

**S510 (k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

K052291

B. Purpose for Submission:

New Device

C. Measurand:

Hemoglobin A, F, A2, S, C, E, D

D. Type of Test:

Quantitative, Qualitative

E. Applicant:

SEBIA

F. Proprietary and Established Names:

CAPILLARYS HEMOGLOBIN(E)

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7515, Abnormal Hemoglobin Assay

2. Classification:

Class II

3. Product code:

GKA, Abnormal Hemoglobin quantiatation

4. Panel:

Hematology (81)

H. Intended Use:

1. Intended use(s):

The CAPILLARYS HEMOGLOBIN(E) kit is designed for the separation of the normal hemoglobins (A, F and A2) and for the detection of the major hemoglobin variants (especially S, C, E or D), by electrophoresis in alkaline buffer (pH 9.4) with the CAPILLARYS System. The CAPILLARYS performs all sequences automatically to obtain a complete hemoglobin profile for qualitative or quantitative analysis of hemoglobins. The assay is performed on red blood cells.

2. Indication(s) for use:

The CAPILLARYS HEMOGLOBIN(E) kit is designed for the detection and the characterization of hemoglobins in human blood with the Sebia CAPILLARYS system, for capillary electrophoresis. The CAPILLARYS performs all procedural sequences automatically to obtain a hemoglobin profile. The CAPILLARYS system automatically mixes the blood sample with hemolysing solution. The hemoglobins, separated in silica capillaries, are directly detected by their absorbance at 415 nm. The electrophoregrams are evaluated visually for the pattern abnormalities. Direct detection of the hemoglobins provides relative quantification of individual hemoglobin fraction of the normal hemoglobin fractions A, A2, F and for the detection of major hemoglobin variants as S, C, E and D using Capillary electrophoresis. For in vitro diagnostic use.

3. Special conditions for use statement(s):

Not applicable.

4. Special instrument requirements:

Not applicable.

I. Device Description:

The CAPILLARYS HEMOGLOBIN(E) kit consist of five components; (1) CAPILLARYS HEMOGLOBIN(E) buffer contains alkaline buffer (pH 9.4), supplied in 700mL vials, (2) Hemolyzing Solution, supplied in 440 ml vials, (3) Washing Solution, supplied in 70 ml vials, (4) Dilution segments, supplied in pack of 90, (5) Filters, three per kit. The CAPILLARYS HEMOGLOBIN(E) kit is used in conjunction with a Sebia CAPILLARYS system in which seven silica capillaries are utilized for analyzing. The hemoglobin, separated in capillaries, are directly detected at an absorbance wave length of 415 nm, resulting electrophoregrams. Direct detection provides relative quantification of individual

hemoglobin fractions.

1. Predicate device name(s):

BIORAD VARIANT (HPLC) - β Thalasemia

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

K051072

3. Comparison with predicate:

Similarities		
Item	<i>CAPILLARYS HEMOGLOBIN(E)</i>	<i>HPLC BIORAD</i>
Intended use	The CAPILLARYS HEMOGLOBIN(E) kit is designed for the separation of the normal hemoglobins (A, F and A2) and for the detection of the major hemoglobin variants (especially S, C, E or D), by electrophoresis in alkaline buffer (pH 9.4) with the CAPILLARYS System. The CAPILLARYS performs all sequences automatically to obtain a complete hemoglobin profile for qualitative or quantitative analysis of hemoglobins. The assay is performed on red blood cells. For in vitro diagnostic use	The VARIANT B-thalasemia Program is intended for the separation and area percent determinations of hemoglobins A2 and F using a whole blood ion-exchange high performance liquid chromatography (HPLC) For in vitro diagnostic use.
Absorbance wave length	415 nm	415 and 690 nm
Analyzed samples	Packed red blood cells	Whole blood
Samples identification	Yes	Yes
Hemolysis	Performed automatically by the system	Performed automatically by the system
Introduction of the samples into the automatic system	Continuous loading	Continuous loading

Differences		
Item	<i>CAPILLARYS HEMOGLOBIN(E)</i>	<i>HPLC BIORAD</i>
Instrument	CAPILLARYS	Bio-Rad VARIANT
Separation System	Capillary electrophoresis in free solution: protein separation in an alkaline buffer (pH 9.4) according to their charge, to the electrolyte pH and electroosmotic flow. Fast separation and good resolution. Electrophoregrams show separated fractions according to their charge.	Ion-exchange high performance liquid chromatography: protein Separation on the column based on their ionic interaction with the cartridge material and elution by buffer gradient with increasing ionic strength. Chromatograms show retention times of eluted fractions.
Materials Included in Kit	Buffer, 2 Vials 700 mL ea Hemolysing solution, 1 vial 440 mL Wash solution , 1 vial 70 mL Dilution segments, 1 pack of 90 Filters, 3 Filters	Elution Buffer -1 Elution Buffer-2 Whole Blood Primer HbA2/F Calibrator set Analytical Cartridge Sample Vials- 100 Wash/Diluent-2 CD ROM
Number of separation units	7 parallel capillaries	1 column
Number of analysis (throughput)	Max 34 samples/hour	9-10 samples/hour

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

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff, May 11, 2005.

L. Test Principle:

The CAPILLARYS system uses the principle of capillary electrophoresis in a free solution. With this technique, charged molecules are separated by their electrophoretic mobility in an alkaline buffer with a specific pH. Separation also occurs according to the electrolyte pH and electroosmotic flow. The CAPILLARYS system has capillaries functioning in parallel allowing 7 simultaneous analyses for hemoglobin quantification. A sample dilution with hemolyzing solution is prepared and injected by aspiration at the anodic end of the capillary. A high voltage protein separation is then performed and direct detection of the hemoglobins is made at 415 nm at the cathodic end of the capillary. The resulting electrophoregrams are evaluated visually for pattern abnormalities. By using alkaline pH buffer, normal and abnormal (or variant) hemoglobins are detected.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Five different blood samples (normal blood 1; blood 2 with increased Hb A2; bloods 3 and 4 with Hb F; blood 5 with increased Hb A2, Hb F and S component) were run seven times with two lots of analysis buffer.

Reproducibility (Within-run) results:

Sample #	Hb A	Hb A2	Hb F	Hb S	Mean (%)	SD	CV (%)
1	X				97.3/97.3	0.05/0.05	0.1/0.1
		X			2.7/2.7	0.05/ 0.05	1.8/1.8
2	X				94.3/94.5	0.06/0.08	0.1/0.1
		X			5.7/5.5	0.06/0.08	0.1/0.1
3	X				80.5/80.4	0.14/0.12	0.2/0.1
		X			2.3/2.3	0.00/0.05	0.0/2.0
			X		17.2/17.3	0.14/0.08	0.8/0.5
4	X				96.8/96.9	0.09/0.11	0.1/0.1
		X			2.4/2.3	0.05/0.03	1.9/1.5
			X		0.8/0.8	0.05/0.08	6.7/10.2
5	X				53.4/53.7	0.17/0.24	0.3/0.4
		X			5.5/4.9	0.05/0.07	1.1/1.4
			X		9.0/8.8	0.05/0.07	0.6/0.8
				X	32.6/32.6	0.17/0.20	0.5/0.6

b. *Linearity/assay reportable range:*

Linearity was conducted using two blood samples (Control 1: normal Hb A and Hb A2 and Control 2: abnormal elevated Hb A2, Hb S and Hb F). The two control samples were mixed at different concentration. Linearity was determined for each fraction (Hb A, Hb A2, Hb S and Hb F). In addition, two blood samples were obtained containing different total hemoglobin concentration values of 10.6 g/dl and 12.5 g/dl. The samples were run neat, diluted 2, 3, and 5. The results demonstrated satisfactory linearity within the entire range of 2.1 – 12.5 g/dL.

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

Stability studies were performed with the CAPILLARYS HEMOGLOBIN(E) kit for samples containing anticoagulants, EDTA, citrate and heparin. Samples were stored for up to 7 days between 2 – 8° C. The percent of each fraction (HbA, HbF, HbS, HbA2 and Hb delta A'2) was measured. All three anticoagulants were found acceptable.

d. Detection limit:

Not applicable.

e. Analytical specificity:

Not applicable.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Comparison studies were performed, with the use of the HPLC system, for Hb A2, Hb F, and Hb S on blood samples (with normal and elevated levels). The results are as follows:

Hb fraction	N	R2	y-intercept	Slope	Range of % values
Hb A2	66	0.947	0.146	0.908	1.6 – 6.0
Hb F	74	0.995	-0.339	0.968	0.0 – 44.9
Hb S	43	0.994	1.769	1.005	9.1 – 92.7

An additional study was performed on seventy (75) blood samples with hemoglobin variants, such as hemoglobin S, C, and E. This study also included the comparison of Hemoglobin A (Hb A). Gel confirmation studies were conducted on all samples tested.

Hemoglobin D studies were not conducted due to infrequency of the hemoglobin variant and sample availability.

All abnormal hemoglobins or abnormal levels detected were in agreement with the comparative method, hospital results and clinical diagnosis.

The blood samples and their diagnostic assessment used for all studies were provided by hospitals in Europe. The diagnosis was based on HPLC and/or on a routine alkaline gel and acid gel electrophoresis.

b. Matrix comparison:

Not applicable.

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):*

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Normal values for individual major electrophoretic hemoglobin zones in the CAPILLARYS system were established from a healthy population of 113 adults (men and women) with normal hemoglobin. See below:

Hemoglobin A (Hb A):	$\geq 96.8 \%$
Hemoglobin F (Hb F):	$< 0.5 \%$
Hemoglobin A2 (Hb A2):	comprised between 2.2 and 3.2 %

It is recommended that each laboratory establish its own threshold values.

N. Instrument Name:

Sebia, CAPILLARYS

O. System Descriptions:

1. Modes of Operation:

Open tube batch mode with the following sequence of automated steps:

Bar code reading of sample tubes
Sample hemolysis and dilution from primary tubes
Capillary washing
Injection of hemolyzed samples
Hemoglobin separation and direct detection of the separated hemoglobins on capillaries

2. Software:

The CAPILLARYS operating system software is designed to work with the instrumentation, CAPILLARYS. The CAPILLARYS instrumentation directed by the software is a fully automated in the performance of the sample identification by barcode labeling, dilution, testing, and calculation of results. The CAPILLARYS software utilizes *Windows 98 or XP as the operating system with Intel based processors with Visual Basic as the programming language.*

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes X or No

3. Specimen Identification:

Bar Code reader

4. Specimen Sampling and Handling:

Red blood cells are allowed to precipitate at 2° – 8° C, or centrifuged at 5000 rpm for 5 minutes. The maximum volume of plasma is removed and the tube is vortexed for 5 seconds. The open tubes are placed in the sample racks.

5. Calibration:

Not applicable

6. Quality Control:

It is necessary to run two analysis sequences with the Normal Hb A2 Control (SEBIA) after having changed buffer lot numbers, after a capillary cleaning, and before starting a new analysis sequence. It is also advised to include into each run of samples an assayed blood control (AFSC Control, Normal Hb A2 Control – SEBIA).

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.