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

510(k) Number:

k162281

B. Purpose for Submission:

New Device

C. Measurand:

Whole blood hemoglobin A1c (HbA1c)

D. Type of Test:

Capillary Electrophoresis

E. Applicant:

Sebia, Inc.

F. Proprietary and Established Names:

CAPI 3 HbA1c

MULTI-SYSTEM HbA1c CAPILLARY Controls (2)

G. Regulatory Information:

Regulation section	Classification	Product code	Panel
21 CFR 864.7470	II	LCP	Hematology (81)
21 CFR 862.1660	Class I, reserved	JJX	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for use below

2. Indication(s) for use:

   The CAPI 3 HbA1c kit is designed for separation and quantification of the HbA1c glycated fraction of hemoglobin in venous whole blood, by capillary electrophoresis in alkaline buffer (pH 9.4) with the CAPILLARYS 3 TERA instrument. Measurement of hemoglobin A1c is effective in monitoring long-term glycemic control in individuals with diabetes mellitus. This test is not for screening or diagnosis of diabetes. The CAPI 3 HbA1c kit is designed for Professional Use Only.

   The Multi-system HbA1c CAPILLARY Controls (2) are designed for the migration control and quality control of human glycated hemoglobin A1c quantification with SEBIA capillary electrophoresis procedures: CAPILLARYS HbA1c performed with the CAPILLARYS 2 FLEX-PIERCING automated instrument, CAPI 3 HbA1c performed with the CAPILLARYS 3 TERA automated instrument and MINICAP HbA1c performed with the MINICAP FLEX-PIERCING automated instrument. The HbA1c CAPILLARY Controls are designed for Professional Use Only.

3. Special conditions for use statement(s):

   For Prescription Use Only.

   The CAPI 3 HbA1c kit should not be used:
   - for "Point-of-Care" use
   - for the screening or diagnosis of diabetes mellitus
   - in monitoring daily glucose control
   - to replace daily home testing of urine and blood glucose levels
   - for analyzing samples from patients with conditions causing shortened red blood cell survival, such as hemolytic diseases, pregnancy and significant acute or chronic blood loss
   - for analyzing samples from patients with total hemoglobin levels of less than 2.9 or greater than 30.5 g/dL and any hemoglobinopathies that may interfere.

   Test results for the CAPI 3 HbA1c kit show that there is not significant interference for Hemoglobin C (≤ 36.9 %), Hemoglobin D (≤ 44.2 %), Hemoglobin E (≤ 26.6 %), Hemoglobin S (≤ 40.4 %), and Hemoglobin F (< 23%).

4. Special instrument requirements:

   CAPILLARYS 3 TERA instrument

I. Device Description:

The CAPI 3 HbA1c kit and controls are to be used with the CAPILLARYS 3 TERA instrument. The components are summarized as follows:

The CAPI 3 HbA1c kit contains a ready to use buffer solution pH 9.4 ± 0.5 (2 vials, 700 mL

each), a ready to use hemolysing solution (1 vial, 700 mL) and filters (4 filters per kit).

The MULTI-SYSTEM HbA1c CAPILLARY Controls (2) consist of a HbA1c CAPILLARY Control 1 (normal HbA1c level, 1 vial) and HbA1c CAPILLARY Control 2 (elevated HbA1c level, 1 vial). The MULTI-SYSTEM HbA1c CAPILLARY Controls (2) are obtained from pools of human blood samples and contain stabilizers and preservatives to maintain the stability of the hemoglobin fractions. The controls are in a stabilized lyophilized form.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   CAPILLARYS HbA1c Kit
   HbA1c CAPILLARY Controls

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

   k122101, k133344

3. Comparison with predicate:

CAPI 3 HbA1c

Similarities/Differences		
Item	CAPI 3 HbA1c Candidate Device (k162281)	CAPILLARYS HbA1c Kit Predicate Device (k122101)
Intended Use	Measurement of hemoglobin A1c is for use in monitoring long-term glycemic control in individuals with diabetes mellitus.	Same
Method	Free solution capillary electrophoresis	Same
Sample type	Whole blood	Same
Collection tubes	K3 EDTA and K2 EDTA	Same
Measuring Range	4.0 to 14.7 % HbA1c	Same
Shelf life	Buffer: 3 years at 2 - 8 °C Hemolysing solution: 3 years at 2 - 30 °C	Same
Instrument	SEBIA CAPILLARYS 3 TERA instrument	SEBIA CAPILLARYS 2 FLEX-PIERCING instrument
Absorbance wavelength	415 nm	Same
Software for data processing	PHORESIS™ software	Same
Number of separation units	12 parallel capillaries	8 parallel capillaries

MULTI-SYSTEM HbA1c CAPILLARY Controls (2)

Similarities/Differences		
Item	Candidate Device: MULTI-SYSTEM HbA1c CAPILLARY Controls (2) (k162281)	Predicate Device: HbA1c CAPILLARY Controls (k122101 and k133344)
Intended Use	Intended for use as quality control materials.	Same
Format	2 levels	Same
Shelf life	3 years at 2 - 8 °C	Same
In use storage	CAPILLARYS HbA1c: When reconstituted the controls are stable for 1 day at 2-8°C, 6 months at -18°C and -30°C. Do not freeze and thaw the reconstituted controls more than 30 times. When hemolyzed, the controls are stable for 8 hours at 2-8°C, 1 month at -18°C and -30°C. Do not freeze and thaw a dilution segment with hemolyzed control more than three times. MINICAP HbA1c and CAPI 3 HbA1c: When reconstituted the controls are stable for 1 day at 2-8°C, 6 months at -18°C and -30°C. Do not freeze and thaw the reconstituted controls more than 30 times.	CAPILLARYS HbA1c : When reconstituted the controls are stable for 1 day at 2-8°C, 6 months at -18°C and -30°C. Do not freeze and thaw the reconstituted controls more than 30 times. When hemolyzed the controls are stable for 8 hours at 2-8°C, 1 month at -18°C and -30°C. Do not freeze and thaw a dilution segment with hemolyzed control more than three times. MINICAP HbA1c : When reconstituted the controls are stable for 1 day at 2-8°C, 6 months at -18°C and -30°C. Do not freeze and thaw the reconstituted controls more than 30 times.

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

CLSI Guideline, EP05-A2: *Evaluation of Precision Performance of Clinical Chemistry Devices*

CLSI Guideline, EP06-A: *Evaluation of the Linearity of Quantitative Analytical Methods*

CLSI Guideline, EP07-A2: *Interference Testing in Clinical Chemistry*

CLSI Guideline, EP09-A2: *Method Comparison and Bias Estimation Using Patient Samples*

CLSI Guideline, EP14-A2: *Evaluation of Matrix Effects*

L. Test Principle:

The CAPILLARYS 3 TERA instrument uses 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 occurs according to the

electrolyte pH and electroosmotic flow.

The CAPILLARYS 3 TERA instrument has silica capillaries functioning in parallel allowing 12 simultaneous analyses of HbA1c quantification in a whole blood sample. A sample dilution with hemolysing 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 the cathodic end of the capillary at 415 nm, which is the absorbance wavelength specific to hemoglobins. Before each run, the capillaries are washed with a wash solution and prepared for the next analysis with buffer.

Direct detection provides accurate relative quantification of individual hemoglobin A1c fraction. In addition, the high resolution of CAPI 3 HbA1c procedure allows the quantification of HbA1c even in the presence of labile HbA1c, carbamylated and acetylated hemoglobins, and major hemoglobin variants.

By using an alkaline pH buffer, normal and abnormal (or variant) hemoglobins are detected in the following order, from cathode to anode: A2/C, E, S/D, F, A0, other Hb (including minor HbA1) and then HbA1c.

At the end of analysis, relative quantification of individual HbA1c fraction is performed automatically. The HbA1c concentrations are standardized and indicated in %HbA1c (DCCT/NGSP) and in mmol/mol (IFCC) units.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Four different EDTA whole blood samples and four whole blood quality control solutions were run using the CAPI 3 HbA1c procedure on three CAPILLARYS 3 TERA instruments. Each sample was analyzed in duplicate on 2 capillaries per run, 2 runs per day. The results are shown below:

Results in NGSP units (%HbA1c) - % CV by Sample

Instruments Combined

Sample	Mean (%)	Within capillary	Between capillary	Between run	Between day	Between lot	Between instrument	Total*
Sample 1	4.8	0.9%	0.5%	0.0%	0.4%	0.5%	0.0%	1.2%
Sample 2	6.4	0.9%	0.4%	0.0%	0.3%	0.3%	0.0%	1.1%
Sample 3	8.9	0.5%	0.4%	0.0%	0.3%	0.4%	0.0%	0.8%
Sample 4	12.0	0.4%	0.3%	0.0%	0.4%	0.3%	0.2%	0.7%
Control 1	5.1	0.9%	0.6%	0.0%	0.4%	0.1%	0.3%	1.3%
Control 2	8.3	0.5%	0.4%	0.0%	0.2%	0.1%	0.9%	1.1%
Calibrator 1	5.3	0.9%	0.6%	0.0%	0.5%	0.0%	0.2%	1.2%
Calibrator 2	9.9	0.6%	0.3%	0.0%	0.3%	0.0%	0.3%	0.7%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day, between-lot and between-instrument.

Instrument 1 (%CV by Sample, NGSP % HbA1c)

Sample	Mean (%)	Within capillary	Between capillary	Between run	Between day	Between lot	Total*
Sample 1	4.8	1.0%	0.5%	0.0%	0.3%	0.4%	1.2%
Sample 2	6.4	1.0%	0.4%	0.0%	0.2%	0.4%	1.1%
Sample 3	8.9	0.6%	0.4%	0.0%	0.4%	0.3%	0.9%
Sample 4	12.0	0.4%	0.4%	0.0%	0.4%	0.2%	0.7%
Control 1	5.1	1.0%	0.5%	0.0%	0.5%	0.0%	1.2%
Control 2	8.3	0.5%	0.4%	0.0%	0.0%	0.1%	0.6%
Calibrator 1	5.3	0.9%	0.7%	0.0%	0.5%	0.0%	1.2%
Calibrator 2	9.9	0.4%	0.3%	0.1%	0.4%	0.0%	0.7%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day and between-lot.

Instrument 2 (%CV by Sample, NGSP % HbA1c)

Sample	Mean (%)	Within capillary	Between capillary	Between run	Between day	Between lot	Total*
Sample 1	4.8	0.9%	0.2%	0.0%	0.5%	0.7%	1.3%
Sample 2	6.4	1.0%	0.0%	0.2%	0.4%	0.4%	1.1%
Sample 3	8.9	0.5%	0.5%	0.0%	0.2%	0.4%	0.8%
Sample 4	12.0	0.5%	0.3%	0.1%	0.3%	0.2%	0.7%
Control 1	5.1	0.9%	0.6%	0.0%	0.4%	0.3%	1.2%
Control 2	8.3	0.5%	0.6%	0.0%	0.2%	0.0%	0.8%
Calibrator 1	5.3	0.7%	0.6%	0.0%	0.5%	0.3%	1.1%
Calibrator 2	9.9	0.6%	0.3%	0.0%	0.3%	0.0%	0.7%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day and between-lot.

Instrument 3 (%CV by Sample, NGSP % HbA1c)

Sample	Mean (%)	Within capillary	Between capillary	Between run	Between day	Between lot	Total *
Sample 1	4.8	0.9%	0.6%	0.0%	0.4%	0.2%	1.2%
Sample 2	6.4	0.8%	0.6%	0.0%	0.4%	0.3%	1.0%
Sample 3	8.9	0.5%	0.3%	0.0%	0.3%	0.4%	0.8%
Sample 4	12.0	0.4%	0.3%	0.0%	0.3%	0.4%	0.7%
Control 1	5.1	0.9%	0.8%	0.0%	0.5%	0.0%	1.3%
Control 2	8.3	0.5%	0.3%	0.0%	0.3%	0.0%	0.7%
Calibrator 1	5.3	1.0%	0.3%	0.0%	0.5%	0.0%	1.2%
Calibrator 2	9.9	0.6%	0.3%	0.0%	0.0%	0.2%	0.7%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day and between-lot.

Results in IFCC units (mmol/mol)

Instruments Combined

Sample	Mean (mmol/mol)	Within capillary	Between capillary	Between run	Between day	Between lot	Between instrument	Total *
Sample 1	29	1.6%	0.9%	0.0%	0.8%	1.0%	0.0%	2.3%
Sample 2	46	1.4%	0.5%	0.0%	0.5%	0.5%	0.1%	1.6%
Sample 3	73	0.6%	0.5%	0.1%	0.4%	0.5%	0.0%	1.0%
Sample 4	108	0.5%	0.5%	0.0%	0.5%	0.2%	0.2%	0.9%
Control 1	33	1.5%	1.2%	0.0%	0.8%	0.4%	0.5%	2.2%
Control 2	67	0.7%	0.5%	0.0%	0.4%	0.0%	1.2%	1.5%
Calibrator 1	35	1.5%	0.8%	0.0%	0.8%	0.0%	0.3%	1.9%
Calibrator 2	85	0.7%	0.3%	0.0%	0.4%	0.1%	0.4%	0.9%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day, between-lot and between-instrument.

Instrument 1 (%CV by Sample, IFCC units)

Sample	Mean (mmol/mol)	Within capillary	Between capillary	Between run	Between day	Between lot	Total*
Sample 1	29	1.7%	1.0%	0.0%	0.7%	0.7%	2.2%
Sample 2	46	1.4%	0.6%	0.0%	0.9%	0.4%	1.8%
Sample 3	73	0.7%	0.4%	0.0%	0.5%	0.4%	1.0%
Sample 4	108	0.4%	0.5%	0.0%	0.5%	0.0%	0.9%
Control 1	33	1.6%	1.4%	0.0%	0.7%	0.5%	2.3%
Control 2	67	0.7%	0.2%	0.3%	0.4%	0.1%	0.9%
Calibrator 1	35	1.5%	1.0%	0.0%	0.7%	0.0%	1.9%
Calibrator 2	85	0.6%	0.2%	0.3%	0.6%	0.0%	0.9%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day and between-lot.

Instrument 2 (%CV by Sample, IFCC units)

Sample	Mean (mmol/mol)	Within capillary	Between capillary	Between run	Between day	Between lot	Total*
Sample 1	29	1.6%	0.5%	0.0%	0.9%	1.4%	2.4%
Sample 2	46	1.6%	0.0%	0.4%	0.0%	0.4%	1.7%
Sample 3	73	0.6%	0.5%	0.0%	0.5%	0.5%	1.0%
Sample 4	108	0.0%	0.0%	0.0%	0.0%	0.0%	0.1%
Control 1	33	1.4%	0.9%	0.0%	0.7%	0.7%	1.9%
Control 2	67	0.6%	0.6%	0.0%	0.4%	0.0%	0.9%
Calibrator 1	35	1.3%	0.3%	0.0%	0.6%	0.0%	1.5%
Calibrator 2	85	0.8%	0.1%	0.0%	0.4%	0.0%	0.9%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day and between-lot.

Instrument 3 (%CV by Sample, IFCC units)

Sample	Mean (mmol/mol)	Within capillary	Between capillary	Between run	Between day	Between lot	Total*
Sample 1	29	1.6%	1.2%	0.0%	0.8%	0.5%	2.2%
Sample 2	46	1.1%	0.7%	0.0%	0.3%	0.6%	1.5%
Sample 3	73	0.6%	0.4%	0.2%	0.3%	0.6%	1.0%
Sample 4	108	0.5%	0.5%	0.0%	0.3%	0.4%	0.8%
Control 1	33	1.4%	1.3%	0.0%	0.9%	0.0%	2.1%
Control 2	67	0.6%	0.6%	0.0%	0.4%	0.0%	1.0%
Calibrator 1	35	1.7%	0.9%	0.0%	1.1%	0.0%	2.2%
Calibrator 2	85	0.7%	0.4%	0.0%	0.0%	0.3%	0.8%

*Total Reproducibility includes: within-capillary, between-capillary, between-run, between-day and between-lot.

b. Linearity/assay reportable range:

The linearity of the CAPI 3 HbA1c procedure was evaluated based on CLSI EP06-A guideline *Evaluation of the Linearity Quantitative Measurement Procedures: A Statistical Approach*. Two blood samples, including a normal sample with HbA1c concentration at 3.8 % HbA1c (18 mmol/mol) and an elevated HbA1c level sample with HbA1c concentration at 17.3 % HbA1c (166 mmol/mol) were mixed within different proportions and the mixtures were electrophoresed with the CAPI 3 Hb A1c procedure. For each mixture, samples were analyzed in triplicate.

The following table summarizes the results obtained for the 1st order linear regression generated using both NGSP (%HbA1c) and IFCC units (mmol/mol).

Units	Slope	y-intercept	Correlation coefficient
NGSP (%HbA1c)	0.9959	-0.2692	0.997
IFCC (mmol/mol)	1.0018	-3.3565	0.998

The study supports the sponsors claimed linearity range of 3.8 - 17.3 % HbA1c (18 - 166 mmol/mol). The reportable range of the device is from 4.0% to 14.7% HbA1c (20 - 138 mmol/mol).

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

Traceability:
The CAPI 3 HbA1c assay is certified with the National Glycohemoglobin Standardization Program (NGSP). The NGSP certification expires in one year. See NGSP website for current certification at http://www.ngsp.org.

Value assignment:
The HbA1c CAPILLARY Calibrators were previously cleared and reviewed in k122101 and k133344. The MULTI-SYSTEM HbA1c CAPILLARY Control (2) values are assigned by multiple measurements using multiple CAPILLARYS 2 FLEX-PIERCING instruments and IFCC traceable calibrators.

Stability:
The stability protocols and acceptance criteria were reviewed and determined to be adequate. The expiration dates of the different components of the CAPI 3 HbA1c kit are indicated as follows:

Kit Component	Shelf-Life	On Board Stability
CAPI 3 HbA1c hemolysing solution	3 years at 2-8°C and 15-30°C	2 months
CAPI 3 HbA1c buffer	3 years at 2-8°C	1 month
CAPI 3 HbA1c wash solution	3 years at 2-8°C and 15-30°C	121 days

The MULTI-SYSTEM HbA1c CAPILLARY Control (2) is demonstrated to be stable for 1 day at 2-8°C, up to 6 months at -22°C/-18°C. The labeling states that the MULTI-SYSTEM HbA1c CAPILLARY Control (2) should not be frozen and thawed more than 30 times.

d. *Detection limit:*

The Limit of Blank (LoB) and Limit of Detection (LoD) were determined by assaying five samples without HbAc1 and five low HbA1c samples, respectively. Both LoB and LoD were tested according to CLSI guideline EP17-A2. The results are as follows:

LoB = 0.1%, LoD = 1.2%

e. Analytical specificity:

i. Endogenous Interference

Studies were performed to assess endogenous substances that could interfere with the CAPI 3 HbA1c assay. The interfering substances were evaluated in venous whole blood EDTA samples that contained two to four different concentrations of HbA1c (including normal, around cut-off and high levels of HbA1c). Samples containing potential interferents were tested and the results compared to those obtained from control samples containing no potential interfering substances. Samples were analyzed in triplicates. The sponsor's definition of non-significant interference is ≤0.3% HbA1c (or ≤ 9.9 mmol/mol) between the tested and the control samples. The results are summarized in the following table:

Concentration at which no significant interference (≤0.3%) was observed

Potential interfering substance	Concentration
Ascorbic Acid	60 mg/dL (3.41 mM)
Bilirubin	35.9 mg/dL (614 mM)
Rheumatoid factor	2178 IU/mL
Triglycerides	3.85 g/dL (43.97mM)
Urea	277 mg/dL (46.1 mM)
Glucose	1000 mg/dL (55 mmol/L)
Total Protein	149.5 g/L

ii. Exogenous Interference

Studies were performed to assess common or known substances that could interfere with the CAPI 3 HbA1c assay. The interfering substances were evaluated in venous whole blood EDTA samples that contained two to four different concentrations of HbA1c (including around cut-off and high levels of HbA1c). Samples containing potential interferents were tested and the results compared to those obtained from control samples containing no potential interfering substances. Samples were analyzed in triplicates. The sponsor's definition of non-significant interference is ≤0.3% HbA1c (or ≤ 9.9 mmol/mol) between the tested and the control samples. The results are summarized in the following table:

Concentration at which no significant interference (≤0.3%) was observed

Potential interfering substance	Concentration
Glybenclamide	3 mg/dL
Acetylsalicylic acid	1000 mg/dL (55.56 mmol/L)
Ibuprofen	500 mg/L (2427 µmol/L)
Acetaminophen	200 mg/L (1325 µmol/L)
Metformin	5 mg/dL (387 µmol/L)

iii. Cross Reactivity with Hemoglobin Derivatives

To study interference from carbamylated hemoglobin, four EDTA whole blood patient samples with HbA1c concentrations at ~5.2%, ~6.9%, ~8.8% and ~11.9% were split into two aliquots. One aliquot, at each HbA1c level, was spiked with 1 mmol/L of potassium cyanate and incubated for 3 hours at 37˚C. Another aliquot, at each HbA1c level, was incubated for 3 hours at 37˚C. Samples were then analyzed on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. Samples were analyzed in triplicate. The sponsor's definition of non-significant interference is ≤ 0.3 HbA1c% between the tested and the control samples.
The sponsor concluded that presence of up to 5.6% carbamylated hemoglobin does not interfere with this assay.

To study interference from labile hemoglobin, four EDTA whole blood patient samples with HbA1c concentrations at ~5.1%, ~6.7%, 8.4% and ~12.3% were split into two aliquots. One aliquot, at each HbA1c level, was spiked with glucose (50 g/L) and incubated for 3 hours at 37˚C. Another aliquot, at each HbA1c level, was incubated for 3 hours at 37˚C. Samples were then analyzed on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. Samples were tested in triplicate. The sponsor's definition of non-significant interference is ≤ 0.3 HbA1c% between the tested and the control samples.
The sponsor concluded that labile HbA1c up to 1257 mg/dL (12.7%) does not interfere with this assay.

To study interference from acetylated hemoglobin, four EDTA whole blood samples with HbA1c concentrations at ~5.7%, 6.3%, 8.1% and ~ 12.1% were split into two aliquots. One aliquot, at each HbA1c level, was used as the control sample and the other aliquot was spiked with acetylsalicylic acid (10 mmol/L) and incubated for 4 hours at 37˚C. All aliquots were tested on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. Samples were tested in triplicate. The sponsor's definition of non-significant interference is ≤ 0.3 HbA1c%.
The sponsor concluded that acetylated hemoglobin up to 2.1% does not interfere with this assay.

iv. Hemoglobin Variant Interference

A hemoglobin variant interference study was carried out using samples known to contain Hemoglobin variants S, E, D and C. These variant samples were tested on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. The sponsor's definition of non-significant interference is ±10% difference between the candidate method and the comparative method. The testing results show there is no significant interference for Hb S (≤ 40.4%), Hb E (≤ 26.6%), Hb D (≤ 44.2%) and Hb C (≤ 36.9%).

The sponsor includes the following limitation in their labeling: "due to the number of variants, the presence of another hemoglobin variant may be observed in the HbA1c migration zone; in the case of a shoulder on HbA1c, no result will be reported by the software."

A variant interference study was carried out to study the variant interference from Hemoglobin F. Twenty-two different EDTA whole blood samples with HbA1c concentrations between 5.1 and 15.1% and varying concentrations of HbF (from 1.5 to 23.7%) were tested on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. The sponsor's definition of non-significant interference is ±10% difference between the candidate method and the comparative method.
The testing results show there is no significant interference for Hb F ≤ 23% therefore the sponsor has included the following limitation in their labeling: Levels of Hb F up to 23 % in the blood sample do not interfere with HbA1c fraction quantification, a result is reported by the software when the Hb F level is higher than 23 % along with a warning message "Atypical profile - Possible quantitative interference if Hb F or variant > 23 %".

An additional variant interference study was carried out to study the variant interference from Hemoglobin A2 (HbA2). Four EDTA whole blood samples with HbA1c concentrations at ~5.0%, 6.7%, 9.0%, and 11.8% were split into two aliquots. One aliquot, at each HbA1c level, was used as the control sample and the other aliquot was spiked with varying concentrations of purified HbA2 (from 9.3 to 11.3%). Samples were analyzed in triplicates on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. The sponsor's definition of non-significant interference is ≤0.3% difference between the tested and the control samples.
The sponsor concluded that Hb A2 up to 11.3% does not interfere with this assay.

f. Assay cut-off:

Not-applicable

2. Comparison studies:

a. Method comparison with predicate device:

The levels of HbA1c were measured in 100 EDTA whole blood samples, both by electrophoretic separations obtained with the CAPI 3 HbA1c procedure on the CAPILLARYS 3 TERA instrument and a commercially available capillary electrophoresis technique for HbA1c quantification that is NGSP standardized. The measured values of HbA1c concentrations and percentages from both procedures were analyzed by a linear regression statistical procedure. The results of linear regression analysis are summarized below:

HbAc1 units	Correlation Coefficient	Intercept	Slope	HbA1c Range
NGSP	0.998	-0.024	1.000	4.1 - 14.2 %
IFCC	0.998	-0.238	1.000	22 - 132 mmol/mol

External sites:

In study No. 1, the levels of HbA1c were measured in 175 EDTA whole blood samples, including samples with normal and elevated HbA1c levels, by electrophoretic separations obtained with CAPI 3 HbA1c procedure with the CAPILLARYS 3 TERA instrument and a commercially available capillary electrophoresis technique for HbA1c quantification that is NGSP standardized. The measured values of HbA1c concentrations and percentages from both procedures were analyzed by a linear regression statistical procedure. The results of linear regression analysis are summarized below:

HbAc1 units	Correlation Coefficient	Intercept	Slope	HbA1c Range
NGSP	0.997	0.045	0.992	4.3 - 14.7 %
IFCC	0.998	0.249	0.993	23 – 138 mmol/mol

In study No. 2, the levels of HbA1c were measured in 117 EDTA whole blood samples, including samples with normal and elevated HbA1c levels, both by electrophoretic separations obtained with CAPI 3 HbA1c procedure with the CAPILLARYS 3 TERA instrument and a commercially available capillary electrophoresis technique for HbA1c quantification that is NGSP standardized. The measured values of HbA1c concentrations and percentages from both procedures were analyzed by a linear regression statistical procedure. The results of linear regression analysis are summarized below:

HbAc1 units	Correlation Coefficient	Intercept	Slope	HbA1c Range
NGSP	0.998	0.205	0.968	4.2 - 13.7%
IFCC	0.998	1.417	0.970	22 – 127 mmol/mol

b. Matrix comparison:

A total of 41 matched sample pairs (K2 EDTA and K3 EDTA) were tested on the CAPILLARYS 3 TERA instrument using the CAPI 3 HbA1c assay kit. The linear regression is presented in the table below:

HbAc1 units	Correlation Coefficient	Intercept	Slope	HbA1c Range
NGSP	0.999	0.085	0.988	4.2 - 13.8%
IFCC	0.999	0.934	0.982	24 - 127 mmol/mol

Venous whole blood samples collected in K2 EDTA and K3 EDTA have been shown to be acceptable for use with the CAPI 3 HbA1c assay using the CAPILLARYS 3 TERA instrument.

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):*

      Not-applicable

4. Clinical cut-off:

   Not-applicable

5. Expected values/Reference range:

   The sponsor states the following:

   Hemoglobin A1c expected value range was cited from the American Diabetes Association (Standards of Medical Care in Diabetes 2012, 35 (Suppl 1) S11 – S63).

   The American Diabetes Association's (ADA) most recent Clinical Practice

Category	HbA1c Range (NGSP/DCCT)
Normal	< 5.7%
Prediabetes (increased risk for diabetes)	5.7% - 6.4%
Diabetes	≥ 6.5%

   The expected HbA1c range for non-diabetic adults is 4 - 6%. However, each laboratory should establish its reference range and HbA1c goal in their country of business taking into account sex, age, ethnicity and individual patient situation.

N. Instrument Name:

CAPILLARYS 3 TERA instrument

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes___X___ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No___X___

2. Software:

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

   Yes ___X___ or No _____

3. Specimen Identification:

   Barcode reader

4. Specimen Sampling and Handling:

   Use K2 EDTA or K3 EDTA whole blood samples. Capped primary sample tubes (containing over 800 µL) are placed on sample racks, which are loaded on the CAPILLARYS 3 TERA instrument. The mixing system with rack inversion allows homogenization before sample collection by the sample probe directly on capped tubes for the HbA1c analysis.

5. Calibration:

   Calibration must be performed for the first use of the HbA1c analysis program with the CAPILLARYS 3 instrument and after having changed the lot number of calibrators. Additional calibration should be performed after having changed the lot number of analysis buffer, after technical operation, in case of analyses of controls giving HbA1c values outside the expected values (and after having confirmed this deviation by a second analysis of blood controls), after having changed capillaries (whatever the number of

replaced capillaries), and at least every 2 months. Calibration is performed using the HbA1c CAPILLARY Calibrators.

6. Quality Control:

   Labeling for the device states that it is recommended to analyze one of the two HbA1c CAPILLARY Controls on whole capillaries after capillaries activation, after each calibration of the instrument performed with the HbA1c CAPILLARY Calibrators, and after a capillary cleaning sequence with CAPICLEAN. In routine, it is recommended to analyze the HbA1c control at the beginning and at the end of the analysis series, alternating the Control 1 and the Control 2. In the case of a migration shift leading to a non-recognition of fractions, it is recommended to analyze immediately one of the two HbA1c controls.

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

Not applicable

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.