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

I Background Information:

A 510(k) Number

K223710

B Applicant

Abbott Point of Care Inc.

C Proprietary and Established Names

i-STAT CG8+ cartridge with the i-STAT 1 System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CGA	21 CFR 862.1345	Glucose Test System	CH – Clinical Chemistry
JJE	21 CFR 862.2160	Discrete photometric chemistry analyzer for clinical use	CH – Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device.

B Measurand:

Glucose

C Type of Test:

Quantitative amperometric

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The i-STAT CG8+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of glucose in arterial, venous or capillary whole blood in point of care or clinical laboratory settings.
Glucose measurements are used in the diagnosis, monitoring, and treatment of carbohydrate metabolism disorders including, but not limited to, diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.

The i-STAT 1 Analyzer is intended for use in the in vitro quantification of various analytes in whole blood or plasma in point of care or clinical laboratory settings. Analyzers and cartridges should be used by healthcare professionals trained and certified to use the system and should be used according to the facility's policies and procedures.
The i-STAT System is for in vitro diagnostics use. Caution: Federal law restricts this device to sale by or on the order of a licensed practitioner.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

For point-of-care or clinical laboratory setting.

Capillary whole blood specimens (e.g., obtained by fingerstick) should not be used in patients receiving intensive medical intervention/therapy because of the potential for pre-analytical collection error and specifically in patients with decreased peripheral blood flow, as it may not reflect the true physiological state. Examples include, but are not limited to, severe hypotension, shock, hyperosmolar-hyperglycemia (with or without ketosis) and severe dehydration.

D Special Instrument Requirements:

i-STAT 1 Analyzer

IV Device/System Characteristics:

A Device Description:

The i-STAT 1 System is an in vitro diagnostic (IVD) medical device, consists of the i-STAT analyzer and single -use disposable cartridges, and is intended for the quantitative determination of various clinical chemistry tests contained within i-STAT cartridges using whole blood.

The i-STAT 1 analyzer is a handheld, in vitro diagnostic analytical device designed to run only i-STAT test cartridges. The instrument interacts with the i-STAT CG8+ cartridge to move fluid across the sensors and generate a quantitative result.

The single-use, disposable i-STAT CG8+ cartridge contains the required sensors, a fluid pack (calibrant pouch), a sample entry well and closure, fluid channels, waste chamber, and the necessary mechanical features for controlled fluid movement within the cartridge. The i-STAT cartridge format allows all the tests in the cartridge to be performed simultaneously. All the test steps and fluid movement occur within the i-STAT CG8+ cartridge. Cartridges require two to three drops of whole blood, which are typically applied to the cartridge using a transfer device, by the trained user before the cartridge is placed within the analyzer.

B Principle of Operation:

Glucose on the i-STAT CG8+ cartridge is measured amperometrically. A voltage is applied to the cartridge electrodes with current generated by the reduction of hydrogen peroxide that was produced by catalytic oxidation of glucose present in the sample by glucose oxidase. The current is directly proportional to the concentration of the glucose in the sample.

C Instrument Description Information:

1. Instrument Name:

   i-STAT 1 Analyzer

2. Specimen Identification:

   The specimen identification may be manually entered or automatically scanned by the device.

3. Specimen Sampling and Handling:

   The sample type must be selected using the device touchscreen. After the sample type is selected the on-screen help appears and the help graphics on the device screen vary based on the sample type selected. The reagent cartridge contains a sample chamber that includes the sample well and the channel leading from the well up to the fill mark. The cartridge label is intended to help the operator fill the cartridge correctly. When filled, the sample chamber contains sufficient sample for testing. Sample volume and placement are monitored by the instrument and an error message will be generated if filled incorrectly. Samples should be remixed thoroughly before testing.

4. Calibration:

   The i-STAT cartridges include an on-board calibration that is performed with each cartridge use. The calibrant solution is automatically released from its foil pack and is positioned over

the sensors. The signals produced by the sensors' responses to the calibrant solution are measured. This one-point calibration adjusts the offset of the stored calibration curve.

5. Quality Control:

The sponsor recommends i-STAT Controls and TriControls for use with the i-STAT cartridges with the i-STAT 1 System.

V Substantial Equivalence Information:

A Predicate Device Name(s):

i-STAT CHEM8+ cartridge with the i-STAT 1 System

B Predicate 510(k) Number(s):

K210958

C Comparison with Predicate(s):

Device & Predicate Device(s):	K223710	K210958
Device Trade Name	i-STAT CG8+ cartridge with the i-STAT 1 System	i-STAT CHEM8+ cartridge with the i-STAT 1 System
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for in vitro quantification of glucose in samples. Glucose measurements are used in the diagnosis, monitoring, and treatment of carbohydrate metabolism disorders including, but not limited to, diabetes mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.	Same
Reportable Range	20 – 700 mg/dL	Same
Traceability	Glucose: NIST SRM965	Same
General Device Characteristic Differences		
Sample Type	Arterial or venous whole blood with and without lithium heparin anticoagulant, lithium heparin capillary whole blood	Arterial and venous whole blood with and without lithium heparin anticoagulant

VI Standards/Guidance Documents Referenced:

Clinical & Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

CLSI EP06: Evaluation of Linearity of Quantitative Measurement Procedures; 2nd ed.

CLSI EP07: Interference Testing in Clinical Chemistry; 3rd ed.

CLSI EP09c: Measurement Procedure Comparison and Bias Estimation using Patient Samples, 3rd ed.

CLSI EP 17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline

CLSI EP37: Supplement Tables for Interference Testing in Clinical Chemistry; 1st ed.

CLSI EP35: Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures; 1st ed.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Internal site precision
A single site precision study for the i-STAT Glucose assay in the i-STAT CG8+ cartridge (white) was conducted following the recommendations in CLSI EP05-A3. Five concentration levels of commercially available calibration verification samples were tested using one lot of i-STAT CG8+ cartridges and ten i-STAT 1 Analyzers. Each sample was measured in duplicates per run, with two runs per day for 20 days by a minimum of two operators resulting in a total of 80 test results per level. The results are summarized below.

Sample	Mean (mg/dL)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	28.4	0.36	1.25	0.20	0.69	0.24	0.85	0.47	1.66
L2	42.0	0.36	0.87	0.29	0.70	0.23	0.56	0.52	1.25
L3	124.7	0.66	0.53	0.55	0.44	0.52	0.42	1.00	0.80
L4	279.4	1.47	0.53	1.79	0.64	1.26	0.45	2.63	0.94
L5	576.8	4.70	0.81	2.35	0.41	2.91	0.50	6.01	1.04

Point of Care Precision (Whole Blood)
A multi-site precision study was conducted using lithium heparin arterial, venous, and capillary whole blood specimens targeted to three levels within the test reportable range of glucose. The whole blood precision was assessed using the duplicate test results collected across multiple point of care sites. The precision results between sites were similar. The combined results for all sites are shown below.

Sample Type	Sample Range	N	Mean	SD	%CV
Venous Whole Blood	20-90	29	73.9	0.86	1.17
	>90-150	102	111.7	1.08	0.96
	>150-250	27	173.4	1.82	1.05
	>250-400	13	308.5	2.08	0.67
	>400-700	9	544.3	7.92	1.46
Arterial Whole Blood	20-90	5	80.8	0.77	0.96
	>90-150	105	113.6	0.75	0.66
	>150-250	35	178.0	1.55	0.87
	>250-400	8	280.7	2.19	0.78
Capillary Whole Blood	20-90	32	77.6	1.08	1.39
	>90-150	107	108.3	2.34	2.16
	>150-700	15	203.8	2.74	1.34

Point of Care (Multi-Site) Precision – aqueous control material
A multi-day precision study was conducted at three POC sites following the recommendations in CLSI EP05-A3. Five concentration levels of commercially available calibration verification samples were tested at three sites. At each site, samples were tested using one lot of i-STAT CG8+ cartridges (white) on six i-STAT 1 Analyzers. Each sample was measured in duplicate per run, with two runs per day for 5 days by two operators. The results are summarized below.

Sample	Mean (mg/dL)	Within-run		Between Day		Between Operator		Within Site		Between Site		Total	
		SD	%CV	SD	SD	%CV	SD	%CV	SD	%CV	SD	SD	%CV
L1	28.1	0.39	1.40	0.16	0.55	0.08	0.29	0.43	1.54	0.11	0.41	0.45	1.59
L2	41.4	0.50	1.21	0.12	0.30	0.17	0.41	0.54	1.32	0.00	0.00	0.54	1.32
L3	124.5	0.64	0.52	0.47	0.38	0.08	0.06	0.8	0.64	0.00	0.00	0.80	0.64
L4	280.3	1.42	0.51	0.33	0.12	0.22	0.08	1.47	0.53	0.44	0.16	1.54	0.55
L5	578.4	4.25	0.73	1.78	0.31	0.00	0.00	4.61	0.80	0.00	0.00	4.61	0.80

Between Lot Precision
The between lot cartridge precision study for the i-STAT Glucose assay in the i-STAT CG8+ cartridge (white) was conducted by testing five levels of i-STAT Calibration Verification fluids with three lots of i-STAT CG8+ cartridges, in five replicates over five non-consecutive days. The results are provided below:

Sample	Mean	Repeatability		Between-lot		Between-Day		Within Laboratory	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
CV1	29.1	0.49	1.69	0.87	2.99	0.11	0.38	1.01	3.46
CV2	42.5	0.37	0.88	0.87	2.05	0.09	0.22	0.95	2.25
CV3	124	0.63	0.51	1.6	1.29	0.13	0.11	1.73	1.39
CV4	283	1.8	0.63	3.46	1.22	0.83	0.29	3.99	1.41
CV5	585.1	4.72	0.81	6.63	1.13	2.41	0.41	8.49	1.45

Between instrument precision

An internal between instrument precision study for the i-STAT Glucose assay in the i-STAT CG8+ cartridge (white) was conducted using five levels of i-STAT Calibration Verification fluids. Each level was tested using three i-STAT 1 Analyzers with one lot of i-STAT CG8+ cartridges, in five replicates over five non-consecutive days. The results are provided below:

Sample	Mean	Repeatability		Between-Instrument		Between-Day		Within Laboratory	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
CV1	29.1	0.43	1.48	0.07	0.25	0.06	0.22	0.44	1.52
CV2	42.3	0.41	0.97	0.06	0.15	0.09	0.21	0.43	1.01
CV3	123.8	0.55	0.45	0.08	0.06	0.09	0.07	0.57	0.46
CV4	282.7	1.13	0.4	0.4	0.14	0.75	0.27	1.42	0.5
CV5	584.2	3.24	0.56	0.51	0.09	0.66	0.11	3.35	0.57

2. Linearity:

The linearity study was designed based on the CLSI EP06 2nd ed guideline. The linearity of the i-STAT Glucose test in the i-STAT CG8+ (white) cartridge with the i-STAT 1 System was evaluated by preparing a total of 11 samples with concentrations spanning the claimed measuring range. Each level was analyzed in replicates of two per cartridge lot for a total of 10 results per level. At each level, the deviation from linearity was less than 3 mg/dL or ≤ 5%.

Reportable Range (mg/dL)	**Range Tested** (mg/dL)	**Slope**	**Intercept**	**R^2**
20 – 700	17.1 – 795.4	0.994	-1.385	0.9993

The linearity data supported the claimed reportable range of 20 to 700 mg/dL.

3. Analytical Specificity/Interference:

The analytical specificity of the i-STAT Glucose assay on the i-STAT CG8+ (white) cartridge was established following the recommendations in the CLSI EP07-3rd ed guideline. Interference from certain exogenous and endogenous substances was assessed using lithium

heparin venous whole blood samples at two glucose concentrations: low (30 – 50 mg/dL and high (210 – 230 mg/dL). The effect of each substance at each analyte level was evaluated by comparing the performance of a test sample spiked to a high concentration of the substance and a control sample spiked with an equal volume of solvent. Each sample was measured in replicates of at least 10 using two lots of the i-STAT CG8+ (white) cartridge. The sponsor identified a substance as an interferent if the difference in the mean between the control and test sample was outside of the predefined allowable error of ± greater of 6 mg/dL or 10% of the control sample.

The following table lists the concentrations of each substance at which no significant interference was found.

Substance	Highest concentration at which no interference was observed
Acetaldehyde	0.2 mg/dL
Acetaminophen	15.6 mg/dL
Acetoacetate (Lithium Acetoacetate)	20 mg/dL
Acetyl Cysteine (N- Acetyl-L-Cysteine)	15 mg/dL
Ammonium (Ammonium Chloride)	10.7 mg/dL
Ascorbic Acid (L- Ascorbic Acid)	5.25 mg/dL
β-Hydroxybutyric Acid	62.46 mg/dL
Bilirubin	40 mg/dL
Bromide (Lithium Bromide)	21.7 mg/dL (2.5 mmol/L)
Cholesterol	400 mg/dL
Creatinine	15 mg/dL
Dopamine (Dopamine Hydrochloride)	0.0621 mg/dL
Ethanol	600 mg/dL
Fluoride (Lithium Fluoride)	0.12 mg/dL
Formaldehyde	0.399 mg/dL
Fructose	18 mg/dL
Galactose	60 mg/dL
Gentamicin (Gentamicin Sulfate)	3 mg/dL
Gentisic Acid	1.5 mg/dL
Glucosamine (Glucosamine Hydrochloride)	0.647 mg/dL
Glutathione, reduced	3 mEq/L
Glycolic Acid	76.05 mg/dL
Guaifenesin	0.45 mg/dL
Hemoglobin	1000 mg/dL
Heparin (Sodium Heparin)	330 U/dL
Ibuprofen	21.9 mg/dL
Intralipid 20%	2891 mg/dL
Lactate (Lithium Lactate)	90 mg/dL
Maltose	360 mg/dL
Mannose [2]	18.02 mg/dL
Nithiodote (Sodium Thiosulfate)	264.04 mg/dL
pH	8.0 pH units
Pyruvate (Lithium Pyruvate)	5 mg/dL

Substance	Highest concentration at which no interference was observed
Salicylate (Lithium Salicylate)	2.86 mg/dL
Thiocyanate (Lithium Thiocyanate)	5.22 mg/dL
Triglyceride	1500 mg/dL
Uric Acid	23.5 mg/dL
Xylose	45.04 mg/dL

For those substances that on initial screening were found to interfere with the glucose results, dose response testing was conducted to establish the concentration limit below which no significant interference is expected. The results are given in the table below:

Substance	Concentration	Interference
Bromide (Lithium Bromide)	≥ 18.09 mmol/L	Decreased glucose results
Hydroxyurea	≥ 0.09 mmol/L	Increased glucose results
Isoniazid	≥ 0.29 mmol/L	Increased glucose results

The sponsor included the following limitations in the labeling:

- Bromide at 2.5 mmol/L is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. Bromide may result in an increased rate of star outs (***).
- Hydroxyurea is a DNA synthesis inhibitor used in the treatment of sickle cell anemia, HIV infection, and various types of cancer. The malignancies that it is used to treat include melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera, thrombocythemia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in a patient's blood may be sustained at approximately 0.1 to 0.5 mmol/L (100 to 500 µmol/L). Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

4. Assay Reportable Range:

   See section A.2 Linearity.

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

   Glucose values assigned to i-STAT controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM965.

   Sample stability
   A study was conducted to verify the whole blood sample stability after sample collection with and without anticoagulants for i-STAT Glucose test using the i-STAT CG8+ cartridge (white) on the i-STAT 1 Analyzer. The results support the sponsor's sample stability claims.

6. Detection Limit:

Detection capability studies of limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ) for the i-STAT glucose assay on the i-STAT CG8+ cartridge (white) with the i-STAT 1 Analyzer were conducted following the recommendations in CLSI EP17-A2.

The LoB was evaluated for the i-STAT CG8+ (white) cartridge using a lithium heparin venous whole blood sample that was altered to create a blank sample. The sample was tested across four days using two lots of i-STAT CG8+ (white) cartridges. The LoB was calculated using a parametric data analysis approach for each of the two lots. The higher of the two LoB values from each lot is reported in the labeling as the LoB.

The LoD was determined using a lithium heparin venous whole blood sample that was altered to create two samples with low concentrations of glucose. Each sample was measured in 20 replicates per day for four days across each of two i-STAT CG8+ (white) cartridge lots. The LoD was calculated using a parametric data analysis approach for each of the two lots. The higher of the two LoD values from each lot is reported as the LoD.

The LoQ was evaluated using lithium heparin venous whole blood samples altered to create four samples with low concentrations of glucose. Each of the four samples was measured in 12 replicates per day for four days across each of two i-STAT CG8+ (white) cartridge lots. The LoQ was calculated for each of the two lots. The sponsor defined LoQ as the greater of the two lots at which the lowest concentration met the pre-defined total error goal of 6.00 mg/dL.

The results from all studies are summarized in the table below.

Analyte (Units)	Reportable range	LoB	LoD	LoQ
Glucose (mg/dL)	20 – 700	0.2	0.9	17.0

7. Assay Cut-Off:

Not Applicable.

8. Accuracy (Instrument):

See Section B1. Method Comparison with Predicate Device.

9. Carry-Over:

Not applicable, the cartridges are single use and disposable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was conducted following the recommendations in CLSI EP09c-3rd ed guideline.

Lithium heparin venous (native n=174, contrived n=8) and arterial (native n=157) whole blood specimens collected across three point of care sites were tested for glucose using the i-STAT CG8+ cartridge (white) on the i-STAT 1 analyzer (candidate device) and the i-STAT CHEM 8+ cartridge on the i-STAT 1 analyzer (predicate device). A Passing-Bablok linear regression analysis was performed using the singlicate result from the candidate device versus the mean results of the comparative method. The sponsor provided acceptable evidence to support pooling the results from venous and arterial samples in the same analysis. Accuracy results for arterial and venous whole blood specimens are shown in the table below.

N	Range tested mg/dL (per comparator)	Slope	Intercept	r
339*	24 - 695	0.98	0.16	1.00

*Includes eight (8) contrived venous specimens tested at an internal site.

Capillary whole blood specimens (n=208, including 22 samples from neonates) collected from skin puncture with balanced heparin capillary tubes collected across six point of care sites were tested for glucose using *i-STAT CG8+* cartridges on the i-STAT 1 analyzer and the epoc Blood Analysis System (comparator method, k200107). A Passing-Bablok linear regression analysis was performed using the singlicate result from the candidate device versus the singlicate result of the comparative method.

Accuracy results for capillary whole blood specimens are shown in the table below.

N	Range tested mg/dL (per comparator)	Slope	Intercept	r
208	26 - 657	1.02	1.21	0.99

2. Matrix Comparison:

A matrix comparison study was conducted to evaluate the performance of the i-STAT Glucose test in the i-STAT CG8+ cartridge (white) on the i-STAT 1 System using non-anticoagulated venous and arterial whole blood specimens following the recommendations in CLSI EP35.

The results of the matrix comparison studies support that the glucose can be tested using lithium heparin and un-anticoagulated venous and arterial whole blood. The assay can also be used for testing heparinized capillary whole blood samples.

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:

Expected values for the Glucose assay on the i-STAT CG8+ (white) cartridge are cited from the literature*:

Age	Reference Range (mg/dL)
Premature	20-60
Neonate	30-60
Newborn 1 day	40-60
Newborn >1 day	50-80
Child	60-100
Adult	70-105

*P.C. Painter, J.Y. Cope, J.L. Smith, "Reference Ranges, Table 41–20" in Tietz Textbook of Clinical Chemistry - Second Edition, C.A. Burtis and E.R. Ashwood, eds. (Philadelphia: W.B. Saunders Company, 1994).

F Other Supportive Instrument Performance Characteristics Data:

The sponsor conducted studies to assess the effect of oxygen on the i-STAT Glucose test in the i-STAT CG8+ cartridge (white) on the i-STAT 1 System. Protocols and results were reviewed and found acceptable to support that the test is insensitive to oxygen levels between 20 and 503 mmHg.

The sponsor conducted studies to assess the effect of hematocrit on the i-STAT Glucose test in the i-STAT CG8+ cartridge (white) on the i-STAT 1 System. Protocols and results were reviewed and found acceptable to support that the test is insensitive to hematocrit levels between 15% to 75%.

The sponsor conducted studies to assess the effect of altitude on the i-STAT Glucose test in the i-STAT CG8+ cartridge (white) on the i-STAT 1 System. Protocols and results were reviewed and found acceptable to support that the test yields accurate results up to approximately 10,000 feet above sea level.

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.