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: K063643.

Submitter:

Bio-Rad Laboratories, Inc.
Clinical System Division
4000 Alfred Nobel Drive,
Hercules, California 94547
Phone: (510) 741-5309
FAX: (510) 741-6471

DEC 27 2006

Contact Person:

Jackie Buckley
Regulatory Affairs Representative III

Date of Summary Preparation:

December 4, 2006

Device Name:

VARIANT™ II Hemoglobin A1c, VARIANT™ II Beta-thalassemia, and VARIANT™ II Total GHb Programs run on the VARIANT II Hemoglobin Testing System using Clinical Management System (CDM) 4.0

Classification Name:

HbA1c: Assay, Glycosylated Hemoglobin
[21CFR 864.7470 / Prod. Code LCP]

HbA2: Hemoglobin A2 Quantitation
[21CFR 864.7400/Prod. Code :JPD]

Predicate Devices:

VARIANT™ II Hemoglobin A1c Program
Bio-Rad Laboratories, Inc.
[K984268, December 17, 1998]]

VARIANT™ II Beta thalassemia Short Program
Bio-Rad Laboratories, Inc.
[K991127, June 10, 1999]]

VARIANT™ II Total GHb Program
Bio-Rad Laboratories, Inc.
[K003280, December 19, 2000]

Intended Use:

This software submission covers three assays with three different intended uses:

Hemoglobin A1c:
The 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 VARIANT II Hemoglobin A1c Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.

Beta-thalassemia:
The VARIANT II Beta thalassemia Short Program is intended for the separation and area percent determinations of hemoglobin A2 and F, and as an aid in the identification of abnormal hemoglobins in human whole blood using ion-exchange high-performance liquid chromatography (HPLC).

The VARIANT II Beta-thalassemia Short Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.

Total GHb:
The VARIANT II Total GHb Program is intended for the separation and area percent determination of total glycated hemoglobin (GHb) in human whole blood using ion-exchange high-performance liquid chromatography (HPLC).

The VARIANT II Total GHb Program with is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.

Indications for Use:

This software submission covers three assays and has two different Indications for Use:

HbA1c & GHb:	Measurement of percent hemoglobin A1c is effective in monitoring long-term glucose control in individuals with diabetes mellitus.
HbA2 and HbF:	Measurement of the percent hemoglobin A_2 and F are effective in screening of β-thalassemia (i.e. hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobin polypeptide chains).

New Device Description

The VARIANT II Hemoglobin Testing System uses the principles of high performance liquid chromatography (HPLC). The VARIANT II Hemoglobin A1c and Beta-thalassemia Short Program are based on chromatographic separation of hemoglobins on a cation exchange cartridge. The Total GHb Program is based on principles of boronate affinity high pressure liquid chromatography to separate glycated hemoglobin from non-glycated hemoglobin.

The new feature in this submission is the upgrade in CDM software. The current software (3.5) requires Windows NT and Object Store N.T. These products are nearing the end of their lifecycle. CDM 4.0 software is needed to transfer the CDM software to Microsoft XP Operating System and Object Store version 4.0.

Technical Characteristics Compared to Predicate

The VARIANT™ II Hemoglobin A1c Program run on the VARIANT II Hemoglobin Testing System with CDM 4.0 has the same basic technical characteristics as the predicate VARIANT II Hemoglobin A1c Program (k) 984268. The technical characteristics between the two submissions are summarized in the following tables on pages 4-A-3 to 4-A-6:

VARIANT™ II Hemoglobin A1c (k) 984268

Summary of Technological Characteristic Similarities in Comparison to Predicate Device		
Characteristics	**New Device:** **VARIANT II Hemoglobin A1c Program run on the VARIANT II Hemoglobin Testing System using CDM 4.0**	**Predicate Device:(k)984268** **VARIANT II Hemoglobin A1c Program run on the VARIANT II Hemoglobin Testing System using CDM 3.5**
Intended Use(s)	The VARIANT II Hemoglobin A1c is intended for the percent determination of hemoglobin A1c in human whole blood using ion-exchange high-performance liquid chromatography (HPLC). For In Vitro Diagnostic Use.	The VARIANT II Hemoglobin A1c is intended for the percent determination of hemoglobin A1c in human whole blood using ion-exchange high-performance liquid chromatography (HPLC). 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.	Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus.
Assay Principle	Cation exchange high performance liquid chromatography	Cation exchange high performance liquid chromatography
CDM Software version	4.0	3.5
Microsoft software	Windows XP	Windows NT
Object Store version	6.0	4.0
Backup and Restore	Use Windows operation to write only data to CD-R	Used Easy CD writer Read/Write
Database Management	Delete data directly from database	Substitute database with a blank database
Standardization for HbA1c	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}.
Firmware upgrade to VARIANT II VCS and VSS	VCS 41.300 VSS 51.381	VCS 41.295 VSS 51.373

VARIANT™ II Beta thalassemia Short Program (k)991127

Summary of Technological Characteristic Similarities in Comparison to Predicate Device		
Characteristics	**New Device:** **VARIANT II Beta thalassemia Short Program run on the VARIANT II Hemoglobin Testing System using CDM 4.0**	**Predicate Device: (k)991127** **VARIANT II Beta thalassemai Short Program run on the VARIANT II Hemoglobin Testing System using CDM 3.5**
Intended Use(s)	The VARIANT II Beta thalassemia Short Program is intended for the separation and area percent determinations of hemoglobin A2 and F, and as an aid in the identification of abnormal hemoglobins in human whole blood using ion-exchange high-performance liquid chromatography (HPLC). The VARIANT II B-thalassemia Short Program is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For In Vitro Diagnostic Use.	The VARIANT II Beta thalassemia Short Program is intended for the separation and area percent determinations of hemoglobin A2 and F, and as an aid in the identification of abnormal hemoglobins in human whole blood using ion-exchange high-performance liquid chromatography (HPLC). The VARIANT II B-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_2 and F are effective in screening of β-thalassemia (i.e. hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobins polypeptide chains).	Measurement of the percent hemoglobin A_2 and F are effective in screening of β-thalassemia (i.e. hereditary hemolytic anemias characterized by decreased synthesis of one or more types of abnormal hemoglobins polypeptide chains).
Assay Principle	Cation exchange high performance liquid chromatography	Cation exchange high performance liquid chromatography
CDM Software version	4.0	3.5
Microsoft software	Windows XP	Windows NT
Object Store version	6.0	4.0
Backup and Restore	Use Windows operation to write only data to CD-R	Used Easy CD writer Read/Write
Database Management	Delete data directly from database	Substitute database with a blank database
Firmware upgrade to VARIANT II VCS and VSS	VCS 41.300 VSS 51.381	VCS 41.295 VSS 51.373

VARIANT™ II GHb (k)003280

Summary of Technological Characteristic Similarities in Comparison to Predicate Device		
Characteristics	**New Device:** **VARIANT II Total GHb Program run on the VARIANT II Hemoglobin Testing System using CDM 4.0**	**Predicate Device: (k) 003280** **VARIANT II Total GHb Program run on the VARIANT II Hemoglobin Testing System using CDM 3.5**
Intended Use(s)	The VARIANT II Total GHb Program is intended for the separation and area percent determination of total glycated hemoglobin (GHb) in whole blood using boronate affinity high-performance liquid chromatography (HPLC). For In Vitro Diagnostic Use.	The VARIANT II Total GHb Program is intended for the separation and area percent determination of total glycated hemoglobin (GHb) in whole blood using boronate affinity high-performance liquid chromatography (HPLC). 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.	Measurement of the percent hemoglobin A_{1c} is effective in monitoring long-term glucose control in individuals with diabetes mellitus.
Assay Principle	Affinity high performance liquid chromatography	Affinity high performance liquid chromatography
CDM Software version	4.0	3.5
Microsoft software	Windows XP	Windows NT
Object Store version	6.0	4.0
Backup and Restore	Use Windows operation to write only data to CD-R	Used Easy CD writer Read/Write
Database Management	Delete data directly from database	Substitute database with a blank database
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}.
Firmware upgrade to VARIANT II VCS and VSS	VCS 41.300 VSS 51.381	VCS 41.295 VSS 51.373

Testing To Establish Substantial Equivalence:

Accuracy:

VARIANT™ II Hemoglobin HbA1c Program

Method correlation between Bio-Rad VARIANT II Hemoglobin A1c Program with CDM 4.0 and VARIANT II Hemoglobin A1c Program with CDM 3.5 was evaluated using 40 EDTA whole blood samples ranging from (4.7% -12.9%) HbA1c. The results are presented in the following table:

VARIANT II Hemoglobin A1c Program Correlation

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9978	1.0119	0.0002

Precision:

VARIANT II Hemoglobin A1c Program

The following precision table provides comparison data on the precision between VARIANT II Hemoglobin A1c Program with CDM 4.0 vs. CDM 3.5 each utilizing EDTA whole blood patient samples.

Method precision was performed using a protocol based on the NCCLS Evaluation protocol, EP5-A for the VARIANT II Hemoglobin A1c Program with CDM 4.0 and 3.5. The protocols for both VARIANT II Hemoglobin A1c Program with CDM 4.0 and 3.5 are similar. In each duplicate daily run for both verification studies, duplicate aliquots of normal HbA1c and diabetic HbA1c patient samples and controls were each analyzed per run. The position of the precision specimens in each run was randomized to simulate normal laboratory conditions. The precision data for the VARIANT II with CDM 3.5 was over 20 working days while the data for VARIANT II with CDM 4.0 was over 10 working days.

Although precision samples are different, since they were run at different time periods, the precision results between the VARIANT II Hemoglobin A1c Program with CDM 4.0 and CDM 3.5 are equivalent. A summary of combined comparative precision results are presented in the following precision table.

VARIANT II HbA1c with CDM 4.0 vs. VARIANT II HbA1c with CDM 3.5 - Precision

	VII HbA1c with CDM 4.0		VII HbA1c with CDM 3.5T	
	Normal Sample	Diabetic Sample	Normal Sample	Diabetic Sample
n= (number of samples)	40	40	80	80
Mean (%HbA_{1c})	5.4	10.4	5.4	13.7
Within run (%CV)	1.1	1.2	1.5	0.7
Total Precision (%CV)	2.6	2.7	2.1	1.7

Accuracy:

VARIANT™ II Beta thalassemia Short Program

Method correlation between Bio-Rad VARIANT II Beta thalassemia Short with CDM 4.0 and VARIANT II Beta thalassemia Short with CDM 3.5 was evaluated using 40 EDTA whole blood samples ranging from (2.0 – 7.0% %) HbA2 and (0.2 – 11.1%) HbF. The results are presented in the following tables:

VARIANT II Beta thalassemia Short Correlation (HbA2)

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9924	1.0070	-0.0034

VARIANT II Beta thalassemia Short Correlation (HbF)

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9991	0.9806	0.0192

Precision:

VARIANT II Beta thalassemia Short Program

The following precision table provides comparison data on the precision between VARIANT II Beta thalassemia Short with CDM 4.0 vs. CDM 3.5 each utilizing EDTA whole blood patient samples.

Method precision was performed using a protocol based on the NCCLS Evaluation protocol, EP5-A for the VARIANT II Beta thalassemia Short with CDM 4.0 and 3.5. The protocols for both VARIANT II Beta thalassemia Short with CDM 4.0 and 3.5 are similar. In each duplicate daily run for both verification studies, duplicate aliquots of normal HbA1c and diabetic HbA1c patient samples and controls were each analyzed per run. The position of the precision specimens in each run was randomized to simulate normal laboratory conditions. The precision data for the VARIANT II with CDM 3.5 was over 20 working days while the data for VARIANT II with CDM 4.0 was over 10 working days.

Although precision samples are different, since they were run at different time periods, the precision results between the VARIANT II Beta thalassemia Short with CDM 4.0 and CDM 3.5 are equivalent. A summary of combined comparative precision results are presented in the following precision tables.

VARIANT II Beta thalassemia Short with CDM 4.0 vs. VARIANT II Beta thalassemia Short with CDM 3.5 - Precision

	VII Beta thalassemia Short with CDM 4.0		VII Beta thalassemia Short with CDM 3.5	
	Normal A2 sample	High A2 sample	Normal A2 sample	High A2 sample
n= (number of samples)	40	40	80	80
Mean (%HbA2)	2.6	2.8	2.8	4.6
Within run (%CV)	1.6	2.2	1.6	0.9
Total Precision (%CV)	3.9	3.1	2.0	2.1

VARIANT II Beta thalassemia Short with CDM 4.0 vs. VARIANT II HbA1c with CDM 3.5 - Precision (continue)

	VII Beta thalassemia Short with CDM 4.0		VII Beta thalassemia Short with CDM 3.5	
	Low HbF sample	Low HbF sample	Low HbF sample	Low HbF sample
n= (number of samples)	40	40	80	80
Mean (%HbF)	2.4	10.6	1.6	8.2
Within run (%CV)	4.8	1.0	2.0	0.6
Total Precision (%CV)	5.5	1.5	3.9	1.4

Accuracy:

VARIANT™ II Total GHb Program

Method correlation between Bio-Rad VARIANT II Total GHb Program with CDM 4.0 and VARIANT II Total GHb Program with CDM 3.5 was evaluated using 40 EDTA whole blood samples ranging from (4.5 – 16.2%) GHb. The results are presented in the following table:

VARIANT II Total GHb Program Correlation

Regression Method	n	r^2	Slope	Intercept
Least Squares	40	0.9991	1.0054	0.042

Precision:

VARIANT II Total GHb Program

The following precision table provides comparison data on the precision between VARIANT II Total GHb Program with CDM 4.0 vs. CDM 3.5 each utilizing EDTA whole blood patient samples.

Method precision was performed using a protocol based on the NCCLS Evaluation protocol, EP5-A for the VARIANT II Total GHb Program with CDM 4.0 and 3.5. The protocols for both VARIANT II Total GHb Program with CDM 4.0 and 3.5 are similar. In each duplicate daily run for both verification studies, duplicate aliquots of normal HbA1c and diabetic HbA1c patient samples and controls were each analyzed per run. The position of the precision specimens in each run was randomized to simulate normal laboratory conditions. The precision data for the VARIANT II with CDM 3.5 was over 20 working days while the data for VARIANT II with CDM 4.0 was over 10 working days.

Although precision samples are different, since they were run at different time periods, the precision results between the VARIANT II Total GHb Program with CDM 4.0 and CDM 3.5 are equivalent. A summary of combined comparative precision results are presented in the following precision table.

VARIANT II Total GHb with CDM 4.0 vs. VARIANT II Total GHb with CDM 3.5 - Precision

	VII Total GHb with CDM 4.0		VII Total GHb with CDM 3.5	
	Normal Sample	**Diabetic Sample**	**Normal Sample**	**Diabetic Sample**
n= (number of samples)	40	40	80	80
Mean (%GHb)	6.1	12.4	5.8	14.5
Within run (%CV)	2.2	1.0	1.5	1.3
Total Precision (%CV)	3.8	2.6	2.9	2.7

Conclusion:

The similarities of the intended use and the general performance characteristics and results of the newly described and evaluated **VARIANT II Hemoglobin A1c , VARIANT II Beta-thalassemia and VARIANT II Total GHb Programs run on the VARIANT II Hemoglobin Testing System with CDM 4.0** are nearly identical to or logical extensions of those for cleared predicate program systems [i.e., VARIANT II Hemoglobin A1c, VARIANT II Beta-thalassemia and VARIANT II Total GHb run on CDM 3.5]. Thus, one may conclude, based on the use of the same HPLC technology, and the nearly equivalent results obtained for the correlation and precision versus the corresponding results obtained with the predicate system that the new **VARIANT II Hemoglobin A1c, VARIANT II Beta-thalassemia and VARIANT II Total GHb Program runs on the VARIANT II Hemoglobin Testing System with CDM 4.0** is substantially equivalent to the cleared and currently marketed predicate system.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Jackie Buckley
Bio-Rad Laboratories, Inc.
Clinical System Division
4000 Alfred Nobel Drive
Hercules, California 94547

DEC 27 2006

Re: k063643
Trade/Device Name: Variant II ™ Hemoglobin A1c Program, Variant™ Beta-thalassemia and Variant ™ II Total Ghb run on the Variant ™ II Hemoglobin Testing System with CDM 4.0
Regulation Number: 21 CFR 864.7400, 21 CFR 864.7470
Regulation Name: Glycosylated hemoglobin assay; Hemoglobin A2 assay
Regulatory Class: Class II
Product Code: LCP, JPD
Dated: December 7, 2006
Received: December 8, 2006

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.

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

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 (240) 276-0490. 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 (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., 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): K063643

Device Name: VARIANT™ II Hemoglobin A1c Program, VARIANT™ II Beta-thalassemia and VARIANT™ II Total GHb run on the VARIANT™ II Hemoglobin Testing System with CDM 4.0

Indications For Use:

Hemoglobin A1c

The Bio-Rad VARIANT II Hemoglobin A1c Program with CDM 4.0 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 with CDM 4.0 is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.

Total GHb

The VARIANT II Total GHb Program with CDM 4.0 is intended for the separation and area percent determination of total glycated hemoglobin (GHb) in whole blood using boronate affinity high performance liquid chromatography (HPLC).

The VARIANT II Total GHb Program with CDM 4.0 is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.

Measurement of percent hemoglobin A1C is effective in monitoring long-term glucose control in individuals with diabetes mellitus.

Beta-thalassemia

The VARIANT II Beta-thalassemia Short Program with CDM 4.0 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 Beta-thalassemia Short Program with CDM 4.0 is intended for use only with the Bio-Rad VARIANT II Hemoglobin Testing System. For in vitro diagnostic use.

Measurement of percent HbA2 and HbF are used for evaluation of Beta-thalassemia, a hereditary hemolytic anemia.

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)

Joan Cooper, M.S., DVM

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K063643