

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

A. 510(k) Number:

k090737

B. Purpose for Submission:

New device – a whole blood, capillary and venous sample collection device for glycosylated hemoglobin

C. Measurand:

Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative, High Performance Liquid Chromatography (HPLC)

E. Applicant:

Bio-Rad Laboratories, Inc

F. Proprietary and Established Names:

Hemoglobin Capillary Collection System (HCCS)

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LCP – Glycosylated Hemoglobin assay	II	864.7470	81, Hematology
JKA – Tubes, vials, systems, serum separators, blood collection	II	862.1675	75, Chemistry

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

The Hemoglobin Capillary Collection System (HCCS) is intended for the collection of human whole blood for the percentage determination of hemoglobin A1c using Bio-Rad HPLC methods.

For In Vitro diagnostic use

The measurement of percent hemoglobin A1c is effective in monitoring long-term glucose control in individuals with diabetes mellitus.

3. Special conditions for use statement(s):

For prescription use

4. Special instrument requirements:

Bio-Rad Variant II Hemoglobin A1c program and D-10 Hemoglobin A1c program

I. Device Description:

Each hemoglobin Capillary Collection System (HCCS) contains a combination of the following components:

Sample Preparation Vials – clear microvials with blue pierceable caps, each contains 1.5 mL of HCCS reagent (aqueous solution of EDTA and potassium cyanide (.25mmol/L). The microvials are 11 mm x 40 mm and have a maximum volume of 2.0 mL.

Capillaries – plastic capillaries (5 µL) in a dispenser

Capillary holder – holder for manipulating the capillaries

Labels – to label prepared samples

J. Substantial Equivalence Information:

1. Predicate device name(s):

VARIANT II Hemoglobin A1c Program and D-10 Hemoglobin A1c Program

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

k070452 and k031043 respectively

3. Comparison with predicate:

Similarities/Differences			
Item	Device	VARIANT II (k070452)	D-10 (k031043)
Intended Use	The Hemoglobin Capillary Collection System (HCCS) is intended for the collection of human whole blood for the percent determination of hemoglobin A1c using Bio-Rad HPLC methods. For <i>in vitro</i> diagnostic use	The Bio-Rad VARIANT II Hemoglobin A1c Program is intended for the percent determination of hemoglobin A1c in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The Bio-Rad VARIANT II Hemoglobin A1c Program is intended for Prescription Use Only.	The Bio-Rad D-10 Hemoglobin A1c Program is intended for the percent determination of hemoglobin A1c in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The Bio-Rad D-10 Hemoglobin A1c Program is intended for Prescription Use Only.
Indication for Use	Measurement of percent hemoglobin A1c is effective in monitoring long-term glucose control in individuals with diabetes mellitus.	Measurement of percent hemoglobin A1c is effective in monitoring long-term glucose control in individuals with diabetes mellitus.	Measurement of percent hemoglobin A1c is effective in monitoring long-term glucose control in individuals with diabetes mellitus.
Formulation	Aqueous solution of EDTA and potassium cyanide	Deionized water with <0.05% sodium azide as a preservative.	Deionized water with <0.05% sodium azide as a preservative.
Sample	Capillary or venous blood from plastic capillary	Venous whole blood sample collected in an EDTA vacuum collection tube.	Venous whole blood sample collected in an EDTA vacuum collection tube.
Purpose of Reagent	Sample dilution for Hemoglobin A1c analysis using Bio-Rad HPLC methods.	Sample dilution for hemoglobin A1c analysis using Bio-Rad HPLC method.	Sample dilution for hemoglobin A1c analysis using Bio-Rad HPLC method
Timing of Dilution Step	Sample dilution at time of sample collection. No further preparation is required; VARIANT II and D-10 Hemoglobin Testing Systems do not perform dilution on samples withdrawn	Dilution with the Wash/Diluent Solution is performed automatically by the VARIANT II Hemoglobin Testing System at time of analysis; when vacuum collection tubes are used.	Dilution with the Wash/Diluent Solution is performed automatically by the D-10 Hemoglobin Testing System at time of analysis; when vacuum collection tubes are used.

Similarities/Differences			
Item	Device	VARIANT II (k070452)	D-10 (k031043)
	from sample vials		
Stability of Sample	Prepared samples can be passed on for analysis or shipped to another location. Samples are stable for: 4 days at 42°C, 2 weeks at 15 to 30°C, or 4 weeks at 2-8°C.	Whole blood specimens may be stored up to 7 days at 2-8°C.	Whole blood specimens may be stored up to 7 days at 2-8°C or 3 days at room temperature (15 to 30°C).

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition
 CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline
 Guidance for Industry and FDA Staff; Replacement Reagent and Instrument Family Policy
 Draft Guidance Document for 510(k) Submission of Glycohemoglobin (Glycated or Glycosylated) Hemoglobin for IVD's
 Format for Traditional and Abbreviated 510(k)s – Guidance for Industry and FDA Staff

L. Test Principle:

The Hemoglobin Capillary Collection System (HCCS) reagent hemolyzes the Red Blood Cells in the blood sample, removes the Schiff base and preserves the sample. Once the sample is collected and prepared it is ready for immediate analysis, storage for future analysis or shipment for analysis at another site.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were conducted by testing three patient whole blood samples at approximately the following levels; low 4-6%, mid 6-8% and high 8-12%. The samples were assayed twice a day for twenty days using one VARIANT II and one D-10 Hemoglobin testing systems. The results are presented in the table below:

	VARIANT II			D-10		
	Low	Mid	High	Low	Mid	High
Mean - % HbA1c	4.85	6.12	10.49	4.90	6.06	10.57
Within run % CV	1.48	0.71	0.53	0.88	0.61	0.63
Between day % CV	1.02	0.23	0.76	0.00	0.54	0.53
Between run % CV	1.66	0.63	0.80	2.00	0.37	0.89
Total precision % CV	2.45	0.98	1.22	1.92	0.90	1.21

b. Linearity/assay reportable range:

Linearity across the assay range was confirmed by inter mixing the level 1 sample of the Bio-Rad Lyphochek hemoglobin A1c linearity set (~ 3.5% HbA1c) with a high patient sample (~ 18.5% HbA1c) creating three pooled sample sets each with 5 levels of HbA1c. One set of samples was diluted with the Hemoglobin Capillary Collection System (HCCS) reagent and two other sets of samples were diluted with the Wash/Diluent solutions one with the VARIANT II and the other with the D-10 Hemoglobin Testing Systems. Each sample was tested in duplicate on each system. Results are presented below:

VARIANT II		
Sample	Theoretical	Measured
1	3.25	3.10
2	6.75	6.91
3	10.70	10.72
4	14.45	14.53
5	18.45	18.34
Regression	$y = 1.0026x - 0.1586$	

D-10		
Sample	Theoretical	Measured
1	3.45	3.26
2	7.3	7.10
3	11.15	10.94
4	15	14.78
5	18.85	18.62
Regression	$y = 0.9974x - 0.181$	

The VARIANT II test system has a reportable range of 3.1-18.5% A1c.
The D-10 test system has a reportable range of 3.8-18.5% A1c.

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

The sponsor has documented traceability to the NGSP's recommended accuracy base for HbA1c by performing a direct comparison with a Secondary Reference Laboratory (SRL) using 40 fresh human specimens. At this time, the assay is NGSP certified. However, NGSP certification expires at the end of one year. For current certifications see the NGSP website at:

<http://www.ngsp.org/prog/index2.html>

Accelerated stability studies have been conducted. Protocols and acceptance criteria were described and found to be acceptable. When stored at room temperature the shelf life of the HCCS device is 24 months.

Stability of whole blood samples prepared with the Hemoglobin Capillary Collection System (HCCS) has been conducted. Protocols and acceptance criteria were described and found to be acceptable. Samples when stored at 2-8°C are stable for 4 weeks, 15-30°C stable for 2 weeks and 42°C stable for 4 days.

d. *Detection limit:*

The reportable range for the VARIANT II is 3.1 to 18.5% HbA1c and the D-10 is 3.8 to 18.5% HbA1c. See the linearity study above for data on recovery of samples across the measuring range.

e. *Analytical specificity:*

A study was conducted to determine if the level of interference for Labile A1c and Carbamylated Hemoglobin in patient samples differs when diluting samples using the HCCS to diluting the sample with Wash/Diluent for the VARIANT II and D-10 Hemoglobin A1c Programs. Two venous whole blood samples representing normal and diabetic A1c levels were split into 2 aliquots. One aliquot of each pool was treated to elevate the Labile A1c. The other aliquot was treated to elevate the Carbamylated Hemoglobin. Next set was diluted using the HCCS reagent and the other with the Wash/Diluent solution of the assay being studied. Samples and controls were run in duplicate on each system. The sponsor's acceptance criteria states that the %difference of HbA1c for samples diluted with HCCS method as compared to samples diluted with Wash/Diluent Solution must be less than ≤ 0.3 % HbA1c for normal samples and ≤ 0.5 % HbA1c for diabetic samples. The study showed that these criteria were met.

To evaluate the effect on hemoglobin variants such as Hb S, C, D and E when tested using the Hemoglobin Capillary Collection System (HCCS), samples with known hemoglobin variants were tested. One sample was prepared using the Wash/Diluent solution (control) and one using the HCCS device (candidate). The sponsor's acceptance criterion required that the % difference of HbA1c between the control and the candidate devices were within +/- 0.2 % HbA1c. The studies found that samples containing HbS, HbC, HbD and HbE showed no significant interference.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted at an external site comparing % HbA1c in capillary samples collected in the HCCS to venous whole blood testing performed on the VARIANT II and D-10 Hemoglobin testing Systems. The following are the correlations:

	Slope	Intercept	R ²	N	Range
VARIANT II	1.0169	-0.092	0.9984	52	3.2 – 18.5%
D-10	1.0176	-0.0342	0.9989	52	3.2 – 18.5%

b. Matrix comparison:

Paired capillary and EDTA venous whole blood samples were diluted using the Hemoglobin Capillary Collection System (HCCS) and were assayed on the VARIANT II and D-10 Hemoglobin Testing Systems. The following are the correlations:

	Slope	Intercept	R ²	N	Range
VARIANT II	1.000	0.000	0.998	31	5 – 12.0%
D-10	1.000	-0.100	0.999	31	4.8 – 12.2%

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 determined from literature (American Diabetes Association. Standards of Medical Care for Patients with Diabetes Mellitus. Diabetes Care 2001, 24 (Suppl. 1), 33-43). Hemoglobin A1c > 8% Action is suggested. Hemoglobin A1c < 7% is the goal. Hemoglobin A1c < 6% is non-diabetic level.

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.