.9
HbA2	26	4.7% - 8.5%	4.7 – 13.3
HbF	19	3% - 27.8%	5.2 - 9.0

The results for the hemoglobin variant study are summarized below:

Hemoglobin Variant	Relative % Bias from Reference Method at Low and High Concentrations	
	~ 6.0 %HbA _{1c}	~ 9.0 %HbA _{1c}
HbC	-1.6	-1.9
HbD	-0.8	1.8
HbE	0.0	4.3
HbS	-1.4	4.7
HbA2	-0.6	-0.5
HbF	Bias exceeds -5% when the amount of HbF in the sample exceeds 5% ^a	

^a A negative bias with HbF is directly proportional in magnitude to the % HbF present in the sample.

NOTE: The presence of multiple variants in a sample may impact the % bias.

The sponsor claims that no significant interference was observed for the HbC, HbD, HbE, HbS, and HbA2 variants at the concentrations tested above.

Hemoglobin F Interference

The interference study results demonstrate there is significant interference due to the presence of HbF in the sample. The extent of interference is directly proportional to the amount of HbF contained within the sample. For example, significant interference that produces a negative bias of 5% in HbA1c results was observed with specimens containing 5% HbF; and a negative bias of 23% in HbA1c results was observed in samples containing 28% HbF.

In addition, the device labeling contains the following prominent boxed warning in the package insert labeling:

WARNING: The Hemoglobin A1c assay has significant interference with the fetal hemoglobin (HbF). Hemoglobin A1c results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin.

iii) A drug interference study was performed using a low level whole blood sample with a concentration value of between 6.0 and 7.0% HbA1c and a high whole blood sample with a concentration value of $\geq 8.0\%$ HbA1c. Test sample were prepared by spiking each drug at the interferent concentrations into the low and high samples. The test and reference samples were tested in a minimum of 12 replicates using 1 lot of HbA1c reagents and calibrators. The sponsor defined significant interference as greater or equal to $\pm 5\%$ difference from the expected concentration.

The sponsor states that the HbA1c assay is not susceptible to interference effects from the following drugs at the listed concentration levels evaluated.

Potential Drug Interferent	Highest Level Tested Showing No Significant Interference.
Acarbose	50 mg/dL
Acetaminophen	200 $\mu\text{g/mL}$
Acetylsalicylate	50.8 mg/dL
Atorvastatin	600 $\mu\text{g Eq/L}$
Captopril	0.5 mg/dL
Chlorpropamide	74.7 mg/dL
Cyanate	50 mg/dL
Furosemide	6.0 mg/dL
Gemfibrozil	7.5 mg/dL
Ibuprofen	0.5 mg/mL
Insulin	450 micro units/mL
Losartan	5 mg/dL
Metformin	5.1 mg/dL
Nicotinic Acid	61 mg/dL
Propranolol	0.2 mg/dL
Repaglinide	60 ng/mL

iv.) A hemoglobin derivative study was performed using a low level whole blood sample with a concentration between 6.0 and 7.0% HbA1c and a high whole blood sample with a concentration of $\geq 8.0\%$ HbA1c. The potentially interfering hemoglobin derivatives were prepared by adding the following substance at the levels shown below.

- Acetylated Hemoglobin ≥ 50 mg/dL of ASA (aspirin)
- Carbamlyated Hemoglobin ≥ 10 mmol/L of Cyanate
- Labile Hemoglobin ≥ 1000 mg/dL of Glucose

The test samples were prepared by spiking the substances at the interferent concentration listed above into the low and high samples. The test and reference samples were tested in a minimum of 12 replicates. Significant interference was defined as $\pm 5\%$ when comparing test samples containing the potentially interfering hemoglobin derivatives to the corresponding reference samples.

The sponsor states that the HbA1c assay is not susceptible to interference effects from the hemoglobin derivatives at the interference levels evaluated.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study using human EDTA whole blood specimens (n=128) was performed based on CLSI EP9-A2, Method Comparison and Bias Estimation Using Patient Samples guidelines. Each sample was analyzed internally in replicates of two, using two lots each of HbA1c reagents and HbA1c calibrators on two ARCHITECT c 8000 analyzers over a minimum of 5 days. The samples were also tested in duplicate with an NGSP secondary reference laboratory using a FDA cleared HPLC-based method, the Tosoh G8. The total number of comparison results obtained was 256. The sample range tested was 4.0 to 13.2% HbA1c. The method comparison was performed using both the hemolysate and whole blood application. The distribution of samples spanned the measuring interval with a concentration of samples around the clinical decision points as follows:

%HbA_{1c} Level*	Number of Samples
< 5.0%	5
5.0 – 5.9%	16
6.0 – 6.4%	32
6.5 – 7.0%	32
7.1 – 8.0%	22
8.1 – 9.0%	11
> 9.0%	10
Total	128

Deming (weighted) and Passing-Bablok regression analyses were performed for the ARCHITECT HbA1c versus the reference method.

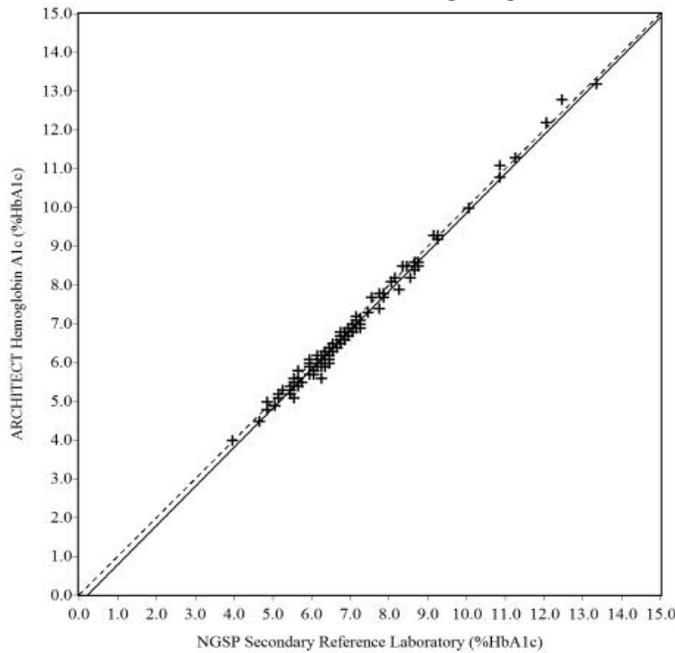
Summary of the first replicate versus first replicate regression analysis results are presented in the tables below for the hemolysate and whole blood applications:

Whole blood application:

Deming: $y=1.01x -0.20$

Passing-Bablok: $y=1.00x-0.20$

Whole Blood Scatter Plot with Deming Regression (NGSP)



Bias and % Bias Summary for Whole Blood (NGSP)

Regression Method	%HbA _{1c}	Bias	% Bias
Deming	5.0	-0.2	-3.7
	6.5	-0.2	-2.7
	8.0	-0.2	-2.0
	12.0	-0.1	-1.1
Passing-Bablok	5.0	-0.2	-4.0
	6.5	-0.2	-3.1

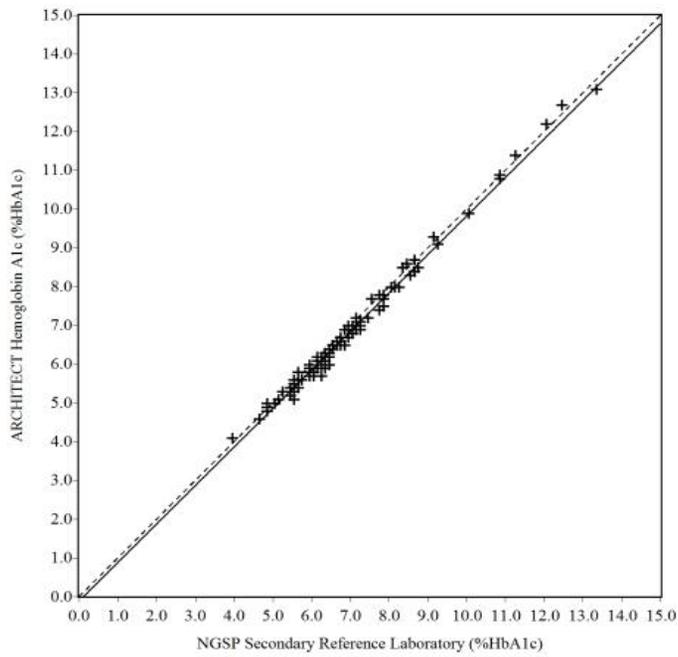
Regression Method	%HbA _{1c}	Bias	% Bias
	8.0	-0.2	-2.5
	12.0	-0.2	-1.7

Hemolysate Application:

Deming: $y=0.99x - 0.10$

Passing-Bablok: $y=1.00x - 0.20$

Hemolysate Scatter Plot with Deming Regression



Hemoglobin A_{1c} Method Comparison (Correlation)
 Bias and %Bias Summary – Hemolysate (NGSP)

Regression Method	%HbA_{1c}	Bias	% Bias
Deming	5.0	-0.2	-3.2
	6.5	-0.2	-2.6
	8.0	-0.2	-2.2
	12.0	-0.2	-1.7
Passing-Bablok	5.0	-0.2	-4.0
	6.5	-0.2	-3.1
	8.0	-0.2	-2.5
	12.0	-0.2	-1.7

Hemoglobin A_{1c} Method Comparison (Correlation) and Predicted Bias

Bias and %Bias Summary - Hemolysate (IFCC)

Regression Method	HbA_{1c} mmol/mol	Bias	% Bias
Deming	31.13	-1.43	-4.6
	47.53	-1.83	-3.9
	63.93	-2.23	-3.5
Passing-Bablok	31.13	-1.98	-6.4
	47.53	-1.98	-4.2
	63.93	-1.98	-3.1

Bias and %Bias Summary – Whole Blood (IFCC)

Regression Method	HbA1c mmol/mol	Bias	% Bias
Deming	31.13	-1.84	-5.9
	47.53	-1.93	-4.1
	63.93	-2.02	-3.2
Passing-Bablok	31.13	-2.22	-7.1
	47.53	-1.94	-4.1
	63.93	-1.66	-2.6

Total Error Near the Cutoff

Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the reproducibility study, Total Error (TE) three concentrations: (5.2%, 6.5% and 8.0%) was calculated as follows: %TE =|%Bias| + 1.96 *%CV*(1+%Bias). The results are presented in the tables below.

Hemoglobin A_{1c} Method Comparison (Correlation) and Predicted Bias

%Total Error Summary – Hemolysate (NGSP)

%HbA _{1c}	Average % Bias	% CV	% TE
5	-3.6	0.8	5.1
6.5	-2.8	0.9	4.5
8	-2.4	1.0	4.3
12.0	-1.7	1.3	4.2

% Total Error Summary – Whole Blood (NGSP)

%HbA_{1c}	Average % Bias	% CV	% TE
5	-3.9	0.6	5.0
6.5	-2.9	0.7	4.2
8	-2.3	0.7	3.6
12.0	-1.4	1.6	4.5

b. Matrix comparison:

A matrix study was performed to determine the suitability of different anticoagulant collection tube types for use in the ARCHITECT HbA_{1c} assay. Specimens with concentration values spanning the measuring interval of the assay (4.0 to 14.0% HbA_{1c}) were collected from a minimum of 43 different donors in the control tube type (Dipotassium EDTA, plastic) and in the following tube types under evaluation:

- Lithium heparin
- Sodium heparin
- Sodium Fluoride/Disodium EDTA
- Tripotassium EDTA

The blood collection tubes collected from one individual constituted one sample set. Each sample was tested in a minimum of 2 replicates, using one lot of HgA_{1c} reagents and HbA_{1c} calibrators on one ARCHITECT c 8000 analyzer.

The regression results are as follows:

Dipotassium-EDTA Control vs Tube Types			
Tube type	Linear fit		
	Slope (95% CI)	Intercept (95% CI)	r value
Sodium Fluoride/Sodium EDTA	1.00	0.0	1.00
	1.00 to 1.00	0.0 to 0.1	
Lithium Heparin	1.00	0.1	1.00

	1.00 to 1.01	0.0 to 0.0	
Tripotassium EDTA	1.00	0.0	1.00
	1.00 to 1.00	0.0 to 0.0	
Sodium Heparin	1.01	0.1	0.98
	1.00 to 1.02	0.0 to 0.1	

The data support the use of the following blood collection tubes with the HbA1c assay:

- Dipotassium EDTA (control tube)
- Lithium heparin
- Sodium heparin
- Sodium Fluoride/Disodium EDTA
- Tripotassium EDTA

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:

Hemoglobin A1c expected value range was cited from American Diabetes Association Standards of Medical Care in Diabetes 2012, 35 (Supplement 1), S11-S63

HbA1c Value	Glycemic Goal
< 8% HbA1c (64 mmol/mol)	Less stringent
< 7% HbA1c (53 mmol/mol)	General (Non-Pregnant Adults)
< 6.5% HbA1c (48 mol/mol)	More stringent

As recommended by the ADA, patients in the range of 5.7 - 6.4% HbA1c (39-46 mmol/mol) would be in the category of increased risk for diabetes and results $\geq 6.5\%$ HbA1c (48 mmol/mol) may aid in the diagnosis of diabetes.

HbA1c levels higher than the upper end of this reference range are an indication of hyperglycemia during the preceding 2 to 3 months or longer. According to the recommendations of the American Diabetes Association values above 48 mmol/mol HbA1c (IFCC) or 6.5 % HbA1c (DCCT/NGSP) are suitable for the diagnosis of diabetes mellitus. Patients with HbA1c values in the range of 39-46 mmol/mol HbA1c (IFCC) or 5.7-6.4 % HbA1c (DCCT/NGSP) may be at a risk of developing diabetes.^{1, 2}

HbA1c levels may reach 195 mmol/mol (IFCC) or 20 % (DCCT/NGSP) or higher in poorly controlled diabetes. Therapeutic action is suggested at levels above 64 mmol/mol HbA1c (IFCC) or 8 % HbA1c (DCCT/NGSP). Diabetes patients with HbA1c levels below 53 mmol/mol HbA1c (IFCC) or 7 % HbA1c (DCCT/NGSP) meet the goal of the American Diabetes Association.^{3, 4}

HbA1c levels below the established reference range may indicate recent episodes of hypoglycemia, the presence of Hb variants, or shortened lifetime of erythrocytes.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

¹International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes. Diabetes Care 2009; 32(7):1327-1334

²Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2010; 33(1):62-69.

³Sacks BW, Bruns DE, Goldstein DE, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002;48:436-472.

⁴American Diabetes Association. Standards of Medical Care for patients with diabetes mellitus. Diabetes Care [Suppl.] 1995;18(1):8-15.

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.