510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k171537

B. Purpose for Submission:

Addition of a diagnostic claim to an existing 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 Hb A1c

G. Regulatory Information:

Product Code	Regulation Name	Classification	Regulation Section	Panel
PDJ	Hemoglobin A1c Test System	Class II	21 CFR 862.1373	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indication for use below.

2. Indication(s) for use:

   The CAPI 3 Hb A1c kit is intended for separation and quantification of the HbA1c glycated fraction of hemoglobin (in IFCC unit (mmol/mol) and NGSP unit (%)) in venous whole human blood, by capillary electrophoresis in alkaline buffer with the CAPILLARYS 3 TERA instrument. Measurement of hemoglobin A1c is used as an aid in diagnosis of diabetes, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus. The CAPI 3 Hb A1c kit is intended for in vitro Diagnostic Use Only.

3. Special conditions for use statement(s):

   For In Vitro Diagnostic Prescription Use.

   The CAPI 3 HbA1c kit should not be used:
   - for point-of-care use
   - in monitoring daily glucose control
   - to replace daily home testing of urine and blood glucose levels
   - to replace glucose testing in pediatric patients, pregnant women, or patients with Type 1 diabetes.
   - 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.
   - to diagnose diabetes during pregnancy or to diagnose gestational diabetes. HbA1c reflects the average blood glucose levels over the preceding 3 months (the average life of a red blood cell), and therefore may be falsely low during pregnancy or any other condition associated with recent onset of hyperglycemia and/or decreased red cell survival,
   - to diagnose diabetes in patients with the following conditions:
     Any condition that alters the life span of the red blood cells, including recent blood loss, transfusion, significant iron deficiency, hemolytic anemia (including hereditary spherocytosis) or other hemolytic diseases, hemoglobinopathies and thalassemias, as the altered red blood cell turnover interferes with the relationship between mean blood glucose and HbA1c values, malignancies or severe chronic hepatic and renal disease.
   - In cases of rapidly evolving Type 1 diabetes, the increase of HbA1c values might be delayed compared to the acute increase in glucose concentrations. In these conditions, diabetes mellitus must be diagnosed based on plasma glucose concentration and/or the typical clinical symptoms.

4. Special instrument requirements:

   CAPILLARYS 3 TERA instrument

I. Device Description:

The CAPI 3 HbA1c kit is to be used with the CAPILLARYS 3 TERA instrument. The reagents

are identical to those cleared in k162281. 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).

CAPILLARYS 3 TERA instrument was cleared in k162281.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Tosoh Automated Glycohemoglobin Analyzer HLC-723G-8

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

   k131580

3. Comparison with predicate:

Similarities		
Item	Candidate Device Sebia CAPI 3 Hb A1c	Predicate Device Tosoh HLC-723G8 (k131580)
Intended Use	Intended for measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mol hemoglobin A1c (IFCC) in whole blood specimens. Measurement of hemoglobin A1c is used as an aid in diagnosis of diabetes, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.	Same
Standardization	Traceable to the Diabetes Control and Complications Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program	Same
Sample type	Venous whole blood	Same

Differences		
Item	Candidate Device Sebia CAPI 3 Hb A1c	Predicate Device Tosoh HLC-723G8 (k131580)
Assay Principle	Capillary electrophoresis	Ion-exchange HPLC
Measuring Range	4.0 – 16.5% (NGSP) 20 – 157 mmol/mol (IFCC)	4.0 – 16.9%

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

CLSI EP05-A3 Evaluation of Precision Performance of Clinical Devices; Approved Guideline

CLSI EP06-A Evaluation of the Linearity of Quantitative Measurement Procedure: A statistical Approach; Approved Guideline

CLSI EP7-A2 Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition

CLSI EP9-A2 Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline

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.

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

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision of the CAPI 3 Hb A1c procedure using the CAPILLARYS 3 TERA was evaluated based on CLSI EP05-A3 Evaluation of Precision Performance of Clinical Devices; Approved Guideline. Four K_2 EDTA venous whole blood samples at the targeted HbA1c concentrations of 5.2, 6.5, 8.1, and 11.9 % were used in the study. The study also included two quality control materials (5.2, and 7.7 % HbA1c) and two calibrators (5.5, and 10.1 % HbA1c). The samples were analyzed in duplicate on two capillaries per run, two runs per day using three lots on each of three instruments over 24 days yielding a total of 1728 results over total testing time of 72 days. 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*
1 Human sample	5.2	0.9%	0.8%	0.0%	0.4%	0.7%	0.3%	1.5%
2 Control sample	5.2	0.9%	0.9%	0.0%	0.6%	0.7%	0.0%	1.6%
3 Calibrator sample	5.5	0.8%	0.8%	0.0%	0.5%	0.7%	0.0%	1.4%
4 Human sample	6.5	0.7%	0.5%	0.3%	0.3%	0.5%	0.0%	1.1%
5 Control sample	7.7	0.7%	0.5%	0.0%	0.5%	0.2%	1.7%	2.0%
6 Human sample	8.1	0.7%	0.5%	0.0%	0.4%	0.3%	0.1%	1.0%
7 Calibrator sample	10.1	0.6%	0.5%	0.0%	0.4%	0.7%	0.0%	1.1%
8 Human sample	11.9	0.6%	0.6%	0.0%	0.5%	1.4%	0.0%	1.7%

*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*
1 Human sample	5.2	0.9%	0.8%	0.0%	0.4%	0.8%	0.8%
2 Control sample	5.2	0.8%	0.9%	0.0%	0.6%	0.9%	0.9%
3 Calibrator sample	5.5	0.8%	0.9%	0.0%	0.7%	0.7%	0.7%
4 Human sample	6.5	0.7%	0.6%	0.3%	0.2%	0.7%	0.7%
5 Control sample	7.7	0.6%	0.6%	0.0%	0.4%	0.1%	0.1%
6 Human sample	8.1	0.7%	0.5%	0.0%	0.4%	0.4%	0.4%
7 Calibrator sample	10.1	0.6%	0.4%	0.0%	0.4%	1.0%	1.0%
8 Human sample	11.9	0.6%	0.6%	0.0%	0.5%	1.8%	1.8%

*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*
1 Human sample	5.2	1.0%	0.9%	0.0%	0.4%	0.9%	1.7%
2 Control sample	5.2	0.9%	1.1%	0.0%	0.4%	0.7%	1.6%
3 Calibrator sample	5.5	0.8%	0.8%	0.0%	0.4%	0.8%	1.4%
4 Human sample	6.5	0.7%	0.5%	0.3%	0.4%	0.4%	1.1%
5 Control sample	7.7	0.7%	0.3%	0.0%	0.6%	0.1%	1.0%
6 Human sample	8.1	0.8%	0.3%	0.1%	0.3%	0.1%	0.9%
7 Calibrator sample	10.1	0.5%	0.5%	0.0%	0.3%	0.5%	1.0%
8 Human sample	11.9	0.6%	0.8%	0.2%	0.6%	1.1%	1.6%

*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 *
1 Human sample	5.2	0.9%	0.8%	0.0%	0.5%	0.2%	1.3%
2 Control sample	5.2	0.9%	0.8%	0.0%	0.6%	0.6%	1.5%
3 Calibrator sample	5.5	0.8%	0.7%	0.0%	0.4%	0.7%	1.3%
4 Human sample	6.5	0.8%	0.6%	0.4%	0.2%	0.4%	1.1%
5 Control sample	7.7	0.6%	0.6%	0.0%	0.4%	0.3%	1.0%
6 Human sample	8.1	0.7%	0.6%	0.0%	0.4%	0.1%	1.0%
7 Calibrator sample	10.1	0.5%	0.4%	0.0%	0.3%	0.6%	1.0%
8 Human sample	11.9	0.5%	0.6%	0.0%	0.4%	1.1%	1.4%

*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 *
1 Human sample	33	1.5%	1.4%	0.0%	0.7%	1.2%	0.6%	2.6%
2 Control sample	34	1.4%	1.5%	0.0%	0.8%	1.5%	0.0%	2.7%
3 Calibrator sample	37	1.2%	1.4%	0.0%	0.7%	1.1%	0.0%	2.3%
4 Human sample	48	1.2%	0.9%	0.5%	0.5%	0.8%	0.0%	1.7%
5 Control sample	61	0.9%	0.7%	0.0%	0.7%	0.1%	2.6%	2.9%

Sample	Mean (mmol/mol)	Within capillary	Between capillary	Between run	Between day	Between lot	Between instrument	Total *
6 Human sample	65	1.0%	0.7%	0.0%	0.5%	0.4%	0.2%	1.3%
7 Calibrator sample	86	0.7%	0.6%	0.0%	0.5%	0.8%	0.0%	1.3%
8 Human sample	107	0.7%	0.8%	0,0%	0.6%	1.7%	0.0%	2.1%

*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*
1 Human sample	33	1.5%	1.3%	0.0%	0.6%	1.3%	2.4%
2 Control sample	34	1.3%	1.4%	0.0%	0.8%	1.8%	2.8%
3 Calibrator sample	37	1.3%	1.2%	0.0%	0.8%	1.2%	2.3%
4 Human sample	48	1.1%	0.8%	0.4%	0.6%	1.0%	1.9%
5 Control sample	61	0.9%	0.8%	0.0%	0.6%	0.1%	1.4%
6 Human sample	65	0.9%	0.6%	0.0%	0.5%	0.8%	1.3%
7 Calibrator sample	86	0.8%	0.5%	0.0%	0.5%	1.2%	1.6%
8 Human sample	107	0.6%	0.7%	0.0%	0.6%	2.2%	2.5%

*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*
1 Human sample	33	1.7%	1.7%	0.0%	0.7%	1.4%	2.8%
2 Control sample	34	1.6%	1.7%	0.0%	0.7%	1.3%	2.7%
3 Calibrator sample	37	1.2%	1.5%	0.0%	0.6%	0.8%	2.2%
4 Human sample	48	1.3%	0.9%	0.8%	0.3%	1.6%	1.9%
5 Control sample	61	0.9%	0.5%	0.0%	0.8%	0.0%	1.3%
6 Human sample	65	1.1%	0.5%	0.0%	0.5%	0.0%	1.3%
7 Calibrator sample	86	0.7%	0.6%	0.0%	0.5%	0.5%	1.1%
8 Human sample	107	0.8%	0.9%	0.0%	0.7%	1.3%	1.9%

*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*
1 Human sample	33	1.3%	1.4%	0.0%	0.9%	1.0%	2.3%
2 Control sample	34	1.4%	1.5%	0.0%	0.9%	1.2%	2.6%
3 Calibrator sample	37	1.1%	1.5%	0.0%	0.8%	1.3%	2.4%

Sample	Mean (mmol/mol)	Within capillary	Between capillary	Between run	Between day	Between lot	Total*
4 Human sample	48	1.1%	1.0%	0.4%	0.4%	0.7%	1.7%
5 Control sample	61	0.9%	0.7%	0.0%	0.7%	0.2%	1.3%
6 Human sample	65	0.9%	0.8%	0.0%	0.4%	0.2%	1.3%
7 Calibrator sample	86	0.7%	0.5%	0.0%	0.4%	0.7%	1.2%
8 Human sample	107	0.6%	0.6%	0.0%	0.5%	1.3%	1.7%

*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 of 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 linear regression results.

Units	Slope	y-intercept	Correlation coefficient
NGSP (%HbA1c)	1.0034	-0.3047	0.999
IFCC (mmol/mol)	1.0016	-3.2377	0.999

The study supports the claimed reportable range of the device from 4.0 to 16.5% HbA1c (20 - 157 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 Hb A1c CAPILLARY CALIBRATORS are required for use with this device. Value

assignment, stability protocols and acceptance criteria were previously reviewed in k162281 and k122101.

Stability:
The stability protocols and acceptance criteria for the different components of the CAPI 3 HbA1c kit were reviewed and determined to be adequate in k162281.
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

d. Detection limit:

The detection limit studies were previously reviewed and cleared in k162281. Those studies were not repeated because the device and procedure has not changed; the intended use has been changed to include a diagnostic claim.

e. Analytical specificity:

i. Endogenous Interference

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 K_2 EDTA samples that contained a blood sample close to the cut-off value 6.4% (46 mmol/mol) and a blood sample with elevated HbA1c level 8.4% (69 mmol/mol). Ten replicates were analyzed using the CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system. The sponsor's definition of non-significant interference is ≤ 7% mean relative deviation between the tested and the control samples.

Concentration at which no significant interference (≤ 7%) was observed

Endogenous interfering factor	Concentration
Bilirubin	70 mg/dL (1197 µM)
D-glucose	1000 mg/dL (55 mM)
Rheumatoid factor	1294 IU/mL
Total Protein	149.5 g/L
Triglycerides	3.58 g/dL (40.9 mM)
Urea	265 mg/dL (44.2 mM)

ii. Exogenous Interference

Interference studies were performed to assess common or known exogenous substances that could interfere with the CAPI 3 HbA1c assay. The interfering substances were evaluated in venous whole blood K_2EDTA samples that contained a blood sample close to the cut-off value 6.4% (46 mmol/mol) and a blood sample with elevated HbA1c level 8.4% (69 mmol/mol). Ten replicates were analyzed using the CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system. The sponsor's definition of non-significant interference is ≤ 7% mean relative deviation between the tested and the control samples

Concentration at which no significant interference (≤ 7%) was observed

Potential interfering substance	Concentration
Acetaminophen	200 mg/L (1325 µM)
Acetylcysteine	200 mg/dL (12.3 mM)
Acetylsalicylic acid	1000 mg/dL (55.56 mM)
Ampicillin-Na	1000 mg/dL (28653 µM)
Ascorbic acid	300 mg/dL (17045 µM)
Cefoxitin	2500 mg/dL (58548 µM)
Cyclosporine	5 mg/L
Doxycycline	50 mg/dL (1123.6 µM)
Glybenclamide	3 mg/dL
Heparin	5000 U/L
Ibuprofen	500 mg/L (2427 µM)
Levodopa	40 mg/dL
Metformin	5 mg/dL
Methyldopa	40 mg/dL (1896 µM)
Metronidazole	200 mg/dL (11696 µM)
Phenylbutazone	400 mg/L
Rifampicin	70 mg/L (85.1 µM)
Theophylline	100 mg/L (556 µM)

iii. Cross Reactivity with Hemoglobin Derivatives

To study interference from carbamylated hemoglobin, four EDTA whole blood patient samples with HbA1c concentrations at 6.3% HbA1c, 8.3% HbA1c, 45 mmol/mol HbA1c and 67 mmol/mol HbA1c 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 and 30 minutes at 37˚C. Another aliquot, at each HbA1c level, without potassium cyanate was incubated for 3 hours and 30 minutes at 37˚C. Ten replicates were analyzed using the CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system. The sponsor's definition of non-significant interference is ≤7% mean relative deviation between the tested and the control samples. The sponsor concluded that presence of ≤ 8.1 mg/mL carbamylated hemoglobin does not interfere with this assay.

To study interference from labile hemoglobin, four EDTA whole blood patient samples

with HbA1c concentrations at 6.3% HbA1c, 8.5% HbA1c, 45 mmol/mol HbA1c and 67 mmol/mol HbA1c 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, without glucose was incubated for 3 hours at 37˚C. Ten replicates were analyzed using the CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system. The sponsor's definition of non-significant interference is ≤7% mean relative deviation between the tested and the control samples. The sponsor concluded that labile HbA1c ≤ 20.0 mg/mL does not interfere with this assay.

To study interference from acetylated hemoglobin, four EDTA whole blood samples with HbA1c concentrations at 6.2% HbA1c, 8.4% HbA1c, 44 mmol/mol HbA1c and 68 mmol/mol HbA1c were split into two aliquots. One aliquot, at each HbA1c level, was spiked with acetylsalicylic acid (10 mmol/L) and incubated for 6 hours at 37˚C. Another aliquot, at each HbA1c level, without acetylsalicylic acid was incubated for 6 hours at 37˚C. Ten replicates were analyzed using the CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system. The sponsor's definition of non-significant interference is ≤7% mean relative deviation between the tested and the control samples. The sponsor concluded that acetylated hemoglobin up to ≤ 4.2 mg/mL does not interfere with this assay.

To study interference from glycated albumin, four EDTA whole blood samples with HbA1c concentrations at 6.2% HbA1c, 8.5% HbA1c, 44 mmol/mol HbA1c and 70 mmol/mol HbA1c were split into two aliquots. One aliquot, at each HbA1c level, was spiked with glycated albumin (0.20 mg/mL) and the other aliquot, at each HbA1c level, was without glycated albumin. Ten replicates were analyzed using the CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system. The sponsor's definition of non-significant interference is ≤7% mean relative deviation between the tested and the control samples. The sponsor concluded that glycated albumin up to ≤ 0.20 mg/mL does not interfere with this assay.

iv. Hemoglobin Variant Interference

A hemoglobin variant study was performed using a total of 131 normal and diabetic whole blood K_2EDTA patent variant samples known to contain hemoglobin variants S, C, E, D, A2, and F. Testing of the samples containing hemoglobin variants S, C, E, and D, A2, and F were performed using CAPI 3 Hb A1c on the CAPILLARYS 3 TERA testing system and compared to results obtained by a NGSP reference method that has been demonstrated to be free from interference by the hemoglobin variants (Trinity Biotech Ultra2 for HbS, HbC, HbD, HbE and Tosoh HLC-723G8 for HbF and HbA2).

Variant samples used in Hemoglobin Variant Study

Hemoglobin Variant	n	Range in % HbVariant	Range in %HbA1c Concentration
Hb A2	20	4.0-7.8	4.5-11.2
Hb F	19	1.5-23.7	5.1-15.1

Hb S	24	33.0-40.8	4.9-14.7
Hb C	24	25.6-37.6	4.9-12.4
Hb D	24	35.5-41.3	5.2-12.0
Hb E	20	21.1-26.8	4.9-9.6

Hemoglobin Variant Study Bias Results

Hemoglobin Variant	Relative % Bias to Comparative Method	
	Relative %Bias (Range of %Bias) for HbA1c	Relative %Bias (Range of %Bias) for HbA1c
	~6.5%	~9.0%
HbS	1.6% (0% - 3.2%)	2.9% (1.1% - 5.4%)
HbC	-1.8% (- 3.1% - 0%)	3.9% (3.3% - 4.5%)
HbD	1.0% (0% - 1.6%)	0.8% (0% - 2.4%)
HbE	1.5% (-1.5% - 1.6%)	1.2 % (0%-2.5%)
HbA2	0.7% (0 % -1.5%)	0.4 % (0% - 1.1%)
HbF	-4.1% (-3.3% - 4.9 %)	-0.8% (0% - 2.0%)

Significant interference was defined as ≥ 7% change in HbA1c value in the presence of the hemoglobin variant relative to control. The results show there is no significant interference for HbS (≤40.8%), HbC (≤37.6%), HbD (≤41.3%), HbE (≤26.8%) and HbA2 (≤7.8%) and HbF (≤ 23.7%) at the concentrations tested in this study.

The package insert labeling contains the following prominent boxed warning;

> **"A significant negative interference has been observed with fetal hemoglobin (Hb F) concentrations >23 %. HbA1c results are invalid for patients with high amounts of Hb F (>23 %) including those with known Hereditary Persistence of Fetal Hemoglobin."**

The package insert labeling states;

> No interference has been observed with HbA1c fraction quantification due to the presence of major abnormal hemoglobins Hb S (≤ 40.8 %), Hb C (≤ 37.6 %), Hb D (≤ 41.3 %) and Hb E (≤ 26.8 %). However, 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 (as in presence of Hb Bart's).

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study of 152 variant-free K_2EDTAwhole blood samples (3.9 – 16.5 % HbA1c concentration range) were evaluated using the CAPI 3 Hb A1c kit and the CAPILLARYS 3 TERA instrument. The results were compared to the testing performed at an NGSP secondary reference laboratory using a previously cleared HPLC HbA1c method (Tosoh HLC-723G8). The distribution of samples follows in the table below.

Distribution of samples

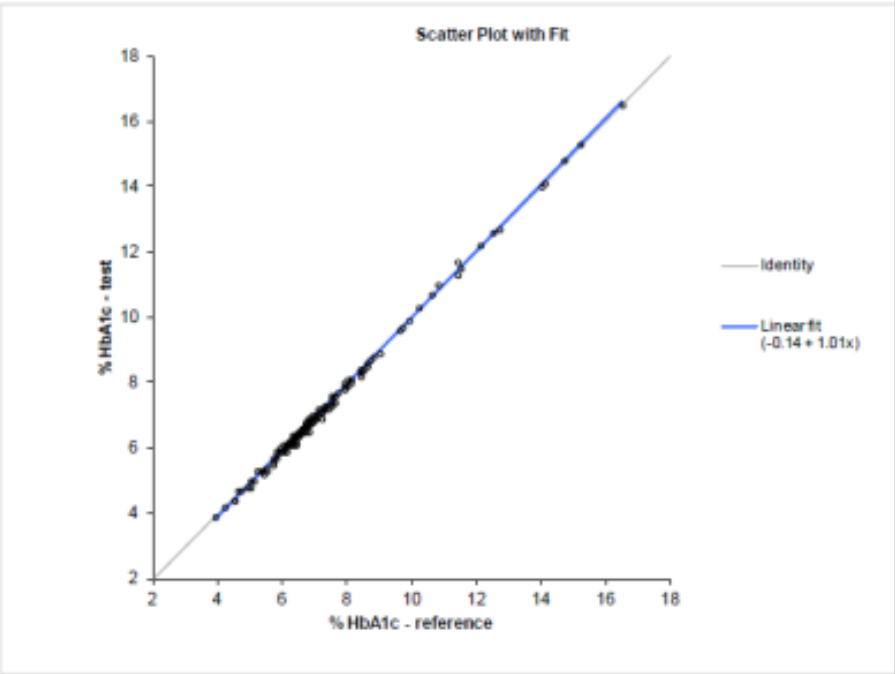
Hemoglobin A1c level	n	% of Samples tested
≤ 5%	9	6
5 – 6%	19	13
6 – 6.5%	35	23
6.5 – 7%	36	24
7 – 8%	23	15
8 – 9%	13	9
> 9%	17	11
Total samples	152	100.0

Linear, Deming (weighted), and Passing-Bablok regression analyses were performed for the CAPI 3 Hb A1c kit and the CAPILLARYS 3 TERA instrument versus the comparative Tosoh HLC-723G8 method (NGSP) and are summarized below:

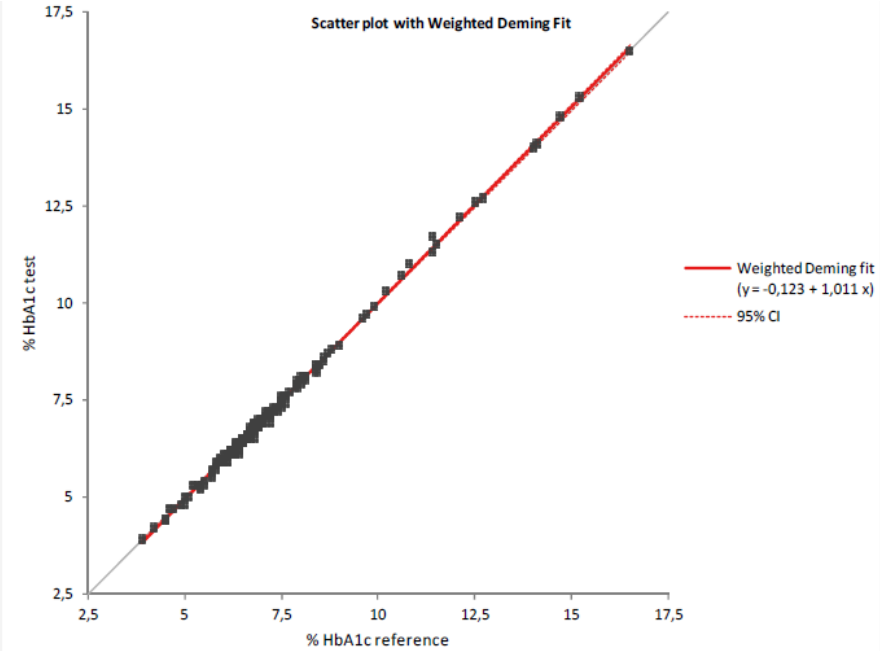
Summary of Method Comparison Results

	Slope	95% CI	y-Intercept	95% CI	R^2
Linear	1.014	1.007 to 1.021	-0.142	-0.197 to -0.087	0.999
Deming	1.011	1.001 to 1.021	-0.123	-0.196 to -0.050	0.999
Passing-Bablok	1.000	1.000 to 1.012	0.000	-0.115 to 0.000	0.999

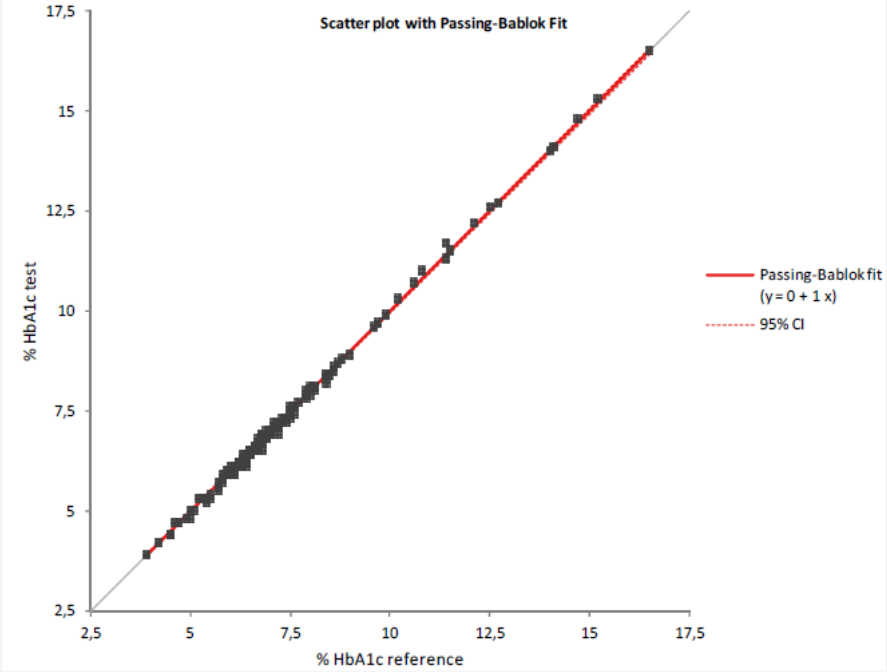
Scatter Plot using Linear Regression Fit, %HbA1c, NGSP vs. CAPI 3 Hb A1c



Scatter Plot using Deming Fit, %HbA1c, NGSP vs. CAPI 3 Hb A1c



Scatter Plot using Passing-Bablok Fit, %HbA1c, NGSP vs. CAPI 3 Hb A1c



Total Error Calculations:
Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the reproducibility study, total error (TE) at four concentrations: (5.0 %, 6.5%, 8.0% and 12.0%) were calculated as follows: %TE=|%Bias| + 1.96 *CV* (1 + %Bias/100). The results are as follows:

Total Error Estimation

% A1c – Decision Level	% Bias	% CV	% TE
5.2	-1.32	1.6	4.4
6.5	-0.77	1.1	2.9
8.1	-0.34	1.0	2.3
11.9	0.22	1.7	3.6

b. Matrix comparison:

The matrix comparison studies were previously reviewed in k162281.
Only K_2 EDTA and K_3 EDTA venous whole blood samples are to be used with this assay.

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:

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.

The following reference was cited: American Diabetes Association. Standards of medical care in diabetes - 2016. *Diabetes Care.* 2016 Jan, 39, Suppl 1.

N. Proposed Labeling:

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

O. Conclusion:

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