510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k162822

B. Purpose for Submission:

New device

C. Measurand:

Whole Blood Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Reversed-Phase Cation Exchange High Performance Liquid Chromatography (HPLC)

E. Applicant:

ARKRAY Factory, Inc.

F. Proprietary and Established Names:

ADAMS A1c HA-8180V

CALIBRATOR 80

G. Regulatory Information:

Regulation Description	Product Code	Classification	Regulation Section	Panel
Hemoglobin A1c Test System	PDJ	Class II	21 CFR 862.1373	Chemistry 75
Glycosylated Hemoglobin Assay	LCP	Class II	21 CFR 864.7470	Hematology 81
Calibrator	JIT	Class II	21 CFR 862.1150	Chemistry 75

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:

   The ADAMS A1c HA-8180V system is intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %) in human whole blood and hemolysate samples using Ion-Exchange high-performance liquid chromatography (HPLC).

   Hemoglobin A1c measurements obtained from the ADAMS A1c HA-8180V are used as an aid in the diagnosis of diabetes mellitus, an aid in the identification of individuals who may be at risk of developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus. The ADAMS H1c HA-8180V is intended for professional use only.

   The CALIBRATOR 80 is for the calibration of the ADAMS A1c HA-8180V system used for the quantitative determination of hemoglobin A1c in human whole blood and hemolysate samples.

   For In Vitro Diagnostic Use Only.

   Special conditions for use statement(s):

   Hemoglobin A1c tests should not be used as a diagnostic aid for diabetes in patients with a hemoglobinopathy but normal red cell turnover (e.g. sickle cell trait).

   Hemoglobin A1c tests should not be used as a diagnostic aid in patients with abnormal red cell turnover (e.g. anemias from hemolysis and iron deficiency), or patients with iron deficiency and hemolytic anemia, various hemoglobinopathies, thalassemias, hereditary spherocytosis, malignancies, and severe chronic hepatic and renal disease.

   Hemoglobin A1c tests should not be used as a diagnostic aid in pregnant women as it reflects the average blood glucose level over the preceding 3 months (average life 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 cell survival.

   Hemoglobin A1c testing should not be used to replace glucose testing for type 1 diabetes in pediatric patients and in pregnant women.

   Hemoglobin A1c testing should not be used in the diagnosis of gestational diabetes.

   Hemoglobin A1c testing should not be used in patients with homozygous sickle cell trait, hemolytic anemia or other hemolytic diseases, or in patients with a recent significant

blood loss.

In cases of rapidly evolving type 1 diabetes the increase of HbA1c values might be delayed compared to the acute increase in glucose concentrations. In these conditions diabetes mellitus must be diagnosed based on plasma glucose concentration and/or the typical clinical symptoms.

The results of interference studies performed to evaluate the effect of hemoglobin variants on the HbA1c measurement show there is no significant interference for HbA2 concentrations of less than or equal to 16%, HbC concentrations of less than or equal to 39%, HbD concentrations of less than or equal to 36%, HbE concentrations of less than or equal to 30%, HbF concentrations of less than or equal to 30%, and HbS concentrations of less than or equal to 40%.

For prescription use only.

3. Special instrument requirements:

ADAMS A1c HA-8180V analyzer.

I. Device Description:

The ADAMS HA-8180V HbA1c system includes two levels of calibrators, diluents used to reconstitute the calibrators, three eluent solutions, a washing solution, and a control dilution set (used for sample dilutions and control material preparation). The components are described below:

CALIBRATOR 80: A boxed set of two levels of calibrator material, CALBRATOR 80 Low and CALIBRATOR 80 High, which are single use, lyophilized calibrators from human-sourced hemoglobin used to calibrate the HA-8180V analyzer. CALIBRATOR 80 Low has a concentration of approximately 5.5% HbA1c (NGSP) and CALIBRATOR 80 High has a concentration of approximately 11.5% HbA1c (NGSP).

CALIBRATOR 80 Diluent: Phosphate- buffered containing surfactant used to reconstitute CALIBRATOR 80 Low and High.

Eluent 80A, Eluent 80B, and Eluent 80CV: Phosphate-buffered solution containing <0.06% sodium azide as preservative used in the chromatographic separation of hemoglobin fractions by elution through column.

Hemolysis Washing Solution 80H: Phosphate-buffered solution containing a surfactant and <0.02% sodium azide as a preservative, used for on-board hemolysis of whole blood samples.

Diluent 80: Phosphate-buffered solution containing a surfactant used for the dilution of liquid controls and whole blood samples.

Reconstitute 80: Phosphate-buffered solution containing a surfactant, used for the dilution of lyophilized controls.

The calibrator set reagents are provided in glass bottles capped with a rubber stopper and plastic cover. The eluents are provided in pouches consisting of a polyethylene (PE), aluminum foil, and polyethylene terephthalate (PET) laminate. The hemolysis washing solution and diluent 80 are provided in PE bottles. The hemolysis washing solution utilizes a polypropylene (PP) cap, while the diluent 80 uses a PE inner cap and PP outer cap. The reconstituent 80 reagent is provided in a PP bottle with a PP cap.

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:

1. Predicate device name(s):

Tosoh Bioscience, Inc. Automated Glycohemoglobin Analyzer HLC-723G8

Tosoh Bioscience, Inc. Hemoglobin A1c Calibrator Set

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

k131580

k071132

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate Device ARKRAY ADAMS A1c HA-8180V	Predicate Device Tosoh Glycohemoglobin Analyzer HLC-723G8 (k131580)
Intended Use	For the quantitative measurement of HbA1c to be used as an aid in diagnosis of diabetes, an aid in the identification of 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.	Same
Assay Principle	Reversed-phase cation exchange high performance liquid chromatography	Cation-exchange high performance liquid chromatography
Detection Method	Dual wavelength (420 nm and 500 nm) LED colorimetric detector)	Dual wavelength (415 nm and unknown) LED colorimetric detector
HbA1c Reporting Units	%HbA1c, mmol/mol, chromatogram	Same
Specimen Type	Human whole blood, hemolysate sample	Human whole blood
Matrix	K3-EDTA and K2-EDTA whole blood	K3-EDTA whole blood
Measuring range	4-15% HbA1c (20-140 mmol/mol) HbA1c	4-16.9% (20-161 mmol/mol) HbA1c
Standardization/Traceability	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP).	Same

Calibrator Similarities and Differences		
Characteristics	Candidate Device CALIBRATOR 80	Predicate Device Tosoh Bioscience, Inc. Hemoglobin A1c Calibrator Set (k071132)
Intended Use	For the calibration of the HbA1c measuring system.	Same
Levels	Bi-level calibrators (low and high) with human-source material.	Same
HbA1c Concentrations	Level 1: 5.0-6.0% Level 2: 10.0-11.0%	Level 1: 5.5-6.5% Level 2: 10.5-11.5%
Matrix	Lyophilized calibrator from human-sourced hemoglobin.	Buffed human red blood cells, 2 mg/mL human hemoglobin
Stability	Shelf life: 18 moths at 2-8^{o}C, Open bottle: 8 hrs. at 2-8 ^{o}C	Shelf life: 2 years at 2-8^{o}C, Open bottle: one week at 2-8 ^{o}C

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

CLSI EP07-A2, Interference Testing in Clinical Chemistry –second edition; Approved Guideline

CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods-second edition; Approved Guideline

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

L. Test Principle:

Hemoglobin test specimens are prepared by automated dilution (1:101) of anticoagulated whole blood in hemolysis washing solution 80H. Alternatively, hemolysates may be prepared "off-line" by manual dilution of anticoagulated whole blood with the diluent 80 provided in control dilution set 80. The sample is then injected into the column, which contains a filter to remove sample impurities. The differing polarity and ionic charges of the released hemoglobin fractions bind with variable strength to the negatively charged stationary phase of the column. The mobile phase, consisting of three eluents of increasing ionic strength, is injected into the column. Hemoglobin fractions eluted from the column are identified and quantified using light absorption, and are measured at 420 nm and 500 nm. The dual wavelength colorimetric analysis of the separated peaks is processed by a microcomputer to obtain peak identification and hemoglobin fraction quantitation.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:
   A precision study was performed in accordance to CLSI EP05 by testing 4 concentrations of unaltered K2-EDTA whole blood samples at the following targeted HbA1c values: ~5%, ~6.5%, ~8% and ~12%. Three levels of controls were also tested. Each sample was tested as whole blood and as hemolysates. All samples were run on three HA-8180V analyzers, each with three lots of each reagent. The aliquots of each sample type were tested in duplicate in two runs on each analyzer per day over a course of 20 days for a total of 720 results per sample. The results are summarized in the tables below for both whole blood and hemolysate applications in NGSP units (%HbA1c) and IFCC units (mmol/mol).

Whole Blood Application: ADAMS HA-8180V analyzer # 1 (NSGP)

Mean %HbA1c	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient1, 5.2%	0.01	0.3%	0.00	0.0%	0.00	0.0%	0.00	0.0%	0.01	0.3%
Patient 2, 6.4%	0.02	0.3%	0.01	0.2%	0.00	0.0%	0.05	0.8%	0.05	0.8%
Patient 3, 7.9%	0.03	0.4%	0.03	0.4%	0.01	0.2%	0.06	0.7%	0.07	0.9%
Patient 4, 11.8%	0.03	0.3%	0.02	0.1%	0.04	0.3%	0.07	0.6%	0.08	0.7%
Control 1, 5.2%	0.03	0.7%	0.03	0.7%	0.02	0.3%	0.02	0.4%	0.05	1.1%
Control 2, 9.0%	0.03	0.3%	0.03	0.3%	0.01	0.2%	0.01	0.1%	0.04	0.5%
Control 3, 13.4%	0.02	0.2%	0.04	0.3%	0.03	0.2%	0.02	0.1%	0.06	0.4%

Whole Blood Application: ADAMS HA-8180V analyzer # 2 (NSGP)

Mean	Repeatability		Between Run		Between Day		Between Lot		Total	
% HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 5.2%	0.02	0.4%	0.01	0.2%	0.00	0.0%	0.01	0.2%	0.03	0.5%
Patient 2, 6.4%	0.01	0.1%	0.00	0.0%	0.00	0.0%	0.06	0.9%	0.06	0.9%
Patient 3, 7.9%	0.03	0.4%	0.02	0.3%	0.01	0.1%	0.08	1.0%	0.09	1.1%
Patient 4, 11.8%	0.05	0.4%	0.01	0.1%	0.03	0.2%	0.10	0.9%	0.12	1.0%
Control 1, 5.2%	0.02	0.4%	0.03	0.5%	0.01	0.3%	0.04	0.9%	0.06	1.1%
Control 2, 9.0%	0.02	0.2%	0.03	0.4%	0.01	0.2%	0.04	0.5%	0.06	0.6%
Control 3, 13.4%	0.03	0.2%	0.03	0.3%	0.04	0.3%	0.05	0.4%	0.08	0.6%

Whole Blood Application: ADAMS HA-8180V analyzer # 3 (NSGP)

Mean	Repeatability		Between Run		Between Day		Between Lot		Total	
% HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 5.2%	0.02	0.4%	0.02	0.4%	0.00	0.0%	0.01	0.2%	0.03	0.6%
Patient 2, 6.4%	0.02	0.4%	0.01	0.2%	0.00	0.0%	0.06	0.9%	0.06	1.0%
Patient 3, 7.9%	0.03	0.4%	0.02	0.2%	0.02	0.3%	0.05	0.7%	0.07	0.9%
Patient 4, 11.8%	0.02	0.2%	0.03	0.2%	0.02	0.2%	0.11	1.0%	0.12	1.0%
Control 1, 5.2%	0.02	0.5%	0.02	0.3%	0.01	0.2%	0.02	0.4%	0.04	0.8%
Control 2, 9.1%	0.03	0.4%	0.03	0.3%	0.03	0.3%	0.05	0.5%	0.07	0.8%
Control 3, 13.4%	0.03	0.2%	0.04	0.3%	0.04	0.3%	0.08	0.6%	0.10	0.7%

Whole Blood Application: ADAMS HA-8180V analyzers combined (NSGP)

Mean % HbA1c	Repeatability		Between Run		Between Day		Between Lot		Between Instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Pt 1, 5.2%	0.02	0.3%	0.02	0.4%	0.01	0.3%	0.01	0.1%	0.00	0.0%	0.03	0.6%
Pt 2, 6.5%	0.02	0.4%	0.02	0.3%	0.02	0.3%	0.04	0.7%	0.02	0.2%	0.06	0.9%
Pt 3, 7.9%	0.02	0.2%	0.02	0.2%	0.02	0.2%	0.05	0.7%	0.01	0.1%	0.06	0.8%
Pt 4, 11.9%	0.03	0.3%	0.03	0.2%	0.03	0.3%	0.09	0.7%	0.03	0.3%	0.11	0.9%
Cntrl 1, 5.2%	0.02	0.5%	0.05	1.1%	0.05	1.0%	0.04	0.7%	0.01	0.3%	0.09	1.7%
Cntrl 2, 9.1%	0.03	0.3%	0.04	0.4%	0.04	0.5%	0.03	0.3%	0.02	0.2%	0.07	0.8%
Cntrl 3, 13.6%	0.03	0.2%	0.05	0.4%	0.05	0.4%	0.05	0.4%	0.03	0.3%	0.10	0.8%

Whole Blood Application: ADAMS HA-8180V analyzer # 1 (IFCC)

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 33	0.2	0.7%	0.2	0.7%	0.0	0.0%	0.3	0.9%	0.4	1.4%
Patient 2, 47	0.3	0.6%	0.2	0.5%	0.1	0.2%	0.4	0.9%	0.5	1.2%
Patient 3, 62	0.3	0.5%	0.1	0.2%	0.1	0.1%	0.6	1.0%	0.7	1.1%
Patient 4, 105	0.3	0.3%	0.2	0.2%	0.2	0.2%	0.7	0.7%	0.8	0.8%
Control 1, 33	0.2	0.7%	0.2	0.7%	0.1	0.2%	0.2	0.5%	0.4	1.1%
Control 2, 75	0.3	0.4%	0.3	0.3%	0.2	0.2%	0.0	0.0%	0.4	0.6%
Control 3, 123	0.2	0.2%	0.4	0.3%	0.2	0.2%	0.2	0.2%	0.6	0.5%

Whole Blood Application: ADAMS HA-8180V analyzer # 2 (IFCC)

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 33	0.2	0.7%	0.1	0.3%	0.0	0.0%	0.5	1.4%	0.5	1.6%
Patient 2, 47	0.3	0.7%	0.0	0.0%	0.2	0.5%	0.5	1.1%	0.7	1.4%
Patient 3, 63	0.4	0.6%	0.2	0.4%	0.2	0.3%	0.8	1.2%	0.9	1.4%
Patient 4, 106	0.5	0.5%	0.3	0.3%	0.2	0.2%	1.1	1.0%	1.2	1.2%
Control 1, 33	0.2	0.7%	0.3	0.8%	0.1	0.4%	0.1	0.5%	0.4	1.2%
Control 2, 75	0.3	0.3%	0.4	0.5%	0.0	0.0%	0.5	0.7%	0.7	0.9%
Control 3, 123	0.3	0.3%	0.3	0.3%	0.3	0.3%	0.6	0.5%	0.8	0.7%

Whole Blood Application: ADAMS HA-8180V analyzer # 3 (IFCC)

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 33	0.2	0.6%	0.2	0.5%	0.0	0.0%	0.5	1.6%	0.6	1.8%
Patient 2, 47	0.3	0.7%	0.2	0.3%	0.2	0.4%	0.3	0.7%	0.5	1.1%
Patient 3, 63	0.3	0.5%	0.2	0.4%	0.3	0.4%	0.6	1.0%	0.8	1.3%
Patient 4, 106	0.3	0.3%	0.3	0.3%	0.3	0.2%	1.3	1.2%	1.4	1.3%
Control 1, 33	0.2	0.6%	0.2	0.5%	0.2	0.6%	0.1	0.4%	0.4	1.1%
Control 2, 75	0.3	0.4%	0.3	0.4%	0.3	0.4%	0.5	0.6%	0.7	0.9%
Control 3, 123	0.3	0.2%	0.4	0.3%	0.4	0.3%	0.9	0.7%	1.1	0.9%

Whole Blood Application: ADAMS HA-8180V analyzers combined (IFCC)

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Between Instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Pt 1, 33	0.22	0.7%	0.17	0.5%	0.06	0.2%	0.44	1.3%	0.07	0.2%	0.53	1.6%
Pt 2, 47	0.31	0.7%	0.14	0.3%	0.27	0.6%	0.35	0.7%	0.27	0.6%	0.61	1.3%
Pt 3, 63	0.32	0.5%	0.20	0.3%	0.24	0.4%	0.64	1.0%	0.21	0.3%	0.81	1.3%
Pt 4, 106	0.39	0.4%	0.29	0.3%	0.33	0.3%	1.00	0.9%	0.31	0.3%	1.20	1.1%
Cntrl 1, 33	0.22	0.7%	0.22	0.7%	0.14	0.4%	0.14	0.4%	0.13	0.4%	0.39	1.2%
Cntrl 2, 75	0.28	0.4%	0.31	0.4%	0.27	0.4%	0.32	0.4%	0.23	0.3%	0.63	0.8%
Cntrl 3, 123	0.28	0.2%	0.40	0.3%	0.43	0.4%	0.53	0.4%	0.34	0.3%	0.90	0.7%

Hemolysate Application: ADAMS HA-8180V analyzer # 1 (NGSP)

Mean % HbA1c	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 5.2%	0.02	0.4%	0.03	0.5%	0.01	0.2%	0.00	0.1%	0.04	0.7%
Patient 2, 6.4%	0.01	0.2%	0.02	0.3%	0.02	0.3%	0.05	0.8%	0.06	0.9%
Patient 3, 7.9%	0.03	0.4%	0.02	0.2%	0.02	0.3%	0.04	0.6%	0.06	0.8%
Patient 4, 11.9%	0.03	0.3%	0.03	0.3%	0.02	0.2%	0.07	0.6%	0.08	0.7%
Control 1, 5.2%	0.03	0.5%	0.07	1.3%	0.06	1.2%	0.05	0.9%	0.11	2.1%
Control 2, 9.1%	0.03	0.3%	0.02	0.2%	0.04	0.4%	0.01	0.2%	0.05	0.6%
Control 3, 13.5%	0.03	0.2%	0.05	0.4%	0.04	0.3%	0.03	0.3%	0.08	0.6%

Hemolysate Application: ADAMS HA-8180V analyzer # 2 (NGSP)

Mean	Repeatability		Between Run		Between Day		Between Lot		Total	
% HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 5.2%	0.01	0.2%	0.02	0.4%	0.02	0.3%	0.01	0.2%	0.03	0.6%
Patient 2, 6.4%	0.02	0.3%	0.01	0.1%	0.02	0.3%	0.05	0.8%	0.06	0.9%
Patient 3, 7.9%	0.02	0.2%	0.02	0.3%	0.01	0.1%	0.06	0.8%	0.07	0.9%
Patient 4, 11.9%	0.03	0.3%	0.02	0.2%	0.03	0.3%	0.10	0.8%	0.11	0.9%
Control 1, 5.2%	0.03	0.5%	0.05	1.0%	0.05	1.0%	0.04	0.8%	0.09	1.7%
Control 2, 9.1%	0.02	0.3%	0.05	0.5%	0.05	0.5%	0.03	0.4%	0.08	0.8%
Control 3, 13.6%	0.03	0.2%	0.05	0.4%	0.05	0.4%	0.06	0.4%	0.10	0.7%

Hemolysate Application: ADAMS HA-8180V analyzer # 3 (NGSP)

Mean	Repeatability		Between Run		Between Day		Between Lot		Total	
% HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 5.2%	0.02	0.3%	0.00	0.0%	0.01	0.3%	0.00	0.1%	0.02	0.4%
Patient 2, 6.5%	0.03	0.5%	0.02	0.4%	0.00	0.0%	0.03	0.5%	0.05	0.8%
Patient 3, 7.9%	0.01	0.1%	0.01	0.1%	0.00	0.0%	0.06	0.7%	0.06	0.8%
Patient 4, 11.9%	0.03	0.2%	0.03	0.2%	0.02	0.2%	0.10	0.9%	0.11	0.9%
Control 1, 5.2%	0.02	0.4%	0.04	0.7%	0.04	0.8%	0.03	0.5%	0.07	1.2%
Control 2, 9.1%	0.03	0.3%	0.04	0.4%	0.03	0.4%	0.04	0.5%	0.07	0.8%
Control 3, 13.6%	0.04	0.3%	0.05	0.4%	0.04	0.3%	0.08	0.6%	0.11	0.8%

Hemolysate Application: ADAMS HA-8180V analyzers combined (NGSP)

Mean % HbA1c	Repeatability		Between Run		Between Day		Between Lot		Between Instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Pt 1, 5.2%	0.02	0.3%	0.02	0.4%	0.01	0.3%	0.01	0.1%	0.00	0.0%	0.03	0.6%
Pt 2, 6.5%	0.02	0.4%	0.02	0.3%	0.02	0.3%	0.04	0.7%	0.02	0.2%	0.06	0.9%
Pt 3, 7.9%	0.02	0.2%	0.02	0.2%	0.02	0.2%	0.05	0.7%	0.01	0.1%	0.06	0.8%
Pt 4, 11.9%	0.03	0.3%	0.03	0.2%	0.03	0.3%	0.09	0.7%	0.03	0.3%	0.11	0.9%
Cntrl 1, 5.2%	0.02	0.5%	0.05	1.1%	0.05	1.0%	0.04	0.7%	0.01	0.3%	0.09	1.7%
Cntrl 2, 9.1%	0.03	0.3%	0.04	0.4%	0.04	0.5%	0.03	0.3%	0.02	0.2%	0.07	0.8%
Cntrl 3, 13.6%	0.03	0.2%	0.05	0.4%	0.05	0.4%	0.05	0.4%	0.03	0.3%	0.10	0.8%

Hemolysate Application: ADAMS HA-8180V analyzer # 1 (IFCC)

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 33	0.3	0.8%	0.3	0.8%	0.2	0.7%	0.4	1.1%	0.6	1.7%
Patient 2, 47	0.3	0.6%	0.2	0.3%	0.2	0.4%	0.2	0.5%	0.4	0.9%
Patient 3, 63	0.3	0.5%	0.3	0.5%	0.2	0.3%	0.5	0.8%	0.7	1.2%
Patient 4, 106	0.3	0.3%	0.3	0.2%	0.2	0.2%	0.7	0.6%	0.8	0.8%
Control 1, 33	0.2	0.6%	0.7	2.0%	0.7	2.0%	0.3	1.0%	1.0	3.0%
Control 2, 76	0.3	0.4%	0.3	0.4%	0.4	0.5%	0.2	0.2%	0.6	0.8%
Control 3, 125	0.3	0.3%	0.6	0.5%	0.5	0.4%	0.4	0.3%	0.9	0.7%

Hemolysate Application: ADAMS HA-8180V analyzer # 2 (IFCC)

Mean	Repeatability		Between Run		Between Day		Between Lot		Total	
mmol/mol	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 33	0.2	0.7%	0.2	0.5%	0.2	0.5%	0.4	1.1%	0.5	1.5%
Patient 2, 47	0.3	0.5%	0.2	0.5%	0.2	0.4%	0.3	0.7%	0.5	1.1%
Patient 3, 63	0.2	0.4%	0.3	0.4%	0.2	0.3%	0.6	1.0%	0.7	1.2%
Patient 4, 107	0.4	0.3%	0.4	0.4%	0.2	0.2%	1.0	0.9%	1.2	1.1%
Control 1, 33	0.2	0.6%	0.6	1.7%	0.7	2.0%	0.2	0.6%	0.9	2.7%
Control 2, 76	0.3	0.4%	0.6	0.8%	0.5	0.7%	0.4	0.6%	0.9	1.2%
Control 3, 125	0.3	0.3%	0.5	0.4%	0.6	0.5%	0.7	0.5%	1.1	0.9%

Hemolysate Application: ADAMS HA-8180V analyzer # 3 (IFCC)

Mean	Repeatability		Between Run		Between Day		Between Lot		Total	
mmol/mol	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1, 33	0.2	0.7%	0.2	0.7%	0.1	0.4%	0.4	1.2%	0.5	1.6%
Patient 2, 47	0.2	0.4%	0.2	0.3%	0.1	0.3%	0.4	0.8%	0.5	1.0%
Patient 3, 63	0.2	0.3%	0.2	0.3%	0.0	0.0%	0.6	1.0%	0.7	1.0%
Patient 4, 107	0.4	0.4%	0.3	0.3%	0.2	0.2%	1.2	1.1%	1.3	1.2%
Control 1, 33	0.2	0.7%	0.5	1.5%	0.4	1.2%	0.2	0.7%	0.7	2.2%
Control 2, 76	0.3	0.4%	0.4	0.5%	0.4	0.5%	0.5	0.6%	0.8	1.0%
Control 3, 125	0.4	0.3%	0.5	0.4%	0.5	0.4%	0.9	0.7%	1.2	0.9%

Hemolysate Application: ADAMS HA-8180V analyzers combined (IFCC)

Mean mmol/mol	Repeatability		Between Run		Between Day		Between Lot		Between Instrument		Total	
	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Pt 1, 33	0.25	0.7%	0.22	0.7%	0.18	0.5%	0.38	1.2%	0.06	0.2%	0.54	1.6%
Pt 2, 47	0.24	0.5%	0.19	0.4%	0.21	0.4%	0.29	0.6%	0.13	0.3%	0.49	1.0%
Pt 3, 63	0.27	0.4%	0.26	0.4%	0.18	0.3%	0.57	0.9%	0.15	0.2%	0.72	1.1%
Pt 4, 107	0.36	0.3%	0.32	0.3%	0.30	0.3%	0.96	0.9%	0.30	0.3%	1.15	1.1%
Cntrl 1, 33	0.21	0.6%	0.57	1.7%	0.57	1.7%	0.28	0.9%	0.00	0.0%	0.88	2.7%
Cntrl 2, 76	0.28	0.4%	0.44	0.6%	0.44	0.6%	0.36	0.5%	0.23	0.3%	0.81	1.1%
Cntrl 3, 125	0.35	0.3%	0.53	0.4%	0.58	0.5%	0.62	0.5%	0.34	0.3%	1.12	0.9%

b. Linearity/assay reportable range:

The linearity of the HA-8180V system was evaluated in accordance with CLSI EP6-A, *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. Linearity across the reportable range was performed using K2-EDTA whole blood patient samples ranging from 3% to 19% (9.3-184.2 mmol/mol) HbA1c. Intermediate HbA1c concentration samples were prepared by performing equal distance dilutions of the high HbA1c sample with the low HbA1c sample. The sample concentrations tested were as follows: 3.0, 4.6, 6.2, 7.8, 9.4, 10.9, 12.5, 14.1, 15.7, 17.37, and 19.0 % HbA1c (9.3, 26.8, 44.3, 61.8, 79.2, 96.7, 114.2, 131.7, 149.2, 166.7, and 184.2 mmol/mol). The samples were tested in replicates of three.

The following linear regression equations were obtained:

NGSP: $y= 0.9958x + 0.0064$, $R^2=0.999$

IFCC: $y= 0.9958x – 0.0275$, $R^2=0.999$

The linearity study supports the measuring range for this device of 4.0-15.0% HbA1c (20-140 mmol/mol HbA1c)

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

Traceability:

The ADAMS HbA1c test method is traceable to the Diabetes Control and Complications Trial Reference Method through The National Glycohemoglobin Standardization Program (NGSP) and has received NGSP certification. See the NGSP website for current certification at http://www.ngsp.org.

The International Federation of Clinical Chemistry (IFCC) units of mmol/mol are calculated using the Master Equation NGSP (%) =0.09148 x IFCC (mmol/mol) + 2.52. HbA1c results are provided to the customers using two different units: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol).

CALIBRATOR 80 Value Assignment:

The value assignment for the ADAMS H1c HA-8180V Calibrators is traceable to the IFCC reference method. Using an ADAMS A1c HA-8180V instrument calibrated with standard material JCCRM-411 (provided by ReCCS), CALIBRATOR 80 Low and High are value assigned by measuring each calibrator 9 times per day over 3 days for a total of 27 values. The mean generated over the 3 days is used as the reference value for each calibrator.

The HbA1c values for the CALIBRATOR 80 are lot specific and target the following % HbA1c concentrations:

CALIBRATOR 80 Low: 5.0-6.0% HbA1c
CALIBRATOR 80 High: 10.0-11.0% HbA1c

CALIBRATOR 80 Stability:

Shelf life: The shelf-life stability study protocol and acceptance criteria were reviewed and found to be acceptable to support the sponsor's shelf-life stability claim that un-opened CALIBRATOR 80 is stable for 18 months when stored at 2-8^{o}C.

Open vial: The open-vial stability study protocol and acceptance criteria were reviewed and found to be acceptable to support the sponsor's open-vial stability claim that upon reconstitution, CALIBRATOR 80 may be stored at 2-8^{o}C for 8 hours. The calibrators are intended for single use only.

d. *Detection limit:*

The claimed measuring range, 4.0% to 15.0% HbA1c (20 to 140 mmol/mol), was validated by the linearity study.

e. Analytical specificity:

i.) Interference

The effect of various potential interfering substances on the HA-8180V HbA1c results was evaluated in accordance with CLSI EP7-A2, *Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition*.

with HbA1c values of 6.5% Human whole blood K2-EDTA samples HbA1c and ~8% HbA1c were analyzed by spiking the interfering substance into each of the two whole blood samples. Samples were analyzed in replicates of ten on the HA-8180V test system and the results were compared to the reference sample (sample containing no interferent). The sponsor defines significant interference as ≥ +/-7% change in %HbA1c value from the control value. The following substances showed no significant interference at the concentrations described below:

Substance	Highest concentration tested with no significant interference
Albumin	20 g/dL
Bilirubin, conjugated	100 mg/dL
Bilirubin, unconjugated	100 mg/dL
Rheumatoid Factor	750 IU/mL
Triglycerides	2,000 mg/dL
Acetaminophen	20 mg/dL
Acetylcysteine	330 mg/dL
Acetylsalicylic Acid (Aspirin)	65 mg/dL
Ampicillin-Na	1,000 mg/dL
Ascorbic Acid	200 mg/dL
Cefoxitin-Na	2,500 mg/dL
Cyclosporine	0.67 mg/dL
Doxycycline	50 mg/dL
Ibuprofen	50 mg/dL
Levodopa	20 mg/dL
Metformin	5 mg/dL
Methyldopa	30 mg/dL
Metronidazole	200 mg/dL
Rifampicin	6.4 mg/dL
Salicylic Acid	60 mg/dL
Theophylline	10 mg/dL

ii.) Cross Reactivity:
Potential interferences from acetylated hemoglobin (Hb), carbamylated Hb, and labile HbA1c were evaluated using Human whole blood K2- EDTA samples with HbA1c values of 6.5%, and 8.0 %. Aliquots of the 6.5% and 8.0% HbA1c samples were spiked with 12.5, 25, 37.5, and 50 mg/dL acetaldehyde solution evaluate the effects of

acetylated hemoglobin; 6.25, 12.5, 18.75, and 25 mg/dL of sodium cyanate solution was added to the A1c samples to evaluate the effects of carbamylated hemoglobin; and 500, 1000, 1500, and 2000 mg/dL glucose solution were added to the A1c samples to evaluate the effects of Labile A1c. The samples were allowed to incubate for two hours at 37^{o} C prior to testing. The samples were run in replicates of ten on one HA-8180V analyzer and the results were compared to the reference sample (sample containing no added solutions). Significant interference was defined as % recovery ≥ +/-7% of the expected 100% recovery.

The results were concluded as follows:

- Acetylated Hb (up to 50 mg/dL) does not interfere with this assay.
- Carbamylated Hb (up to 25 mg/dL) does not interfere with this assay.
- Labile HbA1c (up to 2000 mg/dL) does not interfere with this assay.

iii.) Hemoglobin Variant Interference:
The effect of various hemoglobin variants on the HA-8180V results was evaluated to determine if the variants interfere with HbA1c results. To assess the effects of hemoglobin variant interference, a total of 165 K2-EDTA whole blood samples known to contain Hemoglobin variants A_2, C, D, E, F and S were tested on the HA-8180V and results compared to a NGSP boronate affinity HPLC reference method that has been demonstrated to be free from interference by the hemoglobin variants (Trinity Biotech Ultra2 A1c for HbC, HbD, HbE, and Tosoh G8 HPLC for HbF and HbA2). A minimum of 10 samples were tested in duplicate at each of the two HbA1c concentrations of ~6.5% and ~8.0% containing the Hemoglobin variants A2, C, D, E, F, and S. The table below shows the number and concentrations of the variants and HbA1c concentrations that were tested.

Hemoglobin Variant	Number of Samples	% Concentration of Variant in Sample	%HbA1c Concentration Range
HbA2	30	1.9-25.4%	4.8- 8.9%
HbC	26	26.9-39.0%	4.6-9.2%
HbD	22	31.6-36%	5.7-10.3%
HbE	22	18.0-30.0 %	4.9-9.7%
HbF	24	1.0-30.3%	4.7-11.7%
HbS	41	12.9-42.1%	4.5-11.6%

The results obtained by the HA-8180V were compared to the comparative method and the percent bias was calculated. The sponsor defines acceptable bias as less than or equal to 7%. The result summary is presented below:

Hemoglobin Variant Results Summary

Hemoglobin Variant	%Bias (Range of % Bias) for ~6.5% HbA1c	% Bias (95% CI) for ~8.0% HbA1c
HbA2	-1.6% (-6.7% to -1.5%)	1.2% (-1.3%, 3.4 %)
HbC	0.1% (-5.6% to 4.6%)	-0.5% (-4.7% to 5.7%)
HbD	-1.7% (-6.8% to 1.7%)	-2.6% (-5.7% to 1.2%)
HbE	-0.1% (-3.0% to 4.8%)	-1.1% (-2.8% to 3.5%)
HbF	-0.3% (-6.5% to4.0%)	0.5% (-2.7% to 6.9%)
HbS	0.1% (-8.8% to 5.7%)	-0. 4% (-4.7 to% 5.5%)

The results show there is no significant interference for HbA2 concentrations of less than or equal to 16%, HbC concentrations of less than or equal to 39%, HbD concentrations of less than or equal to 36%, HbE concentrations of less than or equal to 30%, HbF concentrations of less than or equal to 30%, and HbS concentrations of less than or equal to 40%.

The labeling contains the above results summary in the limitations section and the summary and tables are included in the performance characteristic section of the labeling.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

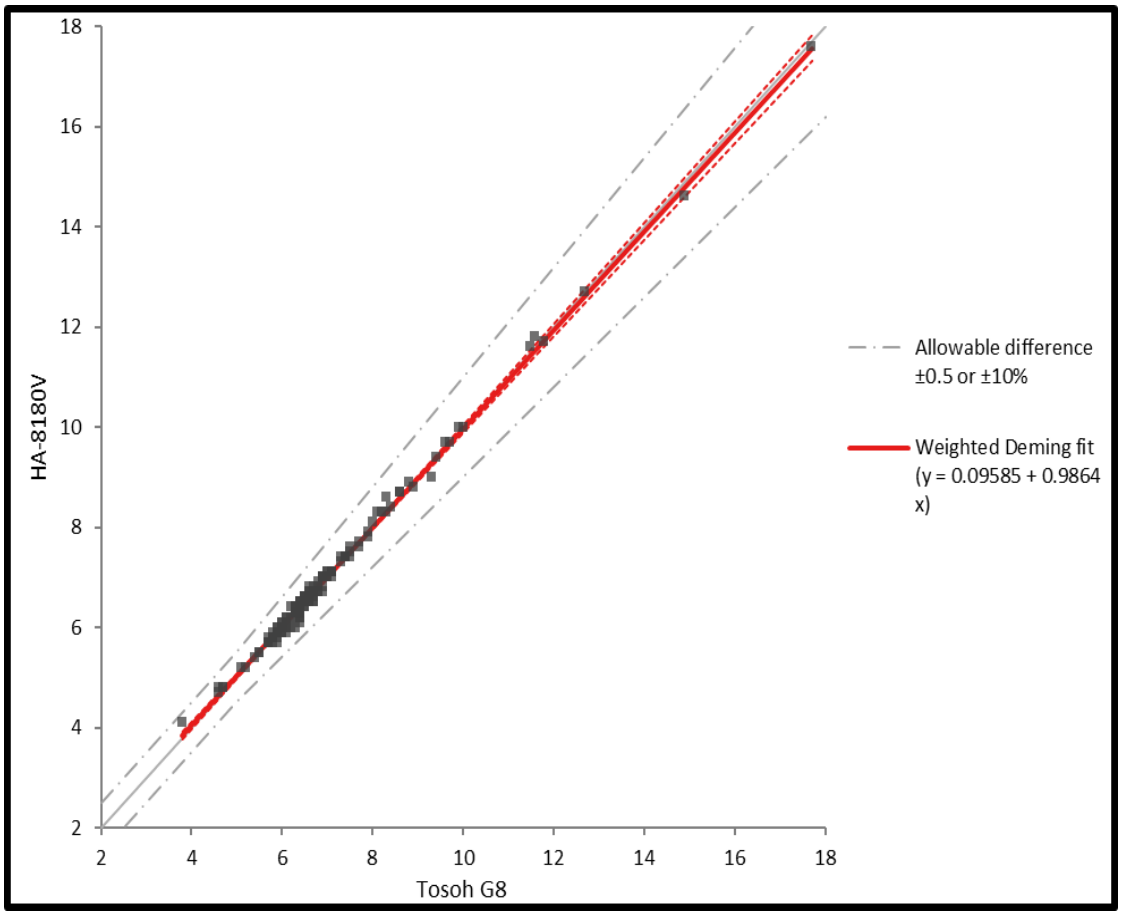
A method comparison study was performed in which %HBA1c was measured in 143 variant-free venous whole blood K2-EDTA samples and hemolysate samples on the candidate HA-8180V device. The candidate device HbA1c results were compared to those obtained from testing performed at secondary NGSP reference laboratory on the Tosoh G8 HPLC method. The distribution of samples spanned the measuring interval (with a higher percentage of samples around the clinical decision points) for both whole blood and hemolysate methods as follows:

Hemoglobin A1c level	Number of samples	%samples tested
≤ 4.9%	5	3%
5 – 5.9%	19	13%
6 – 6.4%	40	28%
6.5 – 6.9%	40	25%
7 – 7.9%	21	15%
8 – 8.9%	10	7%
> 9%	12	89%
Total samples	143	100%

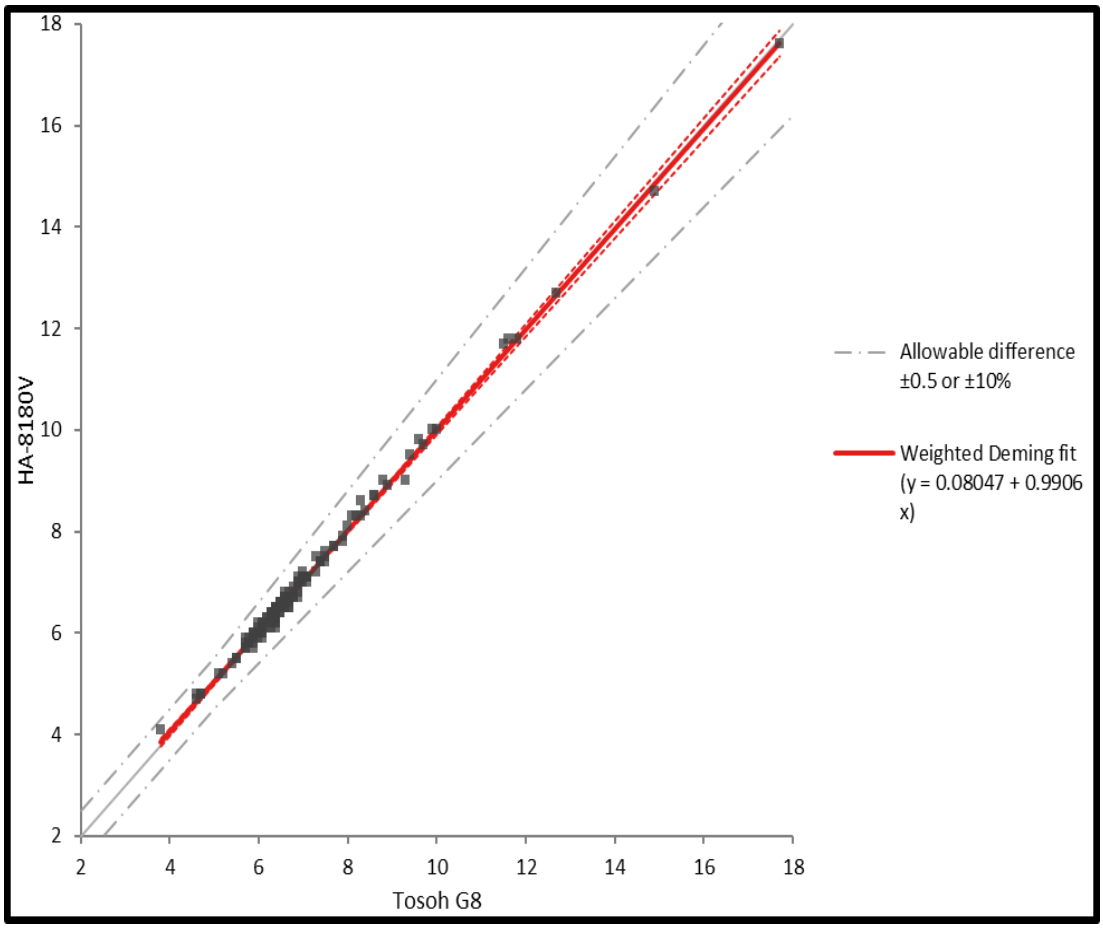
Deming (weighted) regression analysis was performed for the HA-8180V system versus the NGSP SRL reference method. A summary of the results for both the whole blood and the hemolysate methods are provided in the tables below.

Whole Blood	Slope (95% CI)	Intercept (95% CI)	R^2
Weighted Deming	0.9864 (0.9626 to 1.010)	0.09585 (-0.06895 to 0.2670)	0.998
Hemolysate	Slope (95% CI)	Intercept (95% CI)	R^2
Weighted Deming	0.9906 (0.9670-1.014)	0.0847 (-0.08251 to 0.24347)	0.998

Scatter plot using weighted Deming Fit, %HbA1c, Reference Method vs ADAMS A1c HA-8180V (Whole Blood Samples)



Scatter plot using weighted Deming Fit, %HbA1c, Reference Method vs ADAMS A1c HA-8180V (Hemolysate Blood Samples)



The following biases between the candidate HA-8180V system versus the NGSP Reference Method (Tosoh G8 HPLC analyzer) were observed:

Bias Estimation (whole blood)

% HbA1c Level	Bias	%Bias
5.0	0.028	0.56%
6.5	0.007	0.11%
8.0	-0.013	-0.16%
12.0	-0.067	-0.56%

Bias Estimation (hemolysate)

% HbA1c Level	Bias	%Bias
5.0	0.033	0.67%
6.5	0.019	0.30%
8.0	0.005	0.07%
12.0	-0.032	-0.27%

Total Error Near Cutoff

Using the results of bias estimation (%Bias) in the method comparison study and precision estimated in the reproducibility study, Total Error (TE) at four concentrations: (5.0%,6.5%, 8.0% and 12%) was calculated as follows: %TE =|%Bias| + 1.96 x %CV x (1+ (%Bias/100). The results are presented in the tables below:

Whole Blood

Decision Level	%Bias	%CV	%TE
5.0	0.56	0.5	1.5
6.5	0.11	0.9	1.9
8.0	-0.16	1.0	2.1
12.0	-0.56	1.0	2.4

Hemolysate

Decision Level	%Bias	%CV	%TE
5.0	0.67	0.6	1.8
6.5	0.31	0.9	2.1
8.0	0.07	0.8	1.6
12.0	-0.27	0.9	2.0

b. Matrix comparison:

A matrix comparison study was performed to evaluate the effects of the different anticoagulants, K2-EDTA and K3-EDTA, on %HbA1c measurement by the ADAMS A1c HA-8180V system. Venous whole blood specimens with concentrations spanning 4.7 to15.7% HbA1c were collected in K2-EDTA (reference anticoagulant) and K3-EDTA blood tubes from a total of 40 donors. The samples were measured on the candidate device and the results were compared. The following regression equation was obtained :

$y=1.005x-0.047$, $R^2=1.000$

The results of the study support the sponsor ’s claim that blood samples collected in blood collection tubes containing K2-EDTA and K3-EDTA anti-coagulants are

acceptable for use with this device.

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 values reference range cited below is from the American Diabetes Association (ADA), "Diagnosis and Classification of Diabetes Mellitus" Diabetes Care; 39 (Supplement 1): S13-S22; 2016.

Suggested Diagnosis	HbA1c (%)	HbA1c (mmol/mol)
Diabetic	≥ 6.5	≥ 48
Prediabetes	5.7 – 6.4	39 – 47
Normal	< 5.7	< 39

N. Instrument Name:

ADAMS H1c HA-8180V analyzer

O. System Descriptions:

1. Modes of Operation:

   Continuous testing mode

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes ___X_____ or No _____

3. Specimen Identification:

   Manual sample identification or internal barcode reader

4. Specimen Sampling and Handling:
   Hemoglobin test specimens are prepared by automated dilution (1:101) of anticoagulated venous whole blood in hemolysis washing solution 80H. Alternately, hemolysates may be prepared "off-line" by manual dilution of anticoagulated venous whole blood with the diluent 80 provided in control dilution set 80. The samples are placed in plastic racks and placed on the analyzer.

5. Calibration:

   Automatic calibration: The analyzer measures two HbA1c standard solutions (CALIBRATOR 80 Low and High solutions), and uses the results to automatically determine the calibration coefficients. Standard values of the standard solutions can be set by entering the numbers using numeric buttons, or reading the calibration information barcodes during measurement when using the internal barcode reader.

6. Quality Control:

   Recommendations for quality control are described in the labeling. Additionally, users should follow local, state and federal regulations.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not applicable.

Q. Proposed Labeling:

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

R. Conclusion:

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