DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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September 13, 2017

Bio-Rad Laboratories, Inc.
Sweta Patel
Regulatory Affairs Specialist III
4000 Alfred Nobel Drive
Hercules, California 94547

Re: K171664
Trade/Device Name: Hemoglobin Variants System on Newborn Hemoglobin System with GDM and HbReview Software
Regulation Number: 21 CFR 864.7415
Regulation Name: Abnormal hemoglobin assay
Regulatory Class: Class II
Product Code: GKA
Dated: August 14, 2017
Received: August 15, 2017

Dear Sweta Patel:

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 Part 801 and Part 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 regulation (21 CFR Part 801 and Part 809), please contact the Division of Industry and Consumer Education (DICE) 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 (DICE) 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,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology
and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K171664

Device Name
Hemoglobin Variants System on Newborn Hemoglobin System with GDM and HbReview Software

Indications for Use *(Describe)*
The Hemoglobin Variants System is intended as a qualitative screen for the presence of hemoglobins F, A, S, D, C and E in eluates of neonatal blood collected on filter paper by high-performance liquid chromatography (HPLC).
The Hemoglobin Variants System is intended for Professional Use Only. For in vitro diagnostic use.
The Hemoglobin Variants System is for use only with the Newborn Hemoglobin System (NHS).

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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Special 510(k)

VOL_002 Administrative Documents

005_SECTION E: 510(k) Summary of Safety and Effectiveness Document

Hemoglobin Variants System
on the
Newborn Hemoglobin System with GDM and HbReview Software

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:_____.

Date Summary prepared: June 2, 2017

1. **Applicant Name:**
   Bio-Rad Laboratories, Inc.
   Clinical Diagnostics Group
   4000 Alfred Nobel Drive
   Hercules, California 94547

2. **Contact Person(s):**
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3. **Device Name/Trade Name:**

Trade Name:	Hemoglobin Variants System on Newborn Screening System with GDM and HbReview Software.
Classification Name:	Abnormal Hemoglobin Quantitation
Common Name:	Abnormal Hemoglobin Assay
Product Code:	GKA
C.F.R Section:	21 CFR 864.7415
Device classification:	Class II
Panel Classification:	Hematology

4. **Predicate Device:**

Predicate Device Name	**Predicate Device 510(k) Number**
Bio-Rad VARIANT™ nbs Sickle Cell Program	K080911

5. Description of the Instrument:

The instrument, Newborn Hemoglobin System (NHS) utilizes same principles of ion-exchange high-performance liquid chromatography (HPLC). The NHS instrument is a fully automated, high-throughput hemoglobin analyzer. It utilizes principles of ion-exchange high-performance liquid chromatography (HPLC). The NHS provides an integrated method for the separation and determination of relative percent of specific hemoglobins of dried blood spots. The dried blood spot collected from neonatal heel stick is punched and eluted with deionized water. The punched disc is removed and eluted sample is transferred into microplate well. The eluted sample is analyzed to identify specific inherently abnormal (S, D, C, E) as well as normal (F, A) hemoglobins through the system.

The NHS consists of two modules — the Newborn Chromatographic Station (NCS) and the Newborn Auto Sampler (NAS). NCS module delivers buffer solutions (See table 4 for kit components) to the Hemoglobin Variants System CE Mini-Columns and the detector. The NAS module through automatic injection introduces eluted sample from microplate wells. Each sample is processed individually. The mini-column contains a cation exchange gel, and the analyzer makes use of a continuous pre-programmed gradient system. The pre-programmed gradient is designed to have the hemoglobins of interest elute from the mini-column with retention times that fall within pre-determined windows characteristic of known normal and abnormal hemoglobins. The ionic strength of two phosphate buffers passing through the mini-column is changed over three minutes. The eluted hemoglobins introduced through automatic injection are sequentially detected with a dual-wavelength filter photometer, which monitors hemoglobin absorbance at 415 nm and corrects for any gradient induced absorbance changes at 690 nm. Detection is performed at two wavelengths (415 nm and 690 nm) to ensure a stable baseline. Sample of water immediately following a newborn or quality control sample prevents carryover.

A workstation is used to control the Newborn Hemoglobin System using **Genetic Disease Management (GDM) software**. The GDM software is designed to execute the assay protocol on the NHS instrument using the Hemoglobin Variants System reagent kit components. The software processed HPLC data is outputted in a printed report that contains: 1) sample identification, 2) date and time of analysis, 3) report data (i.e., peak names, retention times, area, relative percent), and 4) chromatogram. Also system assigns a presumptive phenotype “pattern” to each sample result. The pattern is calculated by applying a set of “rules” to the peaks identified in the peak table. The purpose of the pattern rules is to eliminate minor peaks from the pattern, identify system or sample problems, and to focus the operator on the samples that may require further investigation. The pattern rules used by the GDM software were derived from those generated by the Genetic Diseases Laboratory for the state of California, USA, after analysis of 2.5 million newborns by HPLC over a four year period (Eastman, et al., 1996)[1]. Laboratories using the Newborn Hemoglobin System pattern rules and assignment should perform an internal validation study to confirm the performance of the system for their application. 1.Eastman, J. W.; Wong, R.; Liao, C. L.; Morales, D. R. Automated HPLC Screening of Newborns for Sickle Cell Anemia and Other Hemoglobinopathies. Clin. Chem. 1996, 42 (5), 704–710.

The HbReview Software is to support the review of transmitted result and release of an approved result for each neonate sample analyzed on Hemoglobin Variants System with Newborn Hemoglobin System. A screening site using Newborn Hemoglobin Systems (NHS) transmits results from the Genetic Disease Management (GDM) software to the central site. The central site uses HbReview software to review results, identify samples for retesting, add comments and release results to the reporting site. Features are provided to assist Reviewers and Approvers in their tasks of examining results from the Hemoglobin Newborn Screening test.

The HbReview software is a Client-Server design. The Review process provides a user interface (client) to a relational database, which is located on a separate computer (the server). The Client software permits an authorized user to make changes to the data maintained on the Server.

6. Intended Use and Indications for Use:

Intended Use:

The Bio-Rad Hemoglobin Variants System is intended as a qualitative screen for the presence of hemoglobins F, A, S, D, C and E in elutes of neonatal blood collected on filter paper by high-performance liquid chromatography (HPLC).

The Bio-Rad Hemoglobin Variants System is intended for Professional Use Only. For in vitro diagnostic use.

The Hemoglobin Variants System is for use only with the Newborn Hemoglobin System (NHS).

Indications for Use:

This device, consisting of the reagents, controls, apparatus, HPLC instrumentation, software is indicated for professional laboratory IVD use to isolate and identify inherently determined abnormal (S, D, C, E) and normal (F, A) hemoglobin types in neonatal blood samples.

7. Substantial Equivalence Information:

Predicate Device Information:

Predicate Device Name	**Model#**	**Predicate Device 510(k) Number**
Bio-Rad VARIANT™ nbs Sickle Cell Program	250-3000	K080911

The comparison of the technological characterizes of the modified device, Hemoglobin Variant System, utilizes principles of ion-exchange high-performance liquid chromatography (HPLC) similar to the same technology of the predicate device Bio-Rad VARIANT™ nbs Sickle Cell Program.

Tables 1 provide the similarities and differences between the modified and the predicate device.

Table 1: Similarities and Differences between modified and predicate device

Summary of Technical Characteristics- Similarity		
Features	**Modified Device** **Hemoglobin Variants Systems**	**Predicate Devices** **Bio-Rad VARIANT™nbs Sickle Cell Program (K080911)**
Intended Use	The Hemoglobin Variants System is intended as a qualitative screen for the presence of hemoglobins F, A, S, D, C, and E in eluates of neonatal blood collected on filter paper by high-performance liquid chromatography (HPLC). The Bio-Rad Hemoglobin Variants System is intended for Professional Use Only The Hemoglobin Variants System is for use only with the Newborn Hemoglobin System (NHS).	The Bio-Rad VARIANT™nbs Sickle Cell Program is intended as a qualitative screen for the presence of hemoglobins F, A, S, D, C, and E in eluates of neonatal blood collected on filter paper by high-performance liquid chromatography (HPLC). The Bio-Rad VARIANTnbs Sickle Cell Program is intended for Professional Use Only.
	For In Vitro Diagnostic Use.	For In Vitro Diagnostic Use.
Target population	Same	Neonates
Design – Assay principle	Same	Cation exchange high performance liquid chromatography.
Design – Assay Detection	Same	Dual Wavelength monitoring at 415 nm and 690 nm.
Design – Analytes Identified	Same	Retention time windows for hemoglobins F, A, E, D, S and C.
Design – Sample Type	Same	Neonatal dried blood spots on filter paper collection cards.
Design – Manual Worklists	Same	Accepts manual worklists.
Safety Standards for Electrical, mechanical and thermal safety	Same	EN ISO 61010 EN ISO 61326 EN ISO 14971 ISO 62304 EN ISO 18113-2 EN ISO 18113-3 EN ISO 15223 EN ISO 13485
Reagents	Same	Elution Buffer 1. Elution Buffer 2. Wash Solution. Analytical Cartridge. Lyophilized Whole Blood Primer. Lyophilized Retention Time Marker 1 (FAES). Lyophilized Retention Time Marker 2 (FADC).
Workstation	Same	HP RP5700 HP RP5800

Software	Same	Bio-Rad Genetic Data Management Software (GDM)
Data Storage	Same	In addition to temporary storage of raw chromatographic data, the system software will be able to store associated sample information including lab site, date, run number, tray number, tray position and full accession number (including site code and calendar year.
Pattern Assignment	Same	Optional Pattern Settings

Summary of Technical Characteristics- Differences		
Features	**New Device** **Hemoglobin Variants Systems**	**Predicate Devices** **Bio-Rad VARIANT™nbs Sickle Cell Program (K080911)**
Instrument Brand name	Newborn Hemoglobin System (NHS).	VARIANTnbs Newborn Screening System
Assay Brand name	Hemoglobin Variants System	VARIANT™nbs Sickle Cell Program
Data Transmission, data collection to Central Site and Data Review (HbReview software)	GDM supports transfer of patient results to the Server. HbReview software are to collect, to access and perform review of the results through the central location (Main administrative office).	No data transmission is performed. The result review is performed the individual laboratories.

8. Risk Management Process for Device Modifications:

In accordance with ISO 14971, and internal risk management processes and procedures a defined risk analysis was used to identify, mitigate or, eliminate potential risks associated with the device modifications. For each identified risk, a Failure Mode and Effect Analysis (FMEA) was conducted. The risk evaluation for the device software modification included in the following tasks:

Reviewed modifications and design inputs to identify potential risks and hazard;
Reviewed existing product risk tables and customer complaints to identify potential risk and hazards;

9. Conclusion:

When considering the similarities of the intended use, the general features and characteristic of the assay and the use of the same technology, it can be concluded that the Hemoglobin Variants System on the Newborn Hemoglobin System using GDM and HbReview software is substantially equivalent to the predicate device.