



Food and Drug Administration
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BIO-RAD LABORATORIES, INC.
JACKIE BUCKLEY
REGULATORY AFFAIRS SUPERVISOR
4000 ALFRED NOBEL DR.
HERCULES CA 94547

October 14, 2016

Re: K161687
Trade/Device Name: D-10 Hemoglobin A1c Program
Regulation Number: 21 CFR 862.1373
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: II
Product Code: PDJ
Dated: August 30, 2016
Received: September 1, 2016

Dear Ms. Buckley:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

k161687

Device Name

D-10™ Hemoglobin A1c Program

Indications for Use (Describe)

The D-10™ Hemoglobin A1c Program is intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %) in human whole blood using ion- exchange high-performance liquid chromatography (HPLC) on the D-10™ Hemoglobin Testing System.

Hemoglobin A1c measurements are used as an aid in diagnosis of diabetes, 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 D-10™ Hemoglobin A1c Program is intended for professional in vitro diagnostic use only.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary (Summary of Safety and Effectiveness)

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

The assigned 510(k) number is: K161687.

Date Summary prepared: Oct. 12, 2016

1. Applicant Name:

Bio-Rad Laboratories, Inc.
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2. Contact Person(s):

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3. Device Name/Trade Name:

Reagents:
Trade Name: D-10™ Hemoglobin A1c
Program
Classification Name: Hemoglobin A1c Test System
Common Name: HbA1c
Product Code: PDJ
C.F.R Section: 21 CFR 862.1373
Device classification: Class II
Panel Classification: Chemistry

4. Predicate Device:

Predicate Device Name	Predicate Device 510(k) Number
VARIANT II TURBO HbA1c Kit -2.0	K142448

5. Description of the Device:

The D-10™ Hemoglobin Testing System utilizes the principles of ion-exchange high-performance liquid chromatography (HPLC). A dual-piston, low pulsation HPLC pump and a proportioning valve deliver the buffer solution to an analytical cartridge and detector. Whole blood samples undergo an automatic two step dilution process and then introduced into the analytical flow path. Pre-diluted samples are aspirated directly and introduced into the analytical flow path. Between sample injections, the sample probe is rinsed with Wash/Diluent Solution to minimize sample carryover.

A programmed buffer gradient of increasing ionic strength delivers the sample to the analytical cartridge where the hemoglobin species are separated based upon their ionic interactions with the cartridge material and the buffer gradient. The separated hemoglobin species then pass through the photometer flow cell where changes in the absorbance are measured at 415 nm and recorded as a digital chromatogram.

The software performs a reduction of raw data collected from each analysis that may indicate use of a calibration factor. A samples report and chromatogram are generated for each sample.

The D-10™ Hemoglobin A1c Program is designed to be used on the D-10™ Hemoglobin Testing System with or without a D-10 Rack Loader.

Reagents:

The D-10™ HbA1c reagents contain the following components:

Description
D-10™ Hemoglobin A_{1c} Analytical Cartridge. Cation exchange cartridge (400 tests), 4.0 mm ID x 30 mm.
D-10™ Wash/Diluent Solution. Each bottle contains 1600 mL of deionized water with <0.05 sodium azide as a preservative.
Floppy diskette with D-10 Hemoglobin A1c "Update Kit" program parameters.
D-10™ Hemoglobin A_{1c} Elution Buffer 1. Each bottle contains 2000 mL of a Bis-Tris/Phosphate buffer. Contains <0.05% sodium azide as a preservative.
D-10™ Hemoglobin A_{1c} Elution Buffer 2. Each bottle contains 1000 mL of a Bis-Tris/Phosphate buffer. Contains <0.05% sodium azide as a preservative.
D-10™ Hemoglobin A_{1c} Calibrator/Diluent Set. One set consisting of 3 vials of Calibrator 1, 3 vials of Calibrator 2, and 1 bottle of Calibrator Diluent. The calibrator vials contain lyophilized human red blood cell hemolysate with gentamicin, tobramycin, and EDTA as preservative. Reconstituted volume is 7mL per vial. Calibrator Diluent contains 100 mL of deionized water with <0.05% sodium azide as preservative.

CD-ROM with D-10 Hemoglobin A1c “Update Kit” program parameters
Whole Blood Primer. Each vial contains lyophilized human red blood cell hemolysate with gentamicin, tobramycin, and EDTA as preservatives. Reconstituted volume is 1.0 mL per vial.
Sample Vials. 100 polypropylene microvials with pierceable caps, 1.5mL

D-10 Hemoglobin A1c Supplemental Reagent Pack. This reagent pack is used as a supplement to the D-10 Hemoglobin A1c Reorder Pack.

6. Indications for Use:

The D-10™ Hemoglobin A1c Program is intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %) in human whole blood using ion-exchange high-performance liquid chromatography (HPLC) on the D-10™ Hemoglobin Testing System.

Hemoglobin A1c measurements are used as an aid in diagnosis of diabetes, 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 D-10™ Hemoglobin A1c Program is intended for professional in vitro diagnostic use only.

7. Substantial Equivalence Information:

Predicate Device Information:

Predicate Device Name	Predicate Device 510(k) Number
VARIANT II TURBO HbA1c Kit -2.0	K142448

The comparison of the technological characterizes of the D-10 Hemoglobin A1c Program (candidate assay) utilizes principles of ion-exchange high-performance liquid chromatography (HPLC) similar to the same technology of the VARIANT II TURBO HbA1c Kit – 2.0 (predicate device).

Tables 1 and 2 provide the similarities and differences between the candidate assay and the predicate assay.

Table 1: Reagent Similarities and Differences

Reagent Similarities and Differences		
Features	Candidate Device: D-10™ Hemoglobin A1c (K)161687	Predicate Device: VARIANT™ II TURBO HbA1c Kit – 2.0 (K)142448
Intended Use	Same	Intended for the quantitative determination of hemoglobin A1c (IFCC mmol/mol and NGSP %)
Platform	D-10™ Hemoglobin Testing System	VARIANT™II TURBO Hemoglobin Testing System and VARIANT™II TURBO Link Hemoglobin Testing System
Measuring Interval	3.9 to 18.8% (NSGP) 19 – 182 mmol/mol HbA1c (IFCC)	3.4 to 20.6 % (NSGP) 14 – 203 mmol/mol HbA1c (IFCC)
Specimen Type	Same	Human Whole blood
Assay Principle	Same	Ion exchange HPLC
Matrices	K ₂ -EDTA, K ₃ -EDTA	K ₂ -EDTA, K ₃ -EDTA Hemoglobin Capillary Collection Kit
Standardization	Same	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP)

8. Summary of Nonclinical Performance Data:

a. Precision/Reproducibility:

The precision of the D-10™ Hemoglobin A1c Program was evaluated based on CLSI EP05-A2 guidelines, Evaluation of Precision Performance of Quantitative Measurement Methods using a modified study design. Four EDTA whole blood samples at the following targeted HbA1c concentrations of ~5%, ~6.5%, ~8% and ~12% were utilized in the study. In addition, five quality control materials were also tested. The samples were run in duplicate in 2 runs per day on 3 instruments for 20 days. The study was repeated using 3 different kit lots, yielding a total of 720 results per sample over a 60-day period. NGSP results are shown in Tables 2-5. IFCC results are shown in Tables 6-9.

Table 2: Instrument 1 % CV by Sample (NGSP)

Sample ID	HbA1c, %	Repeatability		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	5.2	0.07	1.3	0.00	0.0	0.04	0.7	0.08	1.6	0.11	2.2
Patient 2	6.7	0.07	1.0	0.00	0.0	0.07	1.1	0.05	0.7	0.11	1.7
Patient 3	8.4	0.05	0.6	0.01	0.2	0.08	1.0	0.02	0.2	0.10	1.2
Patient 4	12.7	0.09	0.7	0.06	0.5	0.17	1.3	0.21	1.7	0.29	2.3
Control 1	5.6	0.07	1.2	0.00	0.0	0.05	0.9	0.05	0.9	0.10	1.8
Control 2	10.4	0.10	0.9	0.00	0.0	0.12	1.1	0.12	1.2	0.20	1.9
QC 1	5.5	0.06	1.0	0.00	0.0	0.05	0.9	0.08	1.5	0.11	2.1
QC 2	10.0	0.13	1.3	0.00	0.0	0.09	0.9	0.06	0.6	0.17	1.7
QC 3	15.6	0.11	0.7	0.15	1.0	0.08	0.5	0.17	1.1	0.27	1.7

Table 3: Instrument 2 % (CV by Sample (NGSP))

Sample ID	HbA1c, %	Repeatability		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	5.2	0.04	0.9	0.02	0.4	0.04	0.8	0.08	1.5	0.10	1.9
Patient 2	6.6	0.03	0.5	0.04	0.6	0.05	0.8	0.02	0.3	0.08	1.2
Patient 3	8.2	0.04	0.5	0.04	0.4	0.07	0.8	0.02	0.2	0.09	1.0
Patient 4	12.5	0.06	0.5	0.08	0.6	0.13	1.1	0.21	1.7	0.27	2.1
Control 1	5.6	0.04	0.8	0.02	0.3	0.06	1.0	0.07	1.2	0.10	1.7
Control 2	10.1	0.04	0.4	0.06	0.6	0.08	0.8	0.09	0.9	0.14	1.4
QC 1	5.5	0.03	0.6	0.02	0.4	0.06	1.0	0.08	1.5	0.11	1.9
QC 2	9.8	0.07	0.7	0.06	0.6	0.09	0.9	0.04	0.4	0.13	1.4
QC 3	15.2	0.07	0.4	0.08	0.5	0.14	0.9	0.24	1.6	0.29	1.9

Table 4: Instrument 3 (% CV by Sample (NGSP))

Sample ID	HbA1c, %	Repeatability		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	5.2	0.06	1.2	0.00	0.0	0.06	1.2	0.05	0.9	0.10	1.9
Patient 2	6.7	0.05	0.7	0.02	0.3	0.08	1.2	0.00	0.0	0.09	1.4
Patient 3	8.3	0.05	0.6	0.03	0.4	0.11	1.3	0.04	0.5	0.13	1.6
Patient 4	12.7	0.07	0.6	0.07	0.6	0.17	1.3	0.21	1.6	0.29	2.2
Control 1	5.6	0.05	0.9	0.00	0.0	0.07	1.2	0.04	0.8	0.10	1.7
Control 2	10.3	0.08	0.8	0.05	0.5	0.14	1.3	0.08	0.8	0.19	1.8
QC 1	5.5	0.04	0.8	0.02	0.3	0.07	1.2	0.07	1.3	0.11	2.0
QC 2	9.9	0.09	0.9	0.00	0.0	0.12	1.2	0.13	1.3	0.20	2.0
QC 3	15.5	0.10	0.6	0.11	0.7	0.18	1.1	0.07	0.4	0.24	1.6

Table 5: Instruments Combined (% CV by Sample (NGSP))

Sample ID	HbA1c %	Repeatability		Between-Run		Between-Day		Between-Instruments		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	5.2	0.06	1.2	0.00	0.0	0.05	0.9	0.00	0.0	0.07	1.4	0.10	2.0
Patient 2	6.7	0.05	0.8	0.01	0.2	0.07	1.0	0.05	0.8	0.03	0.5	0.11	1.6
Patient 3	8.3	0.05	0.6	0.03	0.3	0.09	1.1	0.08	0.9	0.03	0.3	0.13	1.6
Patient 4	12.7	0.08	0.6	0.07	0.6	0.16	1.2	0.00	0.0	0.21	1.7	0.28	2.2
Control 1	5.6	0.06	1.0	0.00	0.0	0.06	1.0	0.00	0.0	0.05	0.9	0.10	1.7
Control 2	10.3	0.08	0.7	0.04	0.4	0.12	1.1	0.14	1.3	0.10	1.0	0.22	2.2
QC 1	5.5	0.05	0.8	0.00	0.1	0.06	1.0	0.00	0.0	0.08	1.4	0.11	2.0
QC 2	9.9	0.10	1.0	0.00	0.0	0.10	1.0	0.05	0.5	0.09	0.9	0.17	1.8
QC 3	15.4	0.09	0.6	0.12	0.8	0.14	0.9	0.20	1.3	0.17	1.1	0.34	2.2

Table 6: Instrument 1 (% CV by Sample (IFCC Units- mmol/mol))

Sample ID	HbA1c, mmol/mol	Repeatability		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	33	0.76	2.3	0.00	0.0	0.40	1.2	0.89	2.7	1.24	3.7
Patient 2	50	0.76	1.5	0.00	0.0	0.81	1.6	0.54	1.1	1.23	2.5
Patient 3	68	0.53	0.8	0.16	0.2	0.92	1.3	0.17	0.3	1.08	1.6
Patient 4	116	1.01	0.9	0.65	0.6	1.85	1.6	2.31	2.0	3.19	2.8
Control 1	38	0.77	2.0	0.00	0.0	0.56	1.5	0.53	1.4	1.09	2.9
Control 2	91	1.08	1.2	0.00	0.0	1.31	1.4	1.34	1.5	2.16	2.4
QC 1	37	0.63	1.7	0.00	0.0	0.53	1.4	0.93	2.5	1.25	3.4
QC 2	86	1.46	1.7	0.00	0.0	0.96	1.1	0.61	0.7	1.85	2.2
QC 3	147	1.25	0.9	1.67	1.1	0.92	0.6	1.90	1.3	2.96	2.0

Table 7: Instrument 2 (% CV by Sample (IFCC Units- mmol/mol))

Sample ID	HbA1c, mmol/mol	Repeatability		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	33	0.49	1.5	0.20	0.6	0.43	1.3	0.84	2.6	1.08	3.3
Patient 2	49	0.36	0.7	0.42	0.9	0.58	1.2	0.24	0.5	0.83	1.7
Patient 3	66	0.40	0.6	0.38	0.6	0.72	1.1	0.19	0.3	0.93	1.4
Patient 4	113	0.63	0.6	0.88	0.8	1.47	1.3	2.27	2.0	2.91	2.6
Control 1	37	0.46	1.2	0.19	0.5	0.61	1.6	0.70	1.9	1.05	2.8
Control 2	87	0.45	0.5	0.66	0.8	0.89	1.0	0.96	1.1	1.54	1.8
QC 1	37	0.38	1.0	0.21	0.6	0.61	1.7	0.91	2.5	1.18	3.2
QC 2	84	0.72	0.9	0.67	0.8	1.00	1.2	0.43	0.5	1.46	1.7
QC 3	142	0.73	0.5	0.83	0.6	1.52	1.1	2.58	1.8	3.19	2.2

Table 8: Instrument 3 (% CV by Sample (IFCC Units- mmol/mol))

Sample ID	HbA1c, mmol/mol	Repeatability		Between-Run		Between-Day		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	33	0.70	2.1	0.00	0.0	0.66	2.0	0.51	1.6	1.09	3.3
Patient 2	50	0.51	1.0	0.22	0.4	0.85	1.7	0.00	0.0	1.02	2.0
Patient 3	68	0.56	0.8	0.33	0.5	1.20	1.8	0.46	0.7	1.44	2.1
Patient 4	115	0.80	0.7	0.80	0.7	1.81	1.6	2.26	2.0	3.11	2.7
Control 1	37	0.57	1.5	0.00	0.0	0.73	2.0	0.46	1.2	1.03	2.8
Control 2	89	0.87	1.0	0.60	0.7	1.51	1.7	0.93	1.0	2.07	2.3
QC 1	36	0.45	1.2	0.18	0.5	0.73	2.0	0.77	2.1	1.16	3.2
QC 2	85	1.00	1.2	0.00	0.0	1.35	1.6	1.44	1.7	2.21	2.6
QC 3	145	1.05	0.7	1.24	0.9	1.93	1.3	0.74	0.5	2.63	1.8

Table 9: Instruments Combined (% CV by Sample (IFCC Units- mmol/mol))

Sample ID	HbA1c, mmol/mol	Repeatability		Between-Run		Between-Day		Between-Instruments		Between-Lot		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Patient 1	33	0.66	2.0	0.00	0.0	0.51	1.5	0.00	0.0	0.77	2.3	1.13	3.4
Patient 2	50	0.57	1.1	0.13	0.3	0.76	1.5	0.58	1.2	0.34	0.7	1.17	2.3
Patient 3	67	0.50	0.7	0.31	0.5	0.96	1.4	0.84	1.3	0.30	0.4	1.44	2.1
Patient 4	115	0.83	0.7	0.78	0.7	1.72	1.5	0.00	0.0	2.29	2.0	3.08	2.7
Control 1	37	0.60	1.6	0.00	0.0	0.63	1.7	0.00	0.0	0.57	1.5	1.04	2.8
Control 2	89	0.84	0.9	0.48	0.5	1.26	1.4	1.49	1.7	1.09	1.2	2.44	2.7
QC 1	37	0.50	1.4	0.04	0.1	0.63	1.7	0.00	0.0	0.88	2.4	1.20	3.2
QC 2	85	1.10	1.3	0.00	0.0	1.12	1.3	0.59	0.7	0.93	1.1	1.92	2.3
QC 3	145	1.04	0.7	1.29	0.9	1.52	1.0	2.22	1.5	1.90	1.3	3.69	2.5

b. Linearity

A linearity study was performed per CLSI EP06-A: Evaluation of the Linearity of Quantitative Measuring Procedures; A Statistical Approach. Linearity across the reportable range was performed using low (3.9% HbA1c) and high (18.8% HbA1c) EDTA whole blood patient samples. These samples were mixed together in varying ratios. The measured values were compared to the expected values based upon the dilution factor. Polynomial regression analysis (for first, second, and third order polynomials) were performed to determine the statistical significance of non-linearity. The higher order coefficients were found not to be significant and linearity was demonstrated.

% HbA1c (NGSP) using the D-10™ Hemoglobin A1c Program has demonstrated linearity from 3.9 – 18.8% HbA1c with the maximum measured difference of ± 0.1% between the predicted 1st and 2rd order results as shown in Table 10 below. Mmol/mol HbA1c (IFCC) has been demonstrated as linear from 19 – 182 mmol/mol with the maximum measured difference of ±1 mmol/mol as shown in Table 11 below.

Table 10: Results of Linearity Study (NGSP %)

Sample Pool	Predicted 1st Order	Predicted 2nd Order	Difference
Level 1	3.7	3.8	0.1
Level 2	5.2	5.3	0.1
Level 3	6.8	6.8	0.0
Level 4	8.3	8.2	0.1
Level 5	9.8	9.7	0.1
Level 6	11.3	11.2	0.1

Level 7	12.8	12.7	0.1
Level 8	14.3	14.3	0.0
Level 9	15.8	15.8	0.0
Level 10	17.3	17.3	0.0
Level 11	18.8	18.9	0.1

Table 11: Results of Linearity Study (IFCC mmol/mol)

Sample Pool	Predicted 1st Order	Predicted 2nd Order	Difference
Level 1	17	18	1
Level 2	34	34	0
Level 3	50	50	0
Level 4	67	67	0
Level 5	83	83	0
Level 6	100	99	1
Level 7	116	116	0
Level 8	133	133	0
Level 9	149	149	0
Level 10	166	166	0
Level 11	182	183	1

c. Method Comparison

A Method comparison study was performed per CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 128 variant-free whole blood K₃ EDTA samples ranging from 3.9% to approximately 19.0 % (19 to approximately 184 mmol/mol) HbA1c were evaluated using the D-10™ Hemoglobin A1c Program on the D-10™ Hemoglobin Testing System. Samples were tested in a single determination over a 4 day period. The results were compared to testing performed at a secondary NGSP SRL reference laboratory using a cleared HPLC-based HbA1c assay. The distribution of samples spanned the measuring interval listed in Table 12.

Table 12: Distribution of samples

Hemoglobin A1c level	n	% Samples tested
≤ 5%	4	3.1
5 – 6%	19	14.8
6 – 6.5%	33	25.8
6.5 – 7%	33	25.8

7 – 8%	20	15.6
8 – 9%	10	7.8
> 9%	9	7.0
Total samples	128	100

Linear, Deming (weighted) and Passing-Bablok regression analyses were performed for the D-10™ Hemoglobin A1c versus the NGSP SRL reference method. Deming (weighted), Passing-Bablok and Linear regression analyses were performed for the D-10™ Hemoglobin A1c on the D-10 Hemoglobin Testing System versus the reference G8 HPLC method are summarized in Table 13.

Table 13: Summary of Method Comparison Results

	Slope	95% CI	y- Intercept	95% CI	R²
Linear	0.9701	0.9587 – 0.9816	0.1801	0.0980 – 0.2622	0.9955
Deming	0.9722	0.9579 – 0.9866	0.1654	0.0637 – 0.2670	1.0000
Passing-Bablok	1.0000	1.0000 – 1.0000	0.0000	0.0000 – 0.0000	1.0000

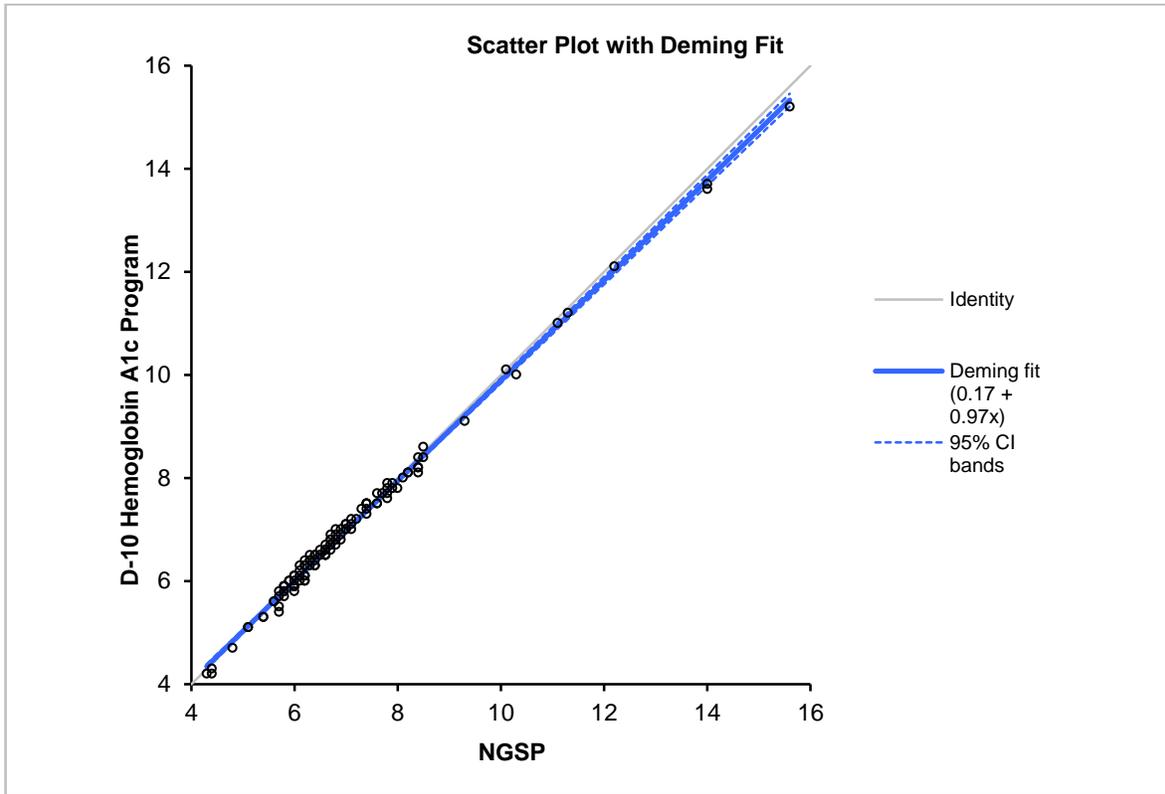


Figure 1: Scatter Plot using Deming Fit, %HbA1c, NGSP SRL vs. D-10 Hemoglobin A1c.

- (1) The following biases between D-10 Hemoglobin A1c versus NGSP SRL Method (Reference method) were observed in Table 14.

Table 14: Bias Estimation

% HbA1c – Decision Level	Bias	% Bias
5.0±0.5	-0.05	-0.96
6.5±0.5	0.00	0.03
8.0±0.5	-0.08	-0.98
12.0±1.0	-0.10	-0.87

Total Error Decision Levels

Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the reproducibility study, Total Error (TE) at four concentrations: (5.0 %, 6.5%, 8.0% and 12.0%) were calculated as follows: $\%TE = |\%Bias| + 1.96 * CV * (1 + \%Bias)$. The results are presented in Table 15.

Table 15: Total Error Estimation

% A1c – Decision Level	% Bias	% CV	% TE
5.0	0.96	2.0	4.9
6.5	0.03	1.6	3.2
8.0	0.98	1.6	4.1
12.0	0.87	2.2	5.2

d. Traceability, Stability, Expected Values (calibrators)

The D-10 Hemoglobin A1c test standardization is traceable to the International Federation of Clinical Chemistry (IFCC) reference calibrators. The D-10 Hemoglobin A1c assay is NGSP certified. The NGSP certification expires in one year. See NGSP website for current certification at <http://www.ngsp.org>. The derived results of (%) from the NGSP correlation are calculated from the individual quantitative results for Hemoglobin A1c (HbA1c). The International Federation of Clinical Chemistry (IFCC) units of mmol/mol are calculated using the Master Equation NGSP (%) = 0.09148 x IFCC (mmol/mol) + 2.152. HbA1c results are provided to the customers using two different units: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol).

Calibrator Materials:

Value assignment for D-10™ Hemoglobin A1c Calibrators which are recommended for use with this device, were previously reviewed under 510(k) submission K031043.

e. Analytical specificity:**i.) Endogenous Interference**

An Endogenous Interference study was performed per CLSI EP07-A2, Interference Testing in Clinical Chemistry. Two EDTA whole blood sample pools were evaluated using a low level whole blood sample with a concentration ~6.5% HbA1c and a high level whole blood sample with a concentration of HbA1c of ~8.0%.

Conjugated bilirubin, unconjugated bilirubin and glucose, available in pure form, were obtained and stock solutions prepared at 10x the intended test concentration. The 10x stock solution of the test substance was pipetted into a low whole blood sample pool (at ~6.5% HbA1c) and a high whole blood sample pool (~8.0% HbA1c), making the test pool. Ten replicates of each pool prepared with the test and control samples were analyzed using the D-10™ Hemoglobin A1c on the D-10™ Hemoglobin Testing System.

Rheumatoid factor, lipemia and total protein were not available as pure standards therefore serum samples with known concentration of these compounds were used. The test pool was prepared by mixing the serum sample known to have a high test substance concentration with a whole blood non-variant sample such that the concentration of test substance in the final mixture would be at the desired level. Ten replicates of each pool prepared with the test and control samples were analyzed using the D-10™ Hemoglobin A1c on the D-10™ Hemoglobin Testing System.

Significant interference was defined as a ± 7% change in %HbA1c value from the control. Results in Table 16 showed no significant interference up to the stated concentrations.

Table 16: Endogenous Interference Study Results

Endogenous substance	Concentration	
	Conventional (US) units	SI Units
Lipemia (Intralipid)	6000 mg/dL	60 g/L
Conjugated bilirubin	60 mg/dL	712 µmol/L
Unconjugated bilirubin	60 mg/dL	1026 µmol/L
Glucose	2000 mg/dL	111 mmol/L
Rheumatoid factor	750 IU/mL	750 kIU/mL
Total protein	21 g/dL	210 g/L

ii.) Drug Interference:

A Drug Interference study was performed based per CLSI EP07-A2, Interference Testing in Clinical Chemistry. Two EDTA whole blood sample pools were evaluated using a low level whole blood sample with a concentration ~6.5%HbA1c and a high level whole blood sample with a concentration ~8.0%HbA1c. Test samples were prepared by spiking each drug at the interferent concentration shown in Table 18. Ten replicates of each drug prepared with the test and control samples were analyzed using the D-10™ Hemoglobin A1c on the D-10™ Hemoglobin Testing System.

Significant interference was defined as a more than $\pm 7\%$ change in %HbA1c value from the control. No significant interference was observed at therapeutic levels up to the stated concentrations in Table 17 on the following page.

Table 17: Drug Interference Study Results

Potential Drug Interferent	Highest Level Tested showing no Significant Interference	
	Conventional (US) units	SI units
Acetylcysteine	166 mg/dL	10.2 mmol/L
Ampicillin-Na	1000 mg/dL	28.65 mmol/L
Ascorbic acid	300 mg/dL	17.05 mmol/L
Cefoxitin	2500 mg/dL	58.55 mmol/L
Heparin	5000 U/L	5000 U/L
Levodopa	20 mg/dL	1015 µmol/L
Methyldopa	20 mg/dL	948 µmol/L
Metronidazole	200 mg/dL	11.7 mmol/L
Doxycyclin	50 mg/dL	1124 µmol/L
Acetylsalicylic acid	1000 mg/dL	55.51 mmol/L
Rifampicin	64 mg/L	78 µmol/L
Cyclosporine	5 mg/L	4 µmol/L
Acetaminophen	200 mg/L	1323 µmol/L
Ibuprofen	500 mg/L	2427 µmol/L
Theophylline	100 mg/L	556 µmol/L
Phenylbutazone	400 mg/L	1299 µmol/L

- iii.) Cross Reactivity with Hemoglobin Derivatives:
 A Hemoglobin Derivatives Interference study was performed based on CLSI EP07-A2, Interference Testing in Clinical Chemistry. Potential interference from Acetylated hemoglobin (Hb), Carbamylated hemoglobin (Hb) and Labile HbA1c were evaluated using a low level whole blood EDTA sample with a concentration ~6.5% HbA1c and a high level whole blood EDTA sample with a concentration of

~8.0% HbA1c. The potentially interfering hemoglobin derivatives were spiked into the low and high level blood samples and each sample was analyzed using ten replicates each in the same analytical run on the D-10™ Hemoglobin Testing System with the D-10™ Hemoglobin A1c.

Significant interference was defined as more than a $\pm 7\%$ change in HbA1c value from the control. The test result conclusions are as follows:

- Acetylated Hb- up to 49 mg/dL does not interfere with this assay.
- Carbamylated Hb – up to 3.5% (or 10 mg/dL potassium cyanate) does not interfere with this assay.
- Labile A1c- up to 6% (or 1000 mg/dL glucose) does not interfere with this assay.

Results showed there was no cross reactivity with these substances at physiological levels.

iv.) Hemoglobin Variant Study:

A Hemoglobin Variant study was performed using a panel of normal and diabetic whole blood EDTA patent variant samples known to contain hemoglobin variants S, C, E, D, A2 and F. Testing of the samples containing hemoglobin variants S, C, E, D, A2 and F were performed in duplicate using the D-10™ Hemoglobin A1c on the D-10™ Hemoglobin Testing System and compared to results obtained by a NGSP reference method that has been demonstrated to be free from the hemoglobin interferent. Table 18 contains the number of samples, range of samples and concentration of samples used in the Hemoglobin Variant Study. Table 19 contains the results for the Hemoglobin Variant study bias.

Table 18: Variant samples used in Hemoglobin Variant Study

Hemoglobin Variant	n	Range in % Abnormal Variant	Range in %HbA1c Concentration
HbS	22	31 – 43	5.6 – 11.5
HbC	20	31 – 40	5.0 – 10.7
HbD	22	35 – 43	5.8 – 10.0
HbE	23	21 – 32	5.9 – 11.6
HbA2	20	5.0 – 6.2	5.0 - 14.5
HbF	24	3.3 – 32.6	4.7 - 14.4

Table 19: Hemoglobin Variant Study Bias Results

Hemoglobin Variant	Relative % Bias to Comparative Method	
	Relative %Bias (Range of %Bias) for HbA1c	Relative %Bias (Range of %Bias) for HbA1c
	~6.5%	~9.0%
HbS	1.1 (-4.7 to 4.9)	0.2 (-6.1 to 5.3)
HbC	2.6 (1.4 to 5.9)	-0.9 (-2.8 to 0.9)
HbD	-0.6 (-3.1 to 4.7)	1.7 (-3.6 to 5.1)
HbE	0.5 (-3.3 to 6.2)	2.8 (1.2 to 5.2)
HbA2	0.6 (-1.8 to 1.8)	-1.7 (-2.8 to -0.7)
HbF	3.1 (-1.5 to 8.8)	-0.6 (-2.5 to 4.8)

This device has significant positive interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Hereditary Persistence of Fetal Hemoglobin.

Hemoglobin F concentrations up to 10% do not interfere with the test. Any sample with HbF>10% may result in higher than expected HbA1c values. Any sample with HbF >5% should be suspected of having a hemoglobinopathy.

No significant interference was observed for HbC (≤ 40%), HbD (≤ 43%), HbS (≤ 43%), HbE (≤ 32%), HbA2 (≤ 6%), and HbF(≤ 10%) at the concentrations tested in this study.

f. Matrix comparison

The data supports the use of the following blood collection tubes with the D-10™ Hemoglobin A1c test in Table 20.

Table 20: Anticoagulant

K ₂ -EDTA
K ₃ -EDTA

g. Expected Values/Reference Range

Hemoglobin A1c expected values range was cited from American Diabetes Association Standards of Medical Care in Diabetes 2014, 37 (Supplement 1) and American Diabetes Association. Standards of Medical Care in Diabetes - 2016 are presented in Table 21.

Table 21: Hemoglobin A1c Expected Values

Hemoglobin A1c		Suggested Diagnosis
NGSP %	IFCC mmol/mol	
≥6.5	≥47	Diabetic
5.7 – 6.4	39-46	Pre-Diabetic
<5.7	<39	Non-Diabetic

Conclusion:

The information and data in this 510(k) document demonstrate that the D-10™ Hemoglobin A1c Program as performed on the D-10™ Hemoglobin Testing System is an accurate, reliable, precise test that correlates well with current cleared methods and NGSP standardized testing for the quantitation of HbA1c. The contents of this submission demonstrates that the D-10™ Hemoglobin A1c Program as performed on the D-10™ Hemoglobin Testing System is substantially equivalent to its predicate device, VARIANT II TURBO HbA1c Kit – 2.0 and, therefore, safe and effective for its intended use. The performance criteria as stipulated by the Special Controls requirements for HbA1c systems that diagnose diabetes have clearly been met. The D-10™ Hemoglobin A1c Program must be found to be substantially equivalent to the predicate and, therefore, cleared by the agency for the intended use requested.