510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

Instrument and Assay

I Background Information:

A 510(k) Number

K232027

B Applicant

Sebia, Inc.

C Proprietary and Established Names

CAPI 3 NEONAT Hb, CAPILLARYS 3 DBS Instrument

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GKA	Class II	21 CFR 864.7415 - Abnormal Hemoglobin Assay	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

Clearance of a new device system

B Measurand:

Hemoglobin variants F, A, S, C, E, D and Bart's

C Type of Test:

Qualitative, Capillary Electrophoresis

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The CAPI 3 NEONAT Hb kit is intended as a qualitative screen for the detection of normal hemoglobins (F and A) and abnormal hemoglobins (S, C, E, D and Bart's) in blood from human new-born collected on filter paper. This analysis is performed by capillary electrophoresis with the CAPILLARYS 3 DBS instrument.

The CAPILLARYS 3 DBS instrument is a capillary electrophoresis based automated analyzer which performs a complete hemoglobin profile for the qualitative analysis of hemoglobins (A, F, S, C, D, E and Bart's). The assay is performed on the hemolysate of whole blood samples previously collected on filter paper.

The test result must be interpreted in conjunction with other biological and clinical findings. In case of abnormal hemoglobin presence, it should be confirmed by additional tests as per local recommendations. The device is intended for professional use only.

For In Vitro Diagnostic Use only.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

CAPILLARYS 3 DBS instrument

IV Device/System Characteristics:

A Device Description:

The CAPI 3 NEONAT Hb kit is intended for the detection of normal hemoglobins (F and A) and abnormal hemoglobins (S, C, E, D and Bart's) in blood from human newborns collected on filter paper. The resulting electrophoregrams are automatically evaluated for pattern abnormalities with identification of normal and pathological patterns.

The CAPI 3 NEONAT Hb kit consists of one CAPILLARYS HEMOGLOBIN(E) buffer, an alkaline buffer (pH 9.4) supplied in three vials, 700 mL each per kit, Filters - five per kit, and CAPILLARYS 3 DBS MICROPLATES - one pack barcoded 96-well microplates consisting of 10 microplates.

The CAPILLARYS 3 DBS instrument has silica capillaries functioning in parallel allowing 12 simultaneous analyses. The CAPILLARYS 3 DBS performs all sequences automatically to obtain a complete hemoglobin profile for the qualitative analysis of hemoglobins. The assay is performed on the hemolysate of whole blood samples previously collected on Guthrie filter paper and punched to obtain a paper circle.

Reagents required to perform the CAPI 3 NEONAT Hb kit on CAPILLARYS 3 DBS instrument but are not supplied in the CAPI 3 NEONAT Hb kit include, CAPI 3 NEONAT Hemolysing solution kit, CAPI 3 NEONAT Hb AF control, CAPILLARYS 3 CAPICLEAN, CAPILLARYS 3 wash solution.

B Principle of Operation:

The CAPI 3 NEONAT Hb kit is intended for the detection of normal hemoglobins (F and A) and abnormal hemoglobins (S, C, E, D and Bart's) in dried blood samples from newborns collected on filter paper. The samples are eluted from the filter paper into microplates.

The CAPILLARYS 3 DBS instrument performs fully automated electrophoresis sequencing on the hemolysate of whole blood samples previously collected on Guthrie filter paper and punched to obtain a paper circle collected in microplates. The CAPI 3 NEONAT Hb kit in conjunction with CAPILLARYS 3 DBS instrument utilizes the principle of capillary electrophoresis in 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 hemoglobins, separated in silica capillaries, are directly detected at an absorbance wavelength of 415 nm. The hemoglobin (Hb) fractions are separated by absorbance spectrophotometry.

C Instrument Description Information:

1. Instrument Name:
   CAPILLARYS 3 DBS instrument

2. Specimen Identification:
   Single use microplates with barcodes

3. Specimen Sampling and Handling:
   Whole blood samples collected from newborns on Guthrie cards (Whatman cards) and dried for a minimum of 4 hours at room temperature (15−30°C).

4. Quality Control:
   CAPI 3 NEONAT Hb AF CONTROL, Hb AFSC CONTROL

V Substantial Equivalence Information:

A Predicate Device Name(s):
Capillarys Neonat Hb

B Predicate 510(k) Number(s):
K091283

C Comparison with Predicate(s):

Device & Predicate Device(s):	K232027	K091283
Device Trade Name	CAPI 3 NEONAT Hb CAPILLARYS 3 DBS Instrument	CAPILLARYS NEONAT Hb with CAPILLARYS 2 System
General Device Characteristic Similarities		
Intended Use/Indications For Use	The CAPI 3 NEONAT Hb kit is intended as a qualitative screen for the detection of normal hemoglobins (F and A) and abnormal hemoglobins (S, C, E, D and Bart's) in blood from human new-born collected on filter paper. This analysis is performed by capillary electrophoresis with the CAPILLARYS 3 DBS instrument. The CAPILLARYS 3 DBS instrument is a capillary electrophoresis based automated analyzer which performs a complete hemoglobin profile for the qualitative analysis of hemoglobins (A, F, S, C, D, E and Bart's). The assay is performed on the hemolysate of whole blood samples previously collected on filter paper.	The CAPILLARYS NEONAT Hb kit is designed for the separation of the normal hemoglobins (F and A) in blood samples from human new-borns, and for the detection of the major hemoglobin variants (S, C, E, D and Bart's), by electrophoresis in alkaline buffer (pH 9.4) with the CAPILLARYS 2 system. The CAPILLARYS NEONAT Hb kit is designed for laboratory use. The CAPILLARYS 2 is an automated analyzer which performs a complete hemoglobin profile for the qualitative analysis of hemoglobins. The assay is performed on the hemolysate of whole blood samples previously collected on filter paper. For In Vitro Diagnostic Use only.

	The test result must be interpreted in conjunction with other biological and clinical findings. In case of abnormal hemoglobin presence, it should be confirmed by additional tests as per local recommendations. The device is intended for professional use only.	
Analytes	Hemoglobin variants (F, A, S, C, E, D and Bart's)	Same
Measurement	Qualitative	Same
Sample Matrix	Blood samples from human newborns collected on filter paper	Same
Technology	Capillary electrophoresis	Same
Instrument Wavelength Measurement	415 nm	Same
Buffer	CAPILLARYS HEMOGLOBIN(E) buffer	Same
Controls	Hb AF Control Hb AFSC Control	Same
General Device Characteristic Differences		
Kit components	• CAPILLARYS HEMOGLOBIN(E) buffer • Filters • CAPILLARYS 3 DBS MICROPLATES	• CAPILLARYS HEMOGLOBIN(E) buffer • Filters • Dilution segments • Hemolyzing Solution • Washing Solution
Dilution Vessel	96 well-microplates	Dilution segments
Punch Size	3.2 mm diameter	3.8 mm diameter
Instrument	CAPILLARYS 3 DBS Instrument	CAPILLARYS 2 SYSTEM

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures, 3rd Edition
- CLSI EP07-A3: Interference Testing in Clinical Chemistry; Approved Guideline. 3rd Edition
- CLSI EP12-A2: User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline. 2nd Edition
- CLSI EP25: Evaluation of Stability of In Vitro Medical Laboratory Test Reagents, 2nd Edition
- CLSI NBS01: Dried Blood Spot Specimen Collection for Newborn Screening, 7th Edition
- IEC 61010-1 Edition 3.1 2017-01, Safety requirements for electrical equipment for measurement, control, & laboratory use - Part 1
- IEC 60601-1-2 Edition 4.1 2020-09, Medical electrical equipment - Part 1-2: General requirements
- IEC 62304 Edition 1.1 2015-06, Medical device software - Software life-cycle processes
- IEC 62366-1:2015+A1:2020, Medical devices Part 1: Application of usability engineering to medical devices

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   Precision of the CAPI 3 NEONAT Hb on the CAPILLARYS 3 DBS instrument was evaluated according to CLSI guideline EP05-A3.

   20-day precision study using hemoglobin control
   Two control materials (AF and AFSC) with different hemoglobin variants were run using one lot of the CAPI 3 NEONAT Hb kit performed with one CAPILLARYS 3 DBS instrument. Each sample was analyzed in one replicate on 12 capillaries per run, two runs per day over 20 days yielding a total of 480 results per sample. Within-run, between-day, between-run, and total precision were determined. All precision estimates for all Hb fractions were within the acceptance criteria.

%Hb F

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
AF	480	69.2	0.40	0.60	0.25	0.40	0.49	0.70	0.68	1.00
AFSC	480	26.0	0.15	0.60	0.07	0.30	0.02	0.10	0.16	0.60

%Hb A

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
AF	480	30.2	0.40	1.30	0.26	0.90	0.51	1.70	0.70	2.30
AFSC	480	46.6	0.30	0.60	0.23	0.50	0.00	0.00	0.38	0.80

%Hb S

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
AFSC	480	16.6	0.14	0.80	0.11	0.70	0.00	0.00	0.17	1.00

%Hb C

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
AFSC	480	10.7	0.08	0.70	0.06	0.60	0.04	0.40	0.11	1.00

Reagent lot-to-lot precision study using hemoglobin control

Two control materials with different hemoglobin variants were run using three lots of the CAPI 3 NEONAT Hb kit performed with one CAPILLARYS 3 DBS instrument. Each sample was analyzed in three replicates per run, two runs per day over five days for each of the three reagent lots yielding a total of 90 results per sample. Within-run, between run, between-day, between-lot and total precision were calculated. All hemoglobin fractions met acceptance criteria demonstrating acceptable reagent lot-to-lot precision.

%Hb F

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AF	90	69.3	0.22	0.30	0.32	0.50	0.00	0.00	0.17	0.20	0.68	1.00
AFSC	90	25.8	0.10	0.40	0.05	0.20	0.04	0.20	0.06	0.20	0.16	0.60

%Hb A

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AF	90	30.3	0.21	0.70	0.34	1.10	0.00	0.00	0.16	0.50	0.43	1.40
AFSC	90	47.1	0.41	0.90	0.00	0.00	0.12	0.30	0.17	0.40	0.46	1.00

%Hb S

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AFSC	90	16.5	0.24	1.5	0.00	0.00	0.04	0.30	0.10	0.60	0.27	1.60

%Hb C

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AFSC	90	10.5	0.14	1.3	0.00	0.00	0.04	0.40	0.13	1.20	0.19	1.80

Between-Instrument Precision using hemoglobin control

Two control materials with different hemoglobin variants were run using one lot of the CAPI 3 NEONAT Hb kit performed with three CAPILLARYS 3 DBS instruments. Each sample

was analyzed in three replicates per run, two runs per day over five days yielding a total of 90 results per sample. The results are expressed as standard deviation (SD) and coefficient of variation (%CV). Within-run, between-run, between-day, between-instrument, and total precision were calculated. All hemoglobin fractions met acceptance criteria demonstrating acceptable between-instrument precision.

%Hb F

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AF	90	69.4	0.33	0.50	0.43	0.60	0.00	0.00	0.45	0.60	0.70	1.00
AFSC	90	25.9	0.11	0.40	0.06	0.20	0.00	0.00	0.09	0.30	0.15	0.60

%Hb A

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Instrument		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AF	90	29.9	0.33	1.10	0.45	1.50	0.00	0.00	0.44	1.50	0.73	2.40
AFSC	90	46.6	0.28	0.60	0.08	0.20	0.05	0.10	0.47	1.00	0.56	1.20

%Hb S

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AFSC	90	16.7	0.14	0.90	0.00	0.00	0.05	0.30	0.20	1.60	0.27	1.70

%Hb C

Control	N	Mean (%)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
AFSC	90	10.8	0.10	1.00	0.05	0.40	0.02	0.20	0.16	1.50	0.20	1.80

Precision study using patient samples

Within-run precision was determined at an internal site by running six newborn whole blood native samples (FA, FAS, FAC, FAD, FAE and FA Bart's patterns) and control samples (FA and AFSC). Each sample was analyzed using one lot of CAPI 3 NEONAT Hb kit in single run on 12 capillaries on one CAPILLARYS 3 DBS instrument. All electropherograms were evaluated visually. All replicates gave concordant results and the patterns corresponded to the hemoglobin type of each tested sample.

Lot-to-lot precision study was performed by running six newborn whole blood native samples (FA, FAS, FAC, FAD, FAE and FA Bart's patterns) and two control samples (FA and AFSC). Each sample was analyzed once per run over two runs with three lots of CAPI 3 NEONAT Hb kit on one CAPILLARYS 3 DBS instrument for three days. One lot of CAPI 3 NEONAT Hb kit was tested on each of the three days. All electropherograms were evaluated visually. All replicates gave concordant results and the patterns corresponded to the hemoglobin type of each tested sample.

Between-instrument precision study was performed by running six newborn whole blood native samples (FA, FAS, FAC, FAD, FAE and FA Bart's patterns) and two control samples (FA and AFSC). Each sample was analyzed once per run over two runs with one lot of CAPI 3 NEONAT Hb kit on three CAPILLARYS 3 DBS instruments. The study was performed for three days with testing performed on one instrument each day. All electropherograms were evaluated visually. All replicates gave concordant results and the patterns corresponded to the hemoglobin type of each tested.

Precision with patient samples

Sample	Identification pattern	Between capillaries		Between-lot		Between-instrument		Between-day	
		Result	Total analyses	Result	Total analyses	Result	Total analyses	Result	Total analyses
1	FA	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
2	FAS	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
3	FAC	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
4	FAD	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
5	FAE	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
6	FA Bart's	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
7	AFSC	100% concordance	12	100% concordance	6	100% concordance	6	100% concordance	10
8	FA	100% concordance	12	100% concordance	72	100% concordance	72	100% concordance	120
Total concordance (95% CI)		**100% (96.2%, 100.0%)**	**96**	**100% (96.7%, 100.0%)**	**114**	**100% (96.7%, 100.0%)**	**114**	**100% (98.0%, 100.0%)**	**190**

2. Linearity:

Not applicable

3. Analytical Specificity/Interference:

The interference studies were conducted in accordance with CLSI EP07-A3 using six neonate whole blood samples collected on Guthrie cards. The samples consisted of FA, FAS, FAC, FAD, FAE, FA Bart's and were analyzed at one internal site. Paired interference testing was performed where test samples were supplemented with the potential interferent, and results were compared to reference samples supplemented with same volume of solvent as the interferent solution. The testing was performed using two lots of CAPI 3 NEONAT kit on two CAPILLARYS 3 DBS instruments with samples run in one replicate. The results were evaluated visually for hemoglobin patterns.

No interference with the CAPI 3 NEONAT Hb kit used on the CAPILLARYS 3 DBS instrument was detected due to the newborn whole blood sample's high concentration of the following interfering factors listed below:

Interference	Maximum concentration tested with no interference
Conjugated bilirubin	40 mg/dL
Unconjugated bilirubin	40 mg/dL
Triglycerides	1500 mg/dL

4. Assay Reportable Range:

   Not Applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   a. Shelf-life Stability

      The sponsor stated that the CAPILLARYS HEMOGLOBIN (E) buffer in the CAPI 3 NEONAT Hb kit is unchanged as in the CAPILLARYS NEONAT Hb kit reviewed in K091283. The established shelf-life for the CAPILLARYS HEMOGLOBIN (E) buffer is up to three years when stored at 2−8°C.

   b. On-board stability of CAPI 3 NEONAT Hb

      On-board reagent stability of the CAPILLARYS HEMOGLOBIN(E) buffer was conducted using one lot of CAPILLARYS HEMOGLOBIN(E) buffer boarded on one CAPILLARYS 3 DBS instrument as per CLSI EP25 Ed2. Six samples: two each of FA and FAS, one of Hb AFSC control and one of Hb AF CAPI 3 NEONAT control were used in the study. Testing was performed on day 1, 15, 31 and 38 days of CAPILLARYS HEMOGLOBIN(E) buffer on board the CAPILLARYS 3 DBS instrument. The results were evaluated visually for hemoglobin patterns and stability was demonstrated if the identification pattern was identical between the reference and time points tested for all replicates. The study supports on-board stability of one month of the CAPILLARYS HEMOGLOBIN(E) buffer once on board the CAPILLARYS 3 DBS instrument.

   c. Sample stability

      The sample stability study was conducted to evaluate the stability of native neonate whole blood samples collected and stored on Guthrie cards. The whole blood samples were comprised of both normal and pathological hemoglobin variants (FA, FAS, FAC, FAE, FCE, FSC, FAX and FA Bart's) collected on Guthrie cards and stored at room temperature (15−30°C) for 16 days, followed by storage at 2−8°C for 2 months +1 day (from day 0 of whole blood collection). The testing was performed using one lot of CAPI 3 NEONAT Hb kit on one CAPILLARYS 3 DBS instrument. The samples were tested at each timepoint in one replicate. The results were evaluated visually for hemoglobin patterns and stability was demonstrated if the identification pattern was identical between the reference and time points tested. The study supports whole blood samples dried on Guthrie cards may be stored for 15 days at room temperature and no longer than 2 months at 2−8°C.

   d. Sample transportation study

The sample transportation study was conducted to evaluate the transportation stability of native neonate whole blood samples collected on Guthrie cards. Two separate studies mimicking different environmental conditions were conducted. Twelve (12) neonate whole blood samples, both normal and pathological (six samples with FA, five samples with FAS ad one sample with FAC) collected on Guthrie cards were used for the study. In the first study, the samples were tested at the beginning of the study (T=0) and after storage period of 8 days at 30°C with exposure of a high hygrometry > 95 %. The results were evaluated visually for hemoglobin patterns and stability was demonstrated if the identification pattern was identical between the reference and time points tested. In the second study, samples after initial analysis (T=0), were stored in a sealed opaque plastic bag, in an envelope for 5 days where samples were cycled between 37°C for 6 hours followed by storage at 2−8°C each day. After sample analysis on day 6, samples were stored at 30°C for another period of 11 days. At the end of 16 days (5 days cycled at different temperatures and 11 days at 30°C) sample analysis was performed. The results were evaluated visually for hemoglobin patterns at T=0, 6 and 16 days, and stability was demonstrated if the identification pattern was identical between the reference and time points tested. The results met the acceptance criteria and samples were found to be stable during transport.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

8. Accuracy (Instrument):

   Not applicable

9. Carry-Over:

   The carryover study was conducted to evaluate sample retention in the capillary. Two neonate whole blood samples, one normal (FA) and one pathological (FS) collected on Guthrie paper were used in the study. Carry-over was assessed by the normal hemoglobin run followed by the pathological hemoglobin run. For all normal samples analyzed after pathological samples, the identification pattern was found unchanged. No carry-over is observed with the CAPI 3 NEONAT Hb kit used on the CAPILLARYS 3 DBS instrument.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   The study was conducted at three sites, one internal and two external sites. The results from CAPI 3 NEONAT Hb kit performed on the CAPILLARYS 3 DBS instrument were compared to the predicate CAPILLARYS NEONAT Hb kit on CAPILLARYS 2 instrument using the CAPILLARYS NEONAT Fast procedure (K091283). A total of 789 newborn

whole blood samples collected on Guthrie cards consisting of 401 normal samples (FA) and 388 pathological samples (FAS, FAC, FAD, FA+ Bart's, FAS+ Bart's, FAE, FS, FSA, FAX, FCS, AFS, FSE, FCX, FE and FAC+ Bart's) were included in the study. One lot of CAPI 3 NEONAT Hb kit and one CAPILLARYS 3 DBS instrument were used at each site. The overall percent agreement (OPA), positive percent agreement (PPA), the negative percent agreement (NPA), and their 95% confidence intervals (95 % CI by Wilson score method) were calculated for the CAPI 3 NEONAT Hb kit compared to the predicate device. The method comparison study showed an OPA of 100% (95%CI: 96.5%, 100%), a PPA of 100% (95%CI: 96.5%, 100%) and an NPA of 100% (95%CI: 96.6%, 100%) between the candidate and the predicate devices.

2. Matrix Comparison:

   Not applicable

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable

2. Clinical Specificity:

   Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not applicable

F Other Supportive Instrument Performance Characteristics Data:

Sample preparation study

The sample preparation study was conducted to evaluate the performance of samples eluted using passive (2 hours or up to 3 days at 2–8°C) and active elution (40 minutes at room temperature) methods and tested using CAPI 3 NEONAT Hb kit on CAPILLARYS 3 DBS instrument. Twelve (12) neonate whole blood samples collected on Guthrie paper comprised of both normal and pathological samples were used in the study (3 FA, 3 FAS, 1 FAC, 1 FAD, 3 FAE and 1 Bart's). Identical electrophoretic patterns were noted between the active and passive elution sample preparation methods.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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