K041444

JUN - 9 2004

Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K_____.

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Date of Summary Preparation:

April 16, 2004

Device Name:

Bio-Rad D-10™ Dual Program

Classification Name:

HbA_{1c}: Assay, Glycosylated Hemoglobin
[21CFR 864.7470 / Prod. Code LCP] and

HbA_2: Hemoglobin A_2 Quantitation
[21CFR 864.7400 / Prod. Code: JPD]

Predicate Devices:

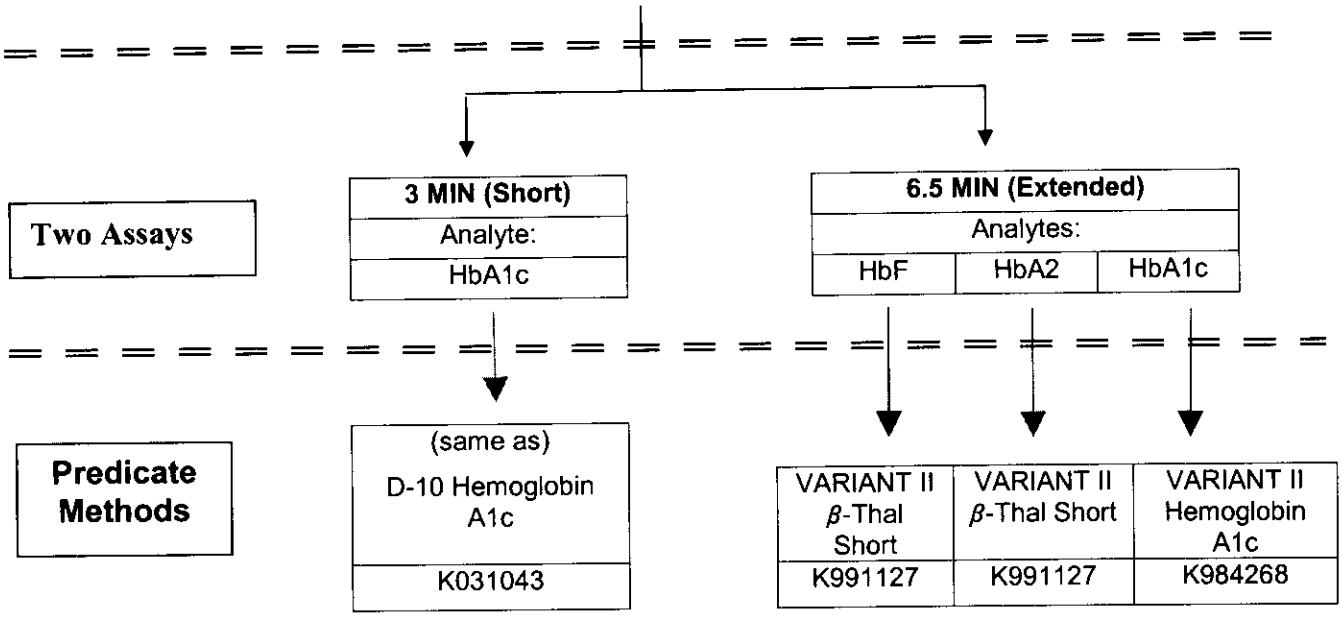
HbA_{1c}: VARIANT™ II Hemoglobin A_{1c} Program
Bio-Rad Laboratories
[K984268; 12/17/98]

HbA_2/F: VARIANT™ II ß-thalassemia Short Program
Bio-Rad Laboratories
[K991127; 06/10/99]

Presumptive Hemoglobin Identification:
VARIANT™ II ß-thalassemia Short Program
Bio-Rad Laboratories
[K991127; 06/10/99]

Special Instrument Requirement:
Bio-Rad D-10™ Hemoglobin Testing System
[K031043; 08/27/03]

PREDICATE MAP for D-10™ DUAL PROGRAM



Indications for Use Statement and Intended Uses:

The Bio-Rad D-10™ Dual Program system is intended for the percent determination of hemoglobins A_{1c}, A_2 and F, and for the detection of abnormal hemoglobins in human whole blood using ion-exchange high performance liquid chromatography (HPLC).

Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus, and measurement of the percent HbA_2 and HbF are effective in long-term monitoring of β–thalassemias (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains).

Detection of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants. The Bio-Rad D-10™ Dual Program is intended for Professional Use Only. For in vitro diagnostic use.

Description of Device

The Bio-Rad D-10™ Dual Program is a new device system that utilizes the principles of high performance liquid chromatography (HPLC), by which chromatographic separation of hemoglobins A_{1c}, A_2, and F occurs on an HPLC cation exchange cartridge. The Bio-Rad D-10™ Dual Program is a new program system that combines the determination of percent hemoglobin A_{1c} used for diabetes monitoring with percent hemoglobins A_2 and F used for evaluation of β – thalassemia. The D-10™ Dual Program system consists of two different reagent programs with two intended uses. The D-10™ Dual Program reagent kit has a short program (3 minutes) for the determination of hemoglobin A_{1c} in which the components exactly the same as the D-10™ Hemoglobin A_{1c} Program (K031043) reagents. The second program includes an extended program (6.5 minutes) that can be used for the determination of HbA_2, HbF as well as HbA_{1c}. The components are exactly the same as the D-10™ Hemoglobin A_{1c} Program (K031043) system and reagents with an additional $HbA_2/F/A_{1c}$ Calibrator/Diluent Set and floppy diskette for the new program parameters.

Technical Characteristics Compared to Predicate

The Bio-Rad D-10™ Dual Program [identified herein as the: **"D-10™ Dual" or "D-10™ Dual Program [6.5 minute)"** system] and its 2 cleared predicates, the **VARIANT™ II Hemoglobin A_{1c}** (K984268) and **VARIANT™ II ß-thalassemia** (K991127) Programs, have the same technical HPLC and general program characteristics that are summarized in the following tables:

HbA_{1c}

Characteristics	Bio-Rad D-10™ Dual Program (6.5 Minutes)	VARIANT II Hemoglobin A_{1c} Program [Cleared: / K984268; 12/17/98]
Intended Use(s)	The Bio-Rad D-10 Dual Program system is intended for the percent determination of hemoglobins A_{1c}, A_2 and F, and for the detection of abnormal hemoglobins in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The Bio-Rad D-10 Dual Program is intended for in Professional Use only. For in vitro diagnostic Use.	The VARIANT II Hemoglobin A_{1c} Program is intended for the determination of hemoglobin A_{1c} in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The VARIANT II Hemoglobin A_{1c} Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.
Indication(s) for Use	Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus, and measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Detection of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.	Measurement of the percent hemoglobin A_{1c} is effective n monitoring long-term glucose control in individuals with diabetes mellitus.
Assay Principle	Cation exchange high performance liquid chromatography	Cation exchange high performance liquid chromatography
Sample Type	Human anticoagulated whole blood (EDTA)	Human anticoagulated whole blood (EDTA)
Visible Detection	415 nm	415 nm
Standardization	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP) for HbA_{1c}.	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP) for HbA_{1c}.
Results	Quantitative Area % HbA_{1c}	Quantitative Area % HbA_{1c}
Time to process sample	6.5 minutes	3.0 minutes
Expected Value Range	4.27 – 6.07 % HbA_{1c}	4.27 – 6.07 % HbA_{1c}
Linearity	3.7 – 18.4 % HbA_{1c}	1.3 – 18.9% HbA_{1c}

HbA_2

Characteristics	Bio-Rad D-10™ Dual Program (6.5 Minutes)	VARIANT II ß-thalassemia Short [Cleared: / K991127; 06/10/1999]
Intended Uses	The Bio-Rad D-10 Dual Program system is intended for the percent determination of hemoglobins A_{1c}, A_2 and F, and for the detection of abnormal hemoglobins in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The Bio-Rad D-10 Dual Program is intended for Professional Use Only. For in vitro diagnostic use.	The VARIANT II ß-thalassemia Short Program is intended for the separation and area percent determinations of hemoglobins A2 and F, and as an aid in the identification of abnormal hemoglobins in whole blood using ion-exchange high performance liquid chromatography. The VARIANT II ß-thalassemia Short Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.
Indication(s) for Use	Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus, and measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Detection of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.	Measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Identification of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.
Assay Principle	Cation exchange high performance liquid chromatography	Cation exchange high performance liquid chromatography
Sample Type	Human anticoagulated whole blood (EDTA)	Human anticoagulated whole blood (EDTA)
Visible Detection	415 nm	415 nm
Standardization	The Joint Committee on Traceability in Laboratory Medicine has not identified a higher order reference method or reference material for the quantitation of HbA_2 and HbF	The Joint Committee on Traceability in Laboratory Medicine has not identified a higher order reference method or reference material for the quantitation of HbA_2 and HbF
Results	Quantitative Area % HbA_2	Quantitative Area % HbA_2
Time to process sample	6.5 minutes	6.5 minutes
Expected Value Range	2.2 – 3.7 % HbA_2	2.3 – 3.3% HbA_2
Linearity	1.5 – 11.4 % HbA_2	1.6 – 18.7% HbA_2

HbF

Characteristics	Bio-Rad D-10™ Dual Program (6.5 Minutes)	VARIANT™ II ß-thalassemia Short [Cleared: / K991127; 06/10/1999]
Intended Uses	The Bio-Rad D-10 Dual Program system is intended for the percent determination of hemoglobins A_{1c}, A_2 and F, and for the detection of abnormal hemoglobins in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The Bio-Rad D-10 Dual Program is intended for Professional Use Only. For in vitro diagnostic use.	The VARIANT II ß-thalassemia Short Program is intended for the separation and area percent determinations of hemoglobins A2 and F, and as an aid in the identification of abnormal hemoglobins in whole blood using ion-exchange high performance liquid chromatography. The VARIANT II ß-thalassemia Short Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.
Indication(s) for Use	Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus, and measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Detection of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.	Measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Identification of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.
Assay Principle	Cation exchange high performance liquid chromatography	Cation exchange high performance liquid chromatography
Sample Type	Human anticoagulated whole blood (EDTA)	Human anticoagulated whole blood (EDTA)
Visible Detection	415 nm	415 nm
Standardization	The Joint Committee on Traceability in Laboratory Medicine has not identified a higher order reference method or reference material for the quantitation of HbA_2 and HbF	The Joint Committee on Traceability in Laboratory Medicine has not identified a higher order reference method or reference material for the quantitation of HbA_2 and HbF
Results	Quantitative Area % HbF	Quantitative Area % HbF
Time to process sample	6.5 minutes	6.5 minutes
Expected Value Range	0- 0.8% HbF	<1.0% HbF
Linearity	0.8 – 16.5 % HbF	1.3 – 44.3% HbF

Hemoglobin Variants

Characteristics	Bio-Rad D-10™ Dual Program (6.5 Minutes)	VARIANT II ß-thalassemia Short [Cleared: / K991127; 06/10/1999]
Intended Uses	The Bio-Rad D-10 Dual Program system is intended for the percent determination of hemoglobins A_{1c}, A_2 and F, and for the detection of abnormal hemoglobins in human whole blood using ion-exchange high performance liquid chromatography (HPLC). The Bio-Rad D-10 Dual Program is intended for Professional Use Only. For in vitro diagnostic use.	The VARIANT II ß-thalassemia Short Program is intended for the separation and area percent determinations of hemoglobins A2 and F, and as an aid in the identification of abnormal hemoglobins in whole blood using ion-exchange high performance liquid chromatography. The VARIANT II ß-thalassemia Short Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.
Indication(s) for Use	Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus, and measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Detection of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.	Measurement of the percent HbA_2 and HbF are effective in monitoring of ß-thalassemia (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains). Identification of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants.
Assay Principle	Cation exchange high performance liquid chromatography	Cation exchange high performance liquid chromatography
Sample Type	Human anticoagulated whole blood (EDTA)	Human anticoagulated whole blood (EDTA)
Visible Detection	415 nm	415 nm
Results	Variant windows for S, C and any additional unknown peaks will be detected as "unknown"	Variant windows for S, C, D and any additional unknown peaks will be detected as "unknown"
Normal Reference Interval	Compared to "normal" pattern of chromatography	Compared to "normal" pattern of chromatography
Time to process sample	6.5 minutes	6.5 minutes

Testing To Establish Substantial Equivalence:

Accuracy:

HbA_{1c}

Method correlation between Bio-Rad D-10™ Dual Program (6.5 minutes) and VARIANT™ II Hemoglobin A_{1c} Program was evaluated using 40 EDTA whole blood samples ranging from 4.7% to 11.2% HbA_{1c}. The results are presented in the following table:

D-10™ Dual Program (6.5 Minutes) Correlation for HbA_{1c}

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9843	0.9906	0.4310

HbA_2

Method correlation between Bio-Rad D-10™ Dual Program (6.5 minutes) and VARIANT™ II β-thalassemia Short Program was evaluated with 40 EDTA whole blood samples ranging from 1.9% to 8.9% HbA_2. The results are presented in the following table:

D-10™ Dual Program (6.5 Minutes) Correlation for HbA_2

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9832	1.0898	-0.2407

HbF

Method correlation between Bio-Rad D-10™ Dual Program (6.5 minutes) and VARIANT™ II β-thalassemia Short Program was evaluated with 40 EDTA whole blood samples ranging from 0% to 12.91% HbF. The results are presented in the following table:

D-10™ Dual Program (6.5 Minutes) Correlation for HbF

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9959	0.9497	-0.1785

Precision:

HbA_{1c}

The following precision table provides comparison data on the precision between D-10™ Dual Program (6.5 Minutes) and VARIANT™ II Hemoglobin A_{1c} Program, each utilizing EDTA whole blood patient samples, and both tested against samples with normal (5.4-5.9) and diabetic (13.1-13.7) % A_{1c} content.

Method precision was performed using a protocol based on the NCCLS Evaluation protocol, Vol.12, No. 4, EP5-A (Feb. 1999) for the D-10™ Dual Program (6.5 Minutes) and NCCLS Evaluation protocol, Vol.12, No. 4, EP5-T2 (Mar. 1992) for the VARIANT II Hemoglobin A_{1c} Program. The protocols for both the D-10™ Dual Program (6.5 Minutes) and VARIANT II Hemoglobin A_{1c} Programs are similar. Using these protocols, 40 runs (2 per day) were performed on one D-10™ (or VARIANT™ II) Hemoglobin Testing System over 20 working days. In each duplicate daily run, duplicate aliquots of normal HbA_{1c} and diabetic HbA_{1c} patient samples were each analyzed per run. Although the precision samples are different, since they were run at different time periods, the precision results between the D-10™ Dual Program (6.5 Minutes) and the VARIANT™ II Hemoglobin A_{1c} (HbA_{1c}) Program are equivalent. A summary of combined comparative precision results is presented in the following precision table.

D-10™ Dual Program (6.5 Minutes) HbA_{1c} vs. VARIANT™ II HbA_{1c} Program - Precision

	D-10™ Dual (6.5 Minutes) HbA_{1c} Program		VARIANT™ II Hemoglobin A_{1c} (HbA_{1c}) Program	
	Normal Sample	Diabetic Sample	Normal Sample	Diabetic Sample
n= (number of samples)	80	80	80	80
Mean (%HbA_{1c})	5.9	13.1	5.4	13.7
Within run (%CV)	0.8	0.3	1.8	0.7
Total Precision (%CV)	1.8	0.9	2.1	1.7

HbA_2

The following precision table provides comparison data on the precision between D-10™ Dual Program (6.5 minutes) and VARIANT™ II β -thalassemia Short Programs, each utilizing EDTA whole blood patient samples. The HbA_2 tested samples had moderate (2.2-2.8) and high (4.6-5.4) % HbA_2 content.

Method precision was performed using a protocol based on the NCCLS Evaluation protocol, Vol.12, No. 4, EP5-A (Feb. 1999) for the D-10™ Dual Program (6.5 minutes) and NCCLS Evaluation protocol, Vol.12, No. 4, EP5-T2 (Mar. 1992) for the VARIANT II β-thalassemia Short Program. The protocols for both the D-10™ Dual Program and VARIANT II β-thalassemia Short Program are similar. Using these protocols, 40 runs (2 per day) were performed on one D-10™ (or VARIANT II) Hemoglobin Testing System over 20 working days. In each duplicate daily run, duplicate aliquots of low HbA_2 and of high HbA_2 patient samples were each analyzed in run. Although the precision samples are different, since they were run at different time periods, the precision results between the D-10™ Dual Program (6.5 minutes) and the VARIANT II β-thalassemia Short Program are equivalent. A summary of combined comparative precision results is presented in the following precision table.

Precision: (continued)

D-10™ Dual Program (6.5 minute HbA_2) vs. VARIANT II β-thalassemia Short(HbA_2)-Precision

	D-10 Dual Program (6.5 Minutes) HbA_2		VARIANT II β-thalassemia Short HbA_2	
	Low Sample	High Sample	Low Sample	High Sample
n= (number of samples)	80	80	80	80
Mean (%HbA_2)	2.2	5.4	2.8	4.6
Within run (%CV)	4.5	1.7	1.6	0.9
Total Precision (%CV)	5.3	3.1	2.0	2.1

HbF

The following precision table provides comparison data on the precision between D-10™ Dual Program (6.5 minutes) and VARIANT™ II β -thalassemia Short Programs, each utilizing EDTA whole blood patient samples. The HbF tested samples had moderate (1.6-2.1) and high (8.2-8.7) % HbF content.

Method precision was performed using a protocol based on the NCCLS Evaluation protocol, Vol.12, No. 4, EP5-A (Feb. 1999) for the D-10™ Dual Program (6.5 minutes) and NCCLS Evaluation protocol, Vol.12, No. 4, EP5-T2 (Mar. 1992) for the VARIANT II β-thalassemia Short Program. The protocols for both the D-10™ Dual Program and VARIANT II β-thalassemia Short Program are similar. Using these protocols, 40 runs (2 per day) were performed on one D-10™ (or VARIANT II) Hemoglobin Testing System over 20 working days. In each duplicate daily run, duplicate aliquots of low HbF and of high HbF patient samples were each analyzed per run. Although the precision samples are different, since they were run at different time periods, the precision results between the D-10™ Dual Program (6.5 minutes) and the VARIANT II β-thalassemia Short Program are equivalent. A summary of combined comparative precision results is presented in the following precision table.

D-10™ Dual Program (6.5 minutes) HbF vs. VARIANT II β-thalassemia Short (HbF) - Precision

	D-10 Dual Program (6.5 minutes) HbF		VARIANT II β-thalassemia Short HbF	
	Low Sample	High Sample	Low Sample	High Sample
n= (number of samples)	80	80	80	80
Mean (%HbF)	2.1	8.7	1.6	8.2
Within run (%CV)	1.7	1.4	2.1	0.6
Total Precision (%CV)	3.3	2.0	3.9	1.4

Linearity:

HbA_{1c}

The following linearity table provides comparison data on the linearity and recovery analyses between D-10 ™ Dual Program (6.5 Minutes) and VARIANT II Hemoglobin A_{1c} Programs, each utilizing eight EDTA-based blood standards (n=2 for each standard). This second linearity study was performed to compare the D-10™ Dual Program with the VARAINT II Hemoglobin A_{1c} linearity using the same standards. The % Recovery for HbA_{1c} by the D-10 ™ Dual Program is essentially the same as the VARIANT II Hemoglobin A_{1c} Program. The results are presented in the following linearity table.

The linear range as stated in the Instruction Manual on the D-10™ Dual Program is 3.7 to 18.4% HbA_{1c} which was performed in the first linearity study, each using a total of seven standards (n=2 for each standard) below, at, and substantially above blood levels of typical normal levels of hemoglobin A_{1c} and found in normal and diabetic patients.

D-10™ Dual Program (6.5 Minutes) vs. VARIANT II Hemoglobin A_{1c} Linearity

		D-10 Dual Program (6.5 Minutes)			VARIANT II Hemoglobin A_{1c}		
% Contribution		Theoretical	Observed	%	Theoretical	Observed	%
Normal	Diabetic	% HbA_{1c}	% HbA_{1c}	Recovery	% HbA_{1c}	% HbA_{1c}	Recovery
100	0	3.8	3.8	100	4.0	4.0	100
90	10	5.3	5.3	100	5.4	5.4	100
80	20	6.8	6.7	98.5	6.8	6.7	98.5
67	33	8.8	8.6	97.7	8.8	8.7	98.9
50	50	11.3	11.1	98.2	11.3	11.3	100
33	67	13.8	13.7	99.3	13.8	13.7	99.3
20	80	15.7	15.7	100	15.8	15.9	100.6
0	100	18.6	18.6	100	19.0	19.0	100

HbA_2

The following linearity table provides comparison data on the linearity and recovery analyses between D-10 ™ Dual Program (6.5 minutes) and VARIANT II β-thalassemia, each utilizing eight EDTA-based blood standards (n=2 for each standard). This second linearity study was performed to compare the D-10 ™ Dual Program with the VARAINT II β-thalassemia Short Program linearity using the same standards. The % Recovery for HbA_2 by the D-10 ™ Dual Program is essentially the same as the VARIANT II β-thalassemia Short Program (HbA_2). Results are presented in the linearity table below.

The linear range as stated in the Instruction Manual on the D-10 ™ Dual Program is 1.5 to 11.4% HbA_2 which was performed in the first linearity study, each using a total of seven standards (n=2 for each standard) below, at, and substantially above blood levels of typical normal levels of hemoglobin A_2 and found in normal patients or patients with β-thalassemia.

Linearity: (continued)

D-10™ Dual Program (6.5 Minutes) vs. VARIANT II Hemoglobin A_{1c} - Linearity

		D-10 Dual Program (6.5 Minutes)			VARIANT II β - thalassemia Short		
% Contribution Low	High	Theoretical % HbA_2	Observed % HbA_2	% Recovery	Theoretical % HbA_2	Observed % HbA_2	% Recovery
100	0	1.7	3.8	100	1.8	1.8	100
90	10	2.5	2.5	100	2.6	2.6	100
80	20	3.4	3.1	91.2	3.4	3.3	97.1
67	33	4.5	4.2	93.3	4.4	4.3	97.1
50	50	6.0	5.8	96.7	5.7	5.6	98.3
33	67	7.4	7.2	97.3	7.0	6.9	98.6
20	80	8.6	8.5	98.8	8.1	8.1	100
0	100	10.3	10.3	100	9.7	9.7	100

HbF

The following linearity table provides comparison data on the linearity and recovery analyses between D-10 ™ Dual Program (6.5 minutes) and VARIANT ™ II β-thalassemia, each utilizing eight EDTA-based blood standards (n=2 for each standard). This second linearity study was performed to compare the D-10 ™ Dual Program with the VARAINT ™ II β-thalassemia Short Program linearity using the same standards. The % Recovery for HbF by the D-10 ™ Dual Program is essentially the same as the VARIANT II β-thalassemia Program. The results are presented in the following linearity table.

The linear range as stated in the Instruction Manual on the D-10 ™ Dual Program is 0.8 to 16.5% HbF which was performed in the first linearity study, each using a total of seven standards (n=2 for each standard) below, at, and substantially above blood levels of typical normal levels of hemoglobin F and found in normal patients or patients with β-thalassemia.

D-10™ Dual Program (6.5 Minutes) vs. VARIANT II β-thalassemia Short (HbF) - Linearity

		D-10 Dual Program (6.5 Minutes HbF)			VARIANT II β-thalassemia Short		
% Contribution Low	High	Theoretical % HbF	Observed % HbF	% Recovery	Theoretical % HbF	Observed % HbF	% Recovery
100	0	0.4	0.4	100	0.1	0.1	100
95	5	1.4	1.5	107.1	1.0	1.1	110.0
90	10	2.4	2.7	112.5	1.9	1.7	89.5
80	20	4.5	4.8	106.7	3.7	4.0	108.1
67	33	7.2	7.7	106.9	6.2	6.6	106.5
50	50	10.8	11.1	102.8	9.4	9.9	105.3
33	67	14.4	14.6	101.4	12.6	13.0	103.2
20	80	17.4	17.5	100.6	15.2	15.5	102.0
0	100	22.0	22.0	100	19.3	19.3	100

Specificity and Interference Testing

HbA_{1c}

In evaluating the specificity of the Bio-Rad D-10™ Dual Program for $\%HbA_{1c}$ in EDTA-treated blood samples, two closely related but chemical derived analogs of HbA_{1c} where evaluated as part of a detailed analytical specificity study. The influence of carbamylated hemoglobin was studied by spiking specimens with sodium cyanate until the carbamylated hemoglobin levels increased to a range of 2.0%. Also, influence of unstable labile hemoglobin A_{1c} was studied by spiking samples with glucose until unstable labile A_{1c} in hemoglobin reached 3.5%. As was the case for the predicate Bio-Rad VARIANT™ II HbA_{1c} system, the results with this new Rad D-10™ Dual Program system demonstrated that the final measurement of $\%HbA_{1c}$ at normal and diabetic levels was not significantly influenced by either added carbamylated hemoglobin or added glucose-labile hemoglobin A_{1c} at the above indicated limits.

Additional normal and diabetic blood samples were obtained as patient bloods that were anticoagulated with EDTA in the standard manner. In three separate trials of patient pools or individual blood samples: a) concentrated bilirubin was added to a final level of 20 mg/dL; b) concentrated lipids were added to a final level of 5680 mg/dL; and c) additional dipotassium EDTA was added to a concentration of ~1980 mg/dL (11x the normal level) to determine the effect of high concentrations of EDTA that can occur in cases of "short draws." For the final measurement of normal and high diabetic HbA_{1c} in blood samples, neither the Bio-Rad D-10™ Dual Program system nor cleared predicate Bio-Rad VARIANT™ II HbA_{1c} Program system were influenced by these excess biochemicals or excess EDTA anticoagulant, as illustrated in the interference evaluation table on the next page.

HbA_2

In evaluating for specificity of the Bio-Rad D-10™ Dual Program for $\%HbA_2$ in EDTA-treated blood samples, additional normal, moderate and high blood $\%HbA_2$ samples were obtained as patient bloods that were anticoagulated with EDTA in the standard manner. In three separate trials of patient pools or individual blood samples: a) concentrated bilirubin was added to a final level of 20 mg/dL; b) concentrated lipids were added to a final level between 5680 mg/dL; and c) additional dipotassium EDTA was added to a concentration of ~1980 mg/dL (11x the normal level) to determine the effect of high concentrations of EDTA that can occur in cases of "short draws." For the final measurement of normal, moderate and high HbA_2 in blood samples, neither the Bio-Rad D-10™ Dual Program system nor the cleared predicate Bio-Rad VARIANT II ß-thalassemia Program system were influenced significantly by these excess biochemicals or excess EDTA anticoagulant, as illustrated in the interference evaluation table on the next page.

Specificity and Interference Testing - continued

HbF

The HbF assay was evaluated using the Bio-Rad D-10™ Dual Program system as part of a detailed analytical specificity study. First the influence of an unstable complex of glucose & hemoglobin known as labile Hemoglobin A_{1c} (which chromatographs in proximity to HbF) was studied by spiking samples with glucose until labile A_{1c} in Hemoglobin reached 0-2.6%. Final measurement of HbF in these blood-based human specimens was not influenced significantly by labile Hemoglobin A_{1c} at the above-indicated limits, as was the case also for the predicate, the Bio-Rad VARIANT™ II ß-thalassemia Program system.

In evaluating for specificity of this Bio-Rad D-10™ Dual Program system for %HbF in EDTA-treated blood samples, additional normal, moderate and high blood samples were obtained as patient bloods that were anticoagulated with EDTA in the standard manner. In three separate trials of patient pools or individual blood samples: a) concentrated bilirubin was added to a final level of 20 mg/dL; b) concentrated lipids were added to a final level between 5680 and 6000 mg/dL; and c) additional dipotassium EDTA was added to a concentration of ~1980 mg/dL (11x the normal level) to determine the effect of high concentrations of EDTA that can occur in cases of "short draws." For the final measurement of HbF, as well as HbA_{1c} and HbA_2, neither the Bio-Rad D-10 Dual Program system, nor cleared predicate Bio-Rad VARIANT II ß-thalassemia Program system were influenced significantly by these excess biochemicals or excess EDTA anticoagulant, as illustrated in the interference evaluation table below.

Summary of Testing for Interfering Substances:

Interfering Substance	D-10™ Dual Program (Extended) (HbA_{1c} & HbA_2/F)	VARIANT™ II Hemoglobin A_{1c} (HbA_{1c})	VARIANT™ II ß-thalassemia Short (HbA_2/F)
Potential Labile Hb (glucose + Hb) Interference	No significant interference up to 3.5% Labile Hb on HbA_{1c}	No significant interference up to 4.8% Labile Hb on HbA_{1c}	Not Applicable
Potential Labile Hb (glucose + Hb) Interference	No significant interference up to 2.6% Labile Hb on HbF	Not Applicable	Not Applicable
Bilirubin	No interference up to 20 mg/dL	No interference up to 20 mg/dL	No interference up to 20 mg/dL
Lipids (Triglycerides)	No interference up to 5680 mg/dL	No interference up to 6000 mg/dL	No interference up to 4600 mg/dL
EDTA	No interference up to 11X EDTA	No interference up to 11X EDTA	No interference up to 11X EDTA

Conclusion:

The similarities of the intended use and the general performance characteristics and results of the newly described and evaluated **Bio-Rad D-10™ Dual Program** system are nearly identical to or logical extensions of those for the two cleared predicate program systems [i.e., the Bio-Rad VARIANT™ II Hemoglobin A_{1c} Program and the Bio-Rad VARIANT™ II ß-thalassemia Short Program]. Thus, one may conclude, based on the use of the same HPLC technology, and the nearly equivalent results obtained for the correlation, precision, linearity, and interfering substances tests versus the corresponding results obtained with the two predicate systems that the new **Bio-Rad D-10™ Dual Program** system is substantially equivalent to these 2 cleared and currently marketed predicate systems.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN - 9 2004

Bio-Rad Laboratories, Inc.
c/o Alfredo J. Quattrone, Ph.D., D.A.B.T.
Third Party 510(k) Review Coordinator
California Department of Health
Food & Drug Branch
1500 Capitol Avenue
Mailstop 7602
Sacramento, CA 95814

Re: k041444
Trade/Device Name: Bio-Rad D-10™ Dual Program
Regulation Number: 21 CFR 864.7470
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: Class II
Product Code: LCP
Dated: May 28, 2004
Received: June 1, 2004

Dear Dr. Quattrone

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Jean M. Cooper MS, DVM.

Jean M. Cooper, MS, D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K041444

Device Name: Bio-Rad D-10™ Dual Program

Indications For Use:

The Bio-Rad D-10™ Dual Program system is intended for the percent determination of hemoglobins A_{1c}, A_2, and F, and for the detection of abnormal hemoglobins in human whole blood using ion-exchange high performance liquid chromatography (HPLC).

Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus, and measurement of the percent HbA_2 and HbF is effective in long-term monitoring of β–thalassemias (i.e., hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains).

Detection of hemoglobin thalassemia variants such as hemoglobins S, C, D and E by HPLC is effective in presumptive identification of these variants. The Bio-Rad D-10™ Dual Program is intended for Professional Use Only. For in vitro diagnostics use.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K041444