510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K230275

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
JGS	Class II	21 CFR 862.1665 - Sodium Test System	CH - Clinical Chemistry
CEM	Class II	21 CFR 862.1600 - Potassium test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device

B Measurand:

Sodium (Na) and Potassium (K)

C Type of Test:

Quantitative, Ion Specific Electrode (Potentiometric method)

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 sodium and potassium in arterial or venous whole blood in point of care or clinical laboratory settings.

The i-STAT CG8+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of sodium in capillary whole blood in point of care or clinical laboratory settings.

Sodium measurements are used for monitoring electrolyte imbalances.

Potassium measurements are used in the diagnosis and monitoring of diseases and clinical conditions that manifest high and low potassium levels.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For point of care or clinical laboratory setting.

D Special Instrument Requirements:

i-STAT 1 Analyzer

IV Device/System Characteristics:

A Device Description:

The candidate device is for the sodium and potassium tests on the i-STAT CG8+ (white) cartridge with the i-STAT 1 System. Additional analytes on the i-STAT CG8+ cartridge (white) with the i-STAT 1 System were cleared in K223710 (glucose), K230285 (pH, pCO2, pO2) and K230300 (ionized calcium and hematocrit).

The i-STAT CG8+ (white) cartridge contains sensors for the measurement of sodium and potassium, a fluid pouch containing aqueous calibrator, a sample entry well and snap closure, fluid channels, waste chamber, and the necessary mechanical features for controlled fluid movement within cartridge. It is a single-use disposable unit that is self-contained. The cartridge tests a sample consisting of two or three drops of whole blood (95 µL). All the test steps and fluid movement occur within the i-STAT CG8+ cartridges.

B Principle of Operation:

Sodium and Potassium tests on the i-STAT CG8+ (white) cartridge are measured by ion-selective electrode potentiometry, measurement of potential difference between the ion selective electrode and the reference electrode. In the calculation of concentration is related to potential through the Nernst equation.

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):
K183688

C Comparison with Predicate(s):

Device & Predicate Device(s):	K230275	K183688
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 sodium and potassium. Sodium measurements are used for monitoring electrolyte imbalances. Potassium measurements are used in the diagnosis and monitoring of diseases and clinical conditions that manifest high and low potassium levels.	Same
Reportable Range	Sodium: 100 -180 mmol/L Potassium: 2.0-9.0 mmol/L	Same
General Device Characteristic Differences		
Sample Type	Sodium and Potassium Test: arterial and venous whole blood with and without balanced heparin or lithium heparin anticoagulant. Sodium Test: capillary	Sodium and Potassium Test: arterial and venous whole blood with lithium heparin anticoagulant

	whole blood with balanced heparin or lithium heparin anticoagulant.	
Analytes	Sodium, Potassium	Sodium, Potassium, Chloride, Blood Urea Nitrogen

VI Standards/Guidance Documents Referenced:

Clinical Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-3rd Edition

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

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:

i-STAT CG8+ cartridge (white) cartridge contains multiple assays. When a cartridge generated a star-out (non-reported result) for one assay, an additional cartridge was run to replace the star-out result, which produced additional test results for other assays. Therefore, the number of replicates per sample in the following precision/reproducibility studies may vary.

Internal within-site precision (aqueous control material)

i. 20-Day precision

A single site precision study for the i-STAT sodium and potassium tests in the i-STAT CG8+ cartridge (white) with the i-STAT 1 system was conducted following the recommendations in CLSI EP 05-A3. Several concentration levels of commercially available calibration verification (CalVer) samples were tested using one lot each of i-STAT CG8+ cartridges and ten i-STAT 1 Analyzers. Each sample was measured in duplicates per run, with two runs per day over 20-days by a minimum of two operators resulting in a total of 80 test results per level. The results are summarized below.

Test	Level	N	Mean (mmol/L)	Repeatability		Between-Run		Between-Day		Within-Laboratory	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV
Na	L 1	80	99.3	0.17	0.17	0.09	0.09	0.05	0.05	0.19	0.20
	L 2	80	121.4	0.20	0.16	0.06	0.05	0.05	0.04	0.22	0.18
	L 3	80	134.8	0.22	0.16	0.06	0.05	0.06	0.05	0.23	0.17
	L 4	80	161.3	0.27	0.16	0.12	0.07	0.07	0.04	0.30	0.19
K	L 1	80	2.09	0.008	0.37	0.003	0.16	0.001	0.04	0.009	0.41
	L 2	80	2.87	0.007	0.25	0.002	0.09	0.002	0.08	0.008	0.28
	L 3	80	3.76	0.012	0.31	0.004	0.10	0.006	0.15	0.014	0.36
	L 4	80	6.41	0.021	0.33	0.008	0.12	0.012	0.18	0.025	0.39
	L 5	80	7.99	0.027	0.33	0.010	0.13	0.014	0.18	0.032	0.40

ii. Between-Lot Precision

The between-lot precision study for the i-STAT sodium and potassium test on the i-STAT CG 8+ cartridge (white) with the i-STAT 1 system was conducted using several concentration levels of commercially available calibration verification (CalVer) samples with three (3) lots of i-STAT CG8 cartridge (white). Each lot was tested in five (5) replicates over five (5) non-consecutive days for each sample. The results are summarized below:

Test	Level	N	Mean (mmol/L)	Repeatability		Between- lot		Between-day		Within-Laboratory	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV
Na	L1	76	100.1	0.22	0.22	0.32	0.32	0.03	0.03	0.39	0.39
	L2	75	122.1	0.26	0.21	0.31	0.25	0.09	0.08	0.41	0.34
	L3	75	135.0	0.34	0.25	0.17	0.13	0.09	0.06	0.39	0.29
	L4	75	162.0	0.33	0.21	0.13	0.08	0.05	0.03	0.36	0.22
K	L1	75	2.10	0.016	0.76	0.013	0.61	0.002	0.12	0.021	0.98
	L2	75	2.86	0.013	0.47	0.012	0.43	0.002	0.08	0.018	0.64
	L3	75	3.74	0.024	0.65	0.007	0.20	0.004	0.11	0.026	0.69
	L4	75	6.40	0.050	0.79	0.017	0.26	0.009	0.13	0.054	0.84
	L5	75	7.95	0.044	0.55	0.043	0.55	0.001	0.02	0.062	0.77

iii. Between-Instrument Precision

The between-instrument precision study for the i-STAT sodium and potassium tests on the i-STAT CG8+ cartridge (white) was conducted using several concentration levels of commercially available calibration verification (CalVer) samples with three (3) i-STAT 1 analyzers. Each fluid level was tested in replicates of five (5) on one lot of i-STAT CG8+

cartridge (white) on each of the three i-STAT analyzers over five (5) non-consecutive days. The results are shown below.

Test	Level	N	Mean (mmol/L)	Repeatability		Between-Instrument		Between-day		Within- Laboratory	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV
Na	L1	76	99.7	0.16	0.16	0.04	0.04	0.02	0.02	0.17	0.17
	L2	75	121.9	0.25	0.20	0.01	0.01	0.04	0.03	0.25	0.20
	L3	76	134.8	0.22	0.17	0.08	0.06	0.03	0.02	0.24	0.18
	L4	75	161.9	0.26	0.16	0.07	0.04	0.09	0.05	0.28	0.17
K	L1	76	2.08	0.010	0.49	0.003	0.15	0.001	0.04	0.011	0.52
	L2	75	2.84	0.011	0.40	0.005	0.17	0.003	0.12	0.013	0.46
	L3	76	3.71	0.018	0.50	0.005	0.14	0.001	0.04	0.019	0.52
	L4	75	6.38	0.030	0.46	0.010	0.16	0.005	0.07	0.032	0.50
	L5	75	7.95	0.030	0.38	0.023	0.29	0.004	0.04	0.038	0.47

Point-of-Care Precision (aqueous control material)

Multiple-day precision testing was performed at three (3) sites using a panel of several levels of calibration verification (CalVer) samples, containing different levels of each analyte. At each site, testing was performed once (1) per day by two (2) operators for five (5) days and each operator performed the test using one (1) lot of i-STAT CG8+ cartridges (white) on three (3) analyzers. The combined precision study results from all sites are summarized below:

Test	Level	N	Mean (mmol/L)	Repeatability		Between-Day		Between-Operator		Within-Site	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV
Na	L 1	91	100 0	0.29	0.29	0.12	0.12	0.08	0.08	0.32	0.32
	L 2	90	121.9	0.28	0.23	0.04	0.04	0.00	0.00	0.29	0.23
	L 3	97	134.9	0.34	0.25	0.00	0.00	0.06	0.04	0.34	0.25
	L 4	90	161.2	0.46	0.29	0.00	0.00	0.00	0.00	0.46	0.29
K	L 1	91	2.10	0.010	0.50	0.000	0.01	0.000	0.00	0.01	0.05
	L 2	90	2.81	0.026	0.91	0.000	0.00	0.012	0.44	0.028	1.01
	L 3	97	3.70	0.014	0.38	0.000	0.00	0.003	0.09	0.014	0.39
	L 4	90	6.32	0.044	0.70	0.000	0.00	0.005	0.08	0.044	0.70
	L 5	90	7.89	0.038	0.48	0.000	0.00	0.006	0.07	0.038	0.48

Test	Level	N	Mean (mmol/L)	Between-Site		Overall	
				SD	%CV	SD	%CV
Na	L 1	91	100	0.00	0.00	0.32	0.32
	L 2	90	121.9	0.00	0.00	0.29	0.23
	L 3	97	134.9	0.03	0.02	0.34	0.26
	L 4	90	161.2	0.21	0.13	0.51	0.32
K	L 1	91	2.10	0.000	0.01	0.01	0.50
	L 2	90	2.81	0.008	0.28	0.029	1.05
	L 3	97	3.70	0.000	0.00	0.014	0.39
	L 4	90	6.32	0.008	0.12	0.045	0.71
	L 5	90	7.89	0.011	0.14	0.040	0.50

Point-of-Care Precision (Whole Blood)

Whole blood precision for the i-STAT Sodium test in the i-STAT CG8+ (white) cartridge on the i-STAT 1 System was evaluated using arterial, venous, and capillary whole blood specimens collected with lithium heparin. Whole blood precision for the i-STAT Potassium tests in the i-STAT CG8+ (white) cartridge on the i-STAT 1 System was evaluated using arterial and venous whole blood specimens collected with lithium heparin. The whole blood precision was assessed using the duplicate test results collected across multiple point of care sites. The results of the whole blood precision are shown below. For each sample type, samples were grouped into subintervals based on their mean values. The precision results between sites were similar. The combined results from all sites are summarized below

Test (units)	Sample Type	Sample Range (mmol/L)	N	Mean	SD	%CV
Na (mmol/L)	Venous Whole Blood	100-130	17	122.6	0.30	0.24
		>130-140	99	137.5	0.45	0.33
		>140-180	67	146.2	0.43	0.30
	Arterial Whole Blood	100-130	2	128.0	0.00	0.00
		>130-140	89	137.4	0.42	0.31
		>140-180	62	142.9	0.37	0.26
	Capillary whole blood	100-130	3	120.8	0.41	0.34
		>130-140	56	138.1	0.61	0.44
		>140-180	95	142.4	0.62	0.44
K (mmol/L)	Venous Whole Blood	2.0-3.5	27	3.22	0.036	1.12
		>3.5-5.0	135	4.12	0.038	0.92
		>5.0-9.0	19	6.49	0.032	0.50
	Arterial Whole Blood	2.0-3.5	23	3.21	0.021	0.65
		>3.5-5.0	124	4.11	0.032	0.79
		>5.0-9.0	6	5.67	0.041	0.72

2. Linearity:

The linearity study was designed based on the CLSI EP06 2nd ed guideline. Lithium heparin venous whole blood was obtained from a healthy subject and was altered to produce a high sample pool and a low sample pool. Samples of intermediate concentrations were prepared by intermixing the high and low pools. A total of eleven (11) samples were prepared for the linearity assessment with the concentrations spanning the claimed measuring range using five CG8+ cartridge lot. Each test sample was tested in replicates of two (2) per cartridge lot for a total of ten (10) results per level. An assessment of linearity was performed using weighted least squares linear regression. At each concentration level, the deviation from linearity was within ± 0.6% for i-STAT Sodium test and within ± 3% for i-STAT Potassium test. The regression parameters for the linearity study are summarized below:

Analyte	Range tested (mmol/L)	Claimed Measuring Range (mmol/L)	Slope	Intercept	R^2
Na	91.3 – 209.8	100 - 180 mmol/L	1.005	-0.525	0.9996
K	1.79 – 10.04	2.0 – 9.0 mmol/L	1.011	0.002	0.9994

3. Analytical Specificity/Interference:

The analytical specificity of the sodium and potassium assays on the i-STAT CG8+ (white) cartridge using the i-STAT 1 system was established by conducting interference testing following the recommendations in CLSI EP07-Edition 3. Interference from certain exogenous and endogenous substances was assessed using lithium heparin venous whole blood samples. A substance was identified as an interferent if the difference in the mean between the control and test sample was outside of the predefined allowable error:

For Sodium: ± 4 mmol/L.
For Potassium: ± 0.5 mmol/L.

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

Sodium:

Substance	Highest concentration at which no significant interference was observed
Acetaminophen	15.6 mg/dL
N-Acetyl-L-Cysteine	15.0 mg/dL
Acetylsalicylic Acid	3.0 mg/dL
Ammonium Chloride	10.7 mg/dL
Ascorbic Acid	5.25 mg/dL
β-Hydroxybutyric Acid	62.46 mg/dL
Bilirubin	40 mg/dL
Calcium Chloride	20 mg/dL

Substance	Highest concentration at which no significant interference was observed
Cholesterol	400 mg/dL
Hemoglobin	1000 mg/dL
Ibuprofen	21.9 mg/dL
Lithium Bromide	325.69 mg/dL (37.5 mmol/L)
Lithium Chloride	13.6 mg/dL
Lithium Lactate	90 mg/dL
Lithium Salicylate	2.86 mg/dL
Magnesium Chloride	10 mg/dL
Intralipid 20%	2395 mg/dL
Sodium Heparin	330 U/dL
Sodium Thiosulfate	2.5 mmol/L
Triglyceride	1500 mg/dL
Uric Acid	23.5 mg/dL

Potassium:

Substance	Highest concentration at which no significant interference was observed
Acetaminophen	15.6 mg/dL
N-Acetyl-L-Cysteine	15.0 mg/dL
Ammonium Chloride	10.7 mg/dL
Ascorbic Acid	5.25 mg/dL
β-Hydroxybutyric Acid	62.46 mg/dL
Benzalkonium Chloride	1.13 mg/dL
Unconjugated Bilirubin	40 mg/dL
Calcium Chloride	20 mg/dL
Cholesterol	400 mg/dL
Hemoglobin	1000 mg/dL
Lithium Bromide	325.69 mg/dL (37.5 mmol/L)
Lithium Chloride	13.6 mg/dL
Lithium Lactate	90 mg/dL
Lithium Salicylate	2.86 mg/dL
Magnesium Chloride	10 mg/dL
Intralipid 20%	3216 mg/dL
Sodium Thiosulfate	264.04 mg/dL (16.7 mmol/L)
Triglyceride	1500 mg/dL

For those substances that on initial screening were found to interfere, 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:

Test	Substance	Concentration	Interference
Sodium	Cholesterol	≥ 425mg/dL	Decreased results
	Nithiodote (Sodium Thiosulfate)	≥ 2.7 mmol/L	Increased results

Limitations included 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 (***).

- Nithiodote (Sodium Thiosulfate) is indicated for the treatment of acute cyanide poisoning. The journal article [1] titled "Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate" indicated that sodium thiosulfate could be used in the treatment of calciphylaxis indicating that the highest concentration likely to be seen in plasma [is] after infusion of a 12.5 g dose of sodium thiosulfate pentahydrate. Assuming that the 12.5 g dose of sodium thiosulfate pentahydrate is distributed in a typical blood volume of 5 L with a hematocrit of 40%, the peak sodium thiosulfate plasma concentration expected is 16.7 mmol/L.

[1] Wendroth Scott M. et.al. "Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate." Clinica Chimica Acta 2014; 431:77-79.

4. Assay Reportable Range:

   See section VII. A.2 Linearity.

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

   Traceability
   The i-STAT sodium and potassium tests on the i-STAT CG8+ (white) cartridge are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material NIST SRM956.

   Sample Stability
   A study was conducted to verify the whole blood sample stability after sample collection with and without anticoagulant for the i-STAT sodium and potassium tests using the i-STAT CG8+ (white) cartridge on the i-STAT 1 Analyzer. The results support the sponsor's sample stability claims. The sample stability claims for sodium and potassium tests are 30 minutes for (arterial, venous) samples with anticoagulant and 3 minutes for (arterial and venous) samples without anticoagulant. The sample stability claims for sodium is 3 minutes for capillary whole blood samples with anticoagulant.

6. Detection Limit:

Linearity studies were used to support the lower end of the measuring range for i-STAT sodium and potassium tests (see section VII. A.2 above). In addition, a limit of quantitation (LoQ) study for each analyte on the i-STAT CG8+(white) cartridge with the i-STAT 1 Analyzer was conducted following the recommendations in CLSI EP17-A2.

The LoQ was evaluated using lithium heparin venous whole blood altered to create four (4) samples with low sodium or potassium concentrations. Each sample was evaluated using two i-STAT CG8+ cartridge (white) lots. The LoQ was calculated for each of the two lots. The sponsor defined LoQ as the lowest concentration that met the pre-defined total error goal listed in the table below for each analyte. The sponsor based the claim on the lot with the highest LoQ estimate. The results are summarized in the table below.

Analyte	Reportable Range	Total Error (TE)	LoQ
Na	100 – 180 mmol/L	≤ 4 mmol/L	92 mmol/L
K	2 – 9.0 mmol/L	≤ 0.5 mmol/L	1.6 mmol/L

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The accuracy of the i-STAT sodium and potassium test with the i-STAT CG8+ cartridge (white) on the i-STAT 1 analyzer was evaluated by a method comparison study for agreement with the comparative methods. The study was conducted following the recommendations in CLSI EP09c-3rd ed. guideline.

A total of 185 lithium heparin arterial whole blood specimen and 157 lithium heparin venous whole blood (5% contrived venous blood samples) specimens collected across three (3) point of care sites were evaluated for sodium and potassium using the i-STAT CG8+ cartridge (white) and i-STAT CHEM8+cartridge (comparative method) on the i-STAT 1 analyzer. The data were analyzed by Passing-Bablok regression analysis comparing the first replicate of the i-STAT CG8+ cartridge to the mean of duplicate results from the comparative method. Accuracy results for arterial and venous whole blood specimens for each analyte are shown in the table below.

Analyte (Units)	Matrix	N	Concentration Range by Comparator (mmol/L)	Slope	Intercept	R	Claimed Range (mmol/L)
Na (mmol/L)	Venous	185	103 – 178	1.00	0.00	1.00	100 – 180
	Arterial	157	128 – 175	1.00	0.00	0.99	
K (mmol/L)	Venous	183	2.4 – 8.8	1.00	0.00	1.00	2 – 9
	Arterial	157	2.4 – 6.3	1.00	0.00	1.00	

Capillary whole blood specimen (including 22 neonate samples) collected from skin punctures with balanced heparin capillary tubes from each study subject across multiple point of care sites were tested for Na using the i-STAT CG8+ cartridge (white) on the i-STAT 1 analyzer and the epoc Blood Analysis System (comparative method). A Passing-Bablok linear regression analysis was performed using the singlicate result from the i-STAT CG8+ cartridge (white) versus the singlicate result of the comparative method. Accuracy results for the capillary whole blood specimen are shown in the table below.

Analyte (Units)	Matrix	N	Concentration Range by Comparator (mmol/L)	Slope	Intercept	R	Claimed Range (mmol/L)
Na (mmol/L)	Capillary blood (All samples)	209	101 -172	1.00	0.00	0.98	100 – 180
	Capillary blood (Native samples only)	194	125-149	1.00	0.00	0.89	

Additionally, the systematic bias and predicted bias at medical decision levels for each analyte per sample type were evaluated and found substantially equivalent to previously cleared sodium and potassium test systems.

2. Matrix Comparison:

The sponsor has provided the information to support that the sodium and potassium in the i-STAT CG8+ cartridge (white) on the i-STAT 1 System can be performed using balanced heparin, lithium heparin and non-anticoagulant venous and arterial whole blood. The sodium assay can also be used for testing heparinized capillary whole blood.

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 sodium and potassium assays on the i-STAT CG8+ cartridges are cited from literature*:

Analyte	Units	Reference Range
Sodium	mmol/L	138-146
Potassium	mmol/L	3.5-4.9

**B.E. Statland, Clinical Decision Levels for Lab Tests (Oradell, NJ: Medical Economics Books, 1987).*

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.