510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K244014

B Applicant

Abbott Point of Care Inc.

C Proprietary and Established Names

i-STAT CG4+ cartridge with the i-STAT 1 System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CHL	Class II	21 CFR 862.1120 - Blood Gases (PCO2, PO2) And Blood Ph Test System	CH - Clinical Chemistry
KHP	Class I, meets the limitations of exemptions per 862.9(c)(9)	21 CFR 862.1450 - Lactic acid test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device

B Measurand:

pH, PO2, PCO2 and lactate

C Type of Test:

Quantitative, amperometric for pH and PCO2

Quantitative, potentiometric for PO2 and lactate

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The i-STAT CG4+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of pH, partial pressure of oxygen (PO2), and partial pressure of carbon dioxide (PCO2) in arterial, venous, or capillary whole blood in point of care or clinical laboratory settings.

The i-STAT CG4+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of lactate in arterial or venous whole blood in point of care or clinical laboratory settings.

pH, PO2, and PCO2 measurements are used in the diagnosis, monitoring, and treatment of respiratory, metabolic, and acid-base disturbances.

Lactate measurements are used in (1) the diagnosis and treatment of lactic acidosis in conjunction with measurements of blood acid/base status, (2) monitoring tissue hypoxia and strenuous physical exertion, and (3) diagnosis of hyperlactatemia.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

Point of Care (POC) or clinical laboratory settings

D Special Instrument Requirements:

i-STAT 1 analyzer

IV Device/System Characteristics:

A Device Description:

The i-STAT CG4+ cartridge is used with the i-STAT 1 analyzer as part of the i-STAT 1 System to measure pH, partial pressure of oxygen (PO2), partial pressure of carbon dioxide (PCO2) in arterial, venous, or capillary whole blood and to measure lactate in arterial or venous whole blood.

Each i-STAT CG4+ cartridge contains a reference electrode, a ground electrode, potentiometric sensors and amperometric sensors for the measurement of specific analytes. It also contains a

buffered aqueous calibrant solution with known concentrations of analytes and preservatives. A list of reactive ingredients relevant for the i-STAT CG4+ cartridge is indicated below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
pH	Hydrogen Ion (H^+)	N/A	6.66 pH
*P*CO2	Carbon Dioxide (CO2)	N/A	25.2 mmHg
Lactate	Lactate	N/A	1.8 mmol/L
	Lactate Oxidase	*Aerococcus viridans*	0.001 IU

B Principle of Operation:

pH is measured by direct potentiometry. In the calculation of results for pH, concentration is related to potential through the Nernst equation.

PO2 is measured amperometrically. The oxygen sensor is similar to a conventional Clark electrode. Oxygen permeates through a gas permeable membrane from the blood sample into an internal electrolyte solution where it is reduced at the cathode. The oxygen reduction current is proportional to the dissolved oxygen concentration.

PCO2 is measured by direct potentiometry. In the calculation of results for PCO2, concentration is related to potential through the Nernst equation.

Lactate is measured amperometrically. The enzyme lactate oxidase, immobilized in the lactate biosensor, selectively converts lactate to pyruvate and hydrogen peroxide (H2O2). The liberated hydrogen peroxide is oxidized at a platinum electrode to produce a current which is proportional to the sample lactate concentration.

Temperature "Correction" Algorithm

pH, PO_2, and PCO_2 are temperature-dependent and are measured at 37°C. The pH, PO_2, and PCO_2 readings at a body temperature other than 37°C can be 'corrected' by entering the patient's temperature on the chart page of the Analyzer. In this case, blood gas results will be displayed at both 37°C and the patient's temperature. pH, PO_2, and PCO_2 at the patient's temperature (T_p) are calculated. The calculations are described in the device labeling.

Calculated Results

The i-STAT 1 Analyzer can be customized to display the following calculated results:

HCO3 (bicarbonate)
TCO2
BE (Base excess)
sO2 (oxygen saturation)

V Substantial Equivalence Information:

A Predicate Device Name(s):
i-STAT G3+ cartridge with the i-STAT 1 System

B Predicate 510(k) Number(s):
K223857

C Comparison with Predicate(s):

Device & Predicate Device(s):	K244014	K223857
Device Trade Name	i-STAT CG4+ (white) cartridge with the i-STAT 1 System	i-STAT G3+ cartridge with the i-STAT 1 System
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended to measure pH, partial pressure of oxygen (PO2), and partial pressure of carbon dioxide (PCO2).	Same
Sample Type	pH, PO2, PCO2 in arterial, venous or capillary whole blood	Same
Sample Volume	95 µL	Same
Reportable Range	pH: 6.500 – 7.800 PO2: 5 – 700 mmHg PCO2: 5 – 130 mmHg	Same Same Same
General Device Characteristic Differences	K244014	K223857
Measurands	pH, PO2, PCO2 and lactate	pH, PO2, PCO2

The sponsor referenced K200492 to support the substantial equivalence of lactate test.

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 the Linearity of Quantitative Measurement Procedures; 2nd Edition.

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

CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; 3rd Edition.

CLSI EP17: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; 2nd Edition.

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

CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The precision of the i-STAT pH, PO2, PCO2, and Lactate tests in the i-STAT CG4+ (white) cartridge with the i-STAT 1 System was evaluated based on the CLSI guideline EP05-A3.

Internal within-Site Precision (aqueous control materials)

The precision of the i-STAT pH, PO2, PCO2, and Lactate tests in the i-STAT CG4+ (white) cartridge with the i-STAT 1 System was evaluated using five (5) levels of aqueous materials. The study was conducted using ten (10) analyzers and one (1) test cartridge lot at one (1) site. 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. 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. The results are summarized below.

pH

Level	N	Mean (pH units)	Repeatability		Between-run		Between-day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	84	6.5701	0.00359	0.05	0.00280	0.04	0.00034	0.01	0.00457	0.07
L2	84	7.0259	0.00178	0.03	0.00105	0.01	0.00068	0.01	0.00218	0.03
L3	83	7.4532	0.00231	0.03	0.00051	0.01	0.00052	0.01	0.00242	0.03
L4	84	7.6338	0.00961	0.13	0.00325	0.04	0.00266	0.03	0.01049	0.14
L5*	84	7.9653	0.00236	0.03	0.00081	0.01	0.00165	0.02	0.00299	0.04

* Results outside of the reportable range may be displayed when performing testing with Calibration Verification material.

PO2

Level	N	Mean (mmHg)	Repeatability		Between-run		Between-day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	84	71.0	1.71	2.41	0.65	0.92	1.03	1.45	2.10	2.96
L2	84	82.6	1.74	2.11	0.58	0.70	0.45	0.54	1.89	2.29
L3	83	108.9	1.86	1.71	1.00	0.91	0.67	0.62	2.22	2.03
L4	84	138.8	2.52	1.82	0.90	0.65	1.12	0.81	2.90	2.09
L5	84	372.9	4.66	1.25	5.29	1.42	2.07	0.56	7.35	1.97

PCO2

Level	N	Mean (mmHg)	Repeatability		Between-run		Between-day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	84	89.41	1.251	1.40	0.626	0.70	0.354	0.40	1.443	1.61
L2	84	56.28	0.621	1.10	0.338	0.60	0.165	0.29	0.726	1.29
L3	83	29.37	0.365	1.24	0.128	0.43	0.141	0.48	0.412	1.40
L4	84	22.69	0.707	3.11	0.196	0.86	0.191	0.84	0.758	3.34
L5	84	12.19	0.377	3.10	0.131	1.07	0.123	1.01	0.418	3.43

Lactate

Level	N	Mean (mmol/L)	Repeatability		Between-run		Between-day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	84	19.791	0.1827	0.92	0.0869	0.44	0.0226	0.11	0.2035	1.03
L2	84	7.874	0.0592	0.75	0.0302	0.38	0.0123	0.16	0.0676	0.86
L3	83	2.110	0.0128	0.61	0.0051	0.24	0.0046	0.22	0.0146	0.69
L4	84	0.820	0.0135	1.64	0.0036	0.44	0.0049	0.60	0.0148	1.80
L5	84	0.410	0.0128	3.13	0.0028	0.70	0.0055	1.35	0.0142	3.47

Point of Care precision (aqueous material)

A multi-site point of care precision study was performed using a panel of five aqueous control solutions containing different levels of pH, PCO2, PO2, and lactate. At each of three (3) point of care site, testing was performed once per day by two (2) operators for five (5) days on six (6) i-STAT 1 Analyzers using one (1) lot of i-STAT CG4+ (white) cartridges, resulting in a total of at least 90 test results per level. 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. Repeatability, between-day, between-operator, within-site, between-site variance components, and reproducibility were calculated by site. These components were also calculated for all sites combined and are provided below.

pH

Level	N	Mean (pH units)	Between-Day		Between-Operator		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	90	6.5725	0.00111	0.02	0.00281	0.04	0.00147	0.02	0.00525	0.08
L2	90	7.0266	0.00133	0.02	0.00124	0.02	0.00201	0.03	0.00340	0.05
L3	90	7.4540	0.00062	0.01	0.00119	0.02	0.00080	0.01	0.00209	0.03
L4	90	7.6373	0.00046	0.01	0.00096	0.01	0.00142	0.02	0.00263	0.03
L5	90	7.9681	0.00062	0.01	0.00093	0.01	0.00107	0.01	0.00248	0.03

PO2

Level	N	Mean (mmHg)	Between-Day		Between-Operator		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	91	76.9	0.95	1.23	2.63	3.42	2.20	2.87	4.53	5.89
L2	90	87.4	0.86	0.98	2.13	2.44	2.56	2.93	3.99	4.57
L3	90	113.4	0.57	0.50	1.57	1.38	3.08	2.71	4.21	3.71
L4	90	141.4	1.50	1.06	1.15	0.82	3.47	2.45	4.74	3.35
L5	90	366.0	2.92	0.80	7.53	2.06	4.66	1.27	11.23	3.07

PCO2

Level	N	Mean (mmHg)	Between-Day		Between-Operator		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	90	89.41	0.501	0.56	0.710	0.79	0.000	0.00	1.618	1.81
L2	90	57.20	0.287	0.50	0.311	0.54	0.000	0.00	0.661	1.16
L3	90	29.99	0.169	0.56	0.063	0.21	0.140	0.47	0.368	1.23
L4	90	23.03	0.092	0.40	0.000	0.00	0.054	0.24	0.353	1.53
L5	90	12.18	0.000	0.00	0.000	0.00	0.000	0.00	0.361	2.96

Lactate

Level	N	Mean (mmol/L)	Between-Day		Between-Operator		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	91	18.928	0.0573	0.30	0.0000	0.00	0.0000	0.00	0.1990	1.05
L2	90	7.636	0.0216	0.28	0.0126	0.16	0.0000	0.00	0.0491	0.64
L3	90	2.087	0.0033	0.16	0.0022	0.11	0.0061	0.29	0.0111	0.53
L4	90	0.838	0.0088	1.05	0.0023	0.28	0.0053	0.63	0.0139	1.65
L5	90	0.433	0.0056	1.29	0.0012	0.27	0.0053	1.21	0.0146	3.39

Whole Blood Precision at Point of Care Sites

A multi-site precision study was conducted using arterial, venous, and capillary whole blood specimens collected with lithium heparin collection devices targeted to levels within the reportable range of pH, PO2, and PCO2. A multi-site precision study was conducted using arterial and venous whole blood for lactate test. The whole blood precision was assessed using the duplicate test results collected across multiple point of care sites. The mean values

for each sample were divided into subintervals for each sample type across the reportable range for each i-STAT test. The results are summarized below.

Analyte Test (units)	Sample Type	Sample Range	N	Mean	SD	% CV
pH (pH units)	Venous Whole Blood	6.500-7.300	9	7.0265	0.00235	0.03
		>7.300 – 7.450	154	7.3745	0.00668	0.09
		>7.450-7.800	12	7.5355	0.00732	0.10
	Arterial Whole Blood	6.500-7.300	9	7.2229	0.00262	0.04
		>7.300 – 7.450	124	7.3816	0.00486	0.07
		>7.450-7.800	43	7.4763	0.00690	0.09
	Capillary Whole Blood	6.500-7.300	3	7.2477	0.01355	0.19
		7.300-7.450	121	7.4099	0.02084	0.28
		>7.450-7.800	32	7.4781	0.02609	0.35
PO2 (mmHg)	Venous Whole Blood	10-40	125	26.2	0.91	3.49
		>40-50	21	43.1	0.98	2.26
		>50-100	24	59.3	1.32	2.23
		>100-250	3	227.7	2.65	1.16
		>250-700	8	508.4	6.96	1.37
	Arterial Whole Blood	>50-100	108	73.2	1.29	1.76
		>100-250	66	135.9	2.90	2.13
		>250-700	3	381.3	8.94	2.35
	Capillary Whole Blood	10-40	15	33.8	4.30	12.74
		>40-50	34	46.0	3.84	8.35
		>50-100	112	63.4	6.04	9.52
		>100-250*	5	166.4	12.95	7.80
		>250-700	8	489.6	8.53	1.74
PCO2 (mmHg)	Venous Whole Blood	5.0-35.0	23	30.17	0.379	1.26
		>35.0-50.0	119	46.48	0.639	1.38
		>50.0-62.5	31	57.05	0.687	1.20
		>62.5-130.0	10	117.05	1.650	1.41
	Arterial Whole Blood	5.0-35.0	48	33.24	0.393	1.18
		>35.0-50.0	105	44.55	0.641	1.44
		>50.0-62.5	16	61.33	1.100	1.79
		>62.5-130.0	6	77.18	1.080	1.40
	Capillary Whole Blood	5.0-35.0	47	32.31	1.736	5.37
		>35.0-50.0	105	40.00	2.258	5.64
		>50.0-62.5	3	58.35	1.967	3.37
		>62.5-130.0	1	68.20	2.263	3.32
Lactate (mmol/L)	Venous Whole Blood	0.30-1.00	100	0.639	0.0127	1.99
		>1.00-5.00	81	1.549	0.0206	1.33
		>5.00-20.00	20	12.476	0.0756	0.61
	Arterial Whole Blood	0.30-1.00	55	0.653	0.0138	2.11
		>1.00-5.00	76	1.771	0.0184	1.04
		>5.00-20.00	3	8.120	0.0252	0.31

* A potential outlier due to preanalytical handling was identified for one (1) subject; *P*O2 precision for capillary whole blood in sample range 100-250 mmHg with this subject excluded (N=4) is as follows: Mean = 177.8 mmHg; SD = 5.50, %CV=3.09

The instrument to instrument and lot to lot precision was evaluated and found to be acceptable.

2. Linearity:

The linearity study was designed based on CLSI EP06-Ed2. The linearity of the i-STAT pH, PO2, PCO2, and Lactate tests in the i-STAT CG4+ (white) cartridge with the i-STAT 1 System was evaluated by preparing venous whole blood samples collected in lithium heparin tubes from healthy subjects of varying analyte levels for each i-STAT test. Each sample for PO2, PCO2, and pH testing was prepared via tonometry to eleven target analyte concentrations. Each test sample was tested in replicates of 3 per cartridge lot for a total of 15 results per level. Each level was tested using 5 lots of i-STAT CG4+ (white) cartridges. For lactate testing, low and high sample levels were prepared by plasma replacement and spiking, then admixed to prepare nine intermediate whole blood samples. The eleven lactate test samples were analyzed using 5 cartridge lots in replicates of two (2) per cartridge lot for a total of 10 results per level.

The linearity study results support that the assays are linear across the following claimed reportable ranges:

i-STAT Test	Reportable Range
pH	6.500 – 7.800 pH Units
PO2	5.0 – 700 mmHg
PCO2	5.0 – 130.0 mmHg
Lactate	0.30 – 20.00 mmol/L

3. Analytical Specificity/Interference:

The analytical specificity of the PO2, PCO2, pH and Lactate tests in the i-STAT CG4+ (white) cartridge using the i-STAT 1 system was established by conducting interference testing following the recommendations in CLSI EP07-A3 and CLSI EP37-ED1. Interference from certain exogenous and endogenous substances was assessed using lithium heparin venous whole blood samples tonometered to two concentrations of low and high: PO2 (20-40 mmHg and 55-95 mmHg) pCO2 (20-40 mmHg and 60-80 mmHg) and pH (7.2-7.4 and 7.3-7.5). Lithium heparin venous whole blood samples were spiked to three concentrations of lactate (0.70 - 1.30 mmol/L, 1.37 - 1.97 mmol/L and ~5.0 mmol/L). Each low and high sample was further divided into two aliquots: control (with no added interferent) and test (with added interferent). Each sample was measured in replicates of 10 using four lots of the i-STAT CG4+ (white) cartridges for the interference assessment and one lot for the dose response testing. 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 PO2: ± greater of 5 mmHg or 10% of the control (mmHg)
For PCO2: ± greater of 5 mmHg or 8% of the control (mmHg)

For pH: ± 0.04 pH units
For Lactate: the greater of ±0.6 mmol/L or ± 12% of the control concentration (mmol/L)

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

PO2, PCO2 and pH

Substance*	Highest concentration at which no significant interference was observed
Acetaminophen	1.03 mmol/L
Atracurium (Atracurium Besylate)	0.0287 mmol/L
Bilirubin	40 mg/dL
Calcium (Calcium Chloride)	20 mg/dL
Ethanol	130 mmol/L
Hemoglobin	10 g/L
Ibuprofen	1.06 mmol/L
Morphine (Morphine Sodium Salt)	0.0273 mmol/L
Potassium (Potassium Chloride)	8 mmol/L
Sodium (Sodium Chloride)	170 mmol/L
Thiopental	1.66 mmol/L
Triglyceride**	1500 mg/dL
Intralipid 20%**	2684 mg/dL

Lactate

Substance*	Highest concentration at which no significant interference was observed
Acetaldehyde	0.045 mmol/L
Acetaminophen	1.03 mmol/L
Acetyl Cysteine (N-Acetyl-Cysteine)	0.92 mmol/L
Ascorbic Acid (L-Ascorbic Acid)	0.298 mmol/L
β-Hydroxybutyric Acid[2]	6 mmol/L
Bilirubin	40 mg/dL
Dopamine (Dopamine Hydrochloride)	4.06 µmol/L
Formaldehyde[2]	0.133 mmol/L
Hemoglobin	10.0 g/L
Hydroxyurea	0.405 mmol/L
Pyruvate (Lithium Pyruvate)	0.570 mmol/L
Salicylate (Lithium Salicylate)	0.207 mmol/L
Thiocyanate (Lithium Thiocyanate)	0.898 mmol/L
Triglyceride**	1500 mg/dL
Intralipid 20%**	3579 mg/dL
Uric Acid	1.4 mmol/L

*The compound tested to evaluate the interfering substance is presented in parenthesis.
**Intralipid 20% and Triglyceride were assessed using the same data set.

For those substances that on initial screening were found to interfere, dose response testing was conducted. The results are summarized in the table below:

Test	Substance	Concentration	Interference
Lactate	Bromide (Lithium Bromide)	> 10.0 mmol/L)	Decreased results. Use Another Method.
	Glycolic Acid	> 0.8/mmol/L	Increased 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. Additionally, bromide may result in an increased rate of star outs (***).
- Glycolic acid is a product of ethylene glycol metabolism. Unexpected increased lactate concentrations caused by glycolic acid may be due to the possibility of ethylene glycol ingestion as the cause of an otherwise unknown high anion gap metabolic acidosis. In a study of 35 patients who had ingested ethylene glycol, initial glycolic acid concentrations of 0 to 38 mmol/L corresponded to ethylene glycol levels of 0.97 – 130.6 mmol/L.

An oxygen sensitivity study was conducted to evaluate the effect of oxygen on the i-STAT Lactate test in the i-STAT CG4+ (white) cartridge. Results demonstrated oxygen as low as 25 mmHg does not impact the lactate test. The sponsor included the following in the labeling:

> PO2 dependence: The dependence of the i-STAT Lactate test with respect to PO2 is as follows: oxygen levels of less than 25 mmHg (3.33 kPa) at 37 °C may decrease results.

4. Assay Reportable Range:

pH: 6.500 – 7.800
PO2: 5 – 700 mmHg
PCO2: 5 – 130 mmHg
Lactate: 0.30 – 20.00 mmol/L

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

Traceability
pH: traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference materials SRMs 186-I, 186-II, 185, and 187 via the IFCC blood reference method.

PO2: traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

PCO2: traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

Lactate: Lactate values assignment is traceable to i-STAT System working calibrator prepared from sodium L-lactate (Sigma-Aldrich Fluka, >99 % purity).

Sample Stability
A study was conducted to verify the whole blood sample stability after sample collection with anticoagulant for i-STAT pH, PO2, PCO2 and Lactate tests in the i-STAT CG4+ (white) cartridge on the i-STAT 1 System. The results support the sponsor's sample stability claims. The sample stability claims for PO2, PCO2, and pH are 10 minutes for arterial and venous samples and three minutes for capillary samples with lithium heparin anticoagulant. Venous and arterial samples are stable for up to three minutes without anticoagulant. The sample stability claim for lactate for all samples is testing the sample immediately after collection.

Altitude effects
A study was conducted to assess the effect of high altitude on the i-STAT CG4+ (white) cartridge pH, PO2, PCO2 and lactate assays. The results support the device performs adequately at an altitude of approximately 10,000 feet.

6. Detection Limit:

The limit of blank (LoB) and limit of detection (LoD) of the i-STAT Lactate test in the i-STAT CG4+ (white) cartridge were evaluated on the i-STAT 1 Analyzer based on CLSI EP17-A2, using whole blood that was altered to achieve a blank lactate concentration for LoB testing and two low lactate concentrations for LoD testing. The studies were conducted across four days using two lots of i-STAT CG4+ (white) cartridges and 40 i-STAT 1 Analyzers for a total of 159 test results for LoB and 315 test results for LoD. The LoB and LoD were calculated using a parametric data analysis for each of the two lots. The higher of the two LoB values and LoD values from each lot is reported in the labeling. The LoB and LoD for the i-STAT Lactate test on the i-STAT 1 Analyzer is shown below.

Analyte	LoB	LoD
Lactate	0.0 mmol/L	0.026 mmol/L

Linearity studies were used to support the lower end of the measuring range for pH, PO2 and PCO2 (see section VII. A.2 above).

The Limit of Quantitation (LoQ) of the i-STAT pH, PO2, PCO2, and Lactate tests in the i-STAT CG4+ (white) cartridge were evaluated on the i-STAT 1 Analyzer using four (4) whole blood samples that were altered using tonometry to below the lower limit of the reportable range for pH, PO2 and PCO2, and by plasma replacement to low lactate concentrations. The testing for pH, PO2 and PCO2 was conducted over four (4) days in replicates of twelve per event using two (2) cartridge lots for a total of 96 results per test. For lactate, testing was conducted over four (4) events in replicates of fifteen per event using two (2) cartridge lots for a total of 120 results.

The sponsor defined LoQ as the greater of the two lots at which the lowest concentration met the pre-defined total error goals given in the following table.

Analyte	Total Error goals
pH	≤ 0.04 pH units
PO2	≤ 5.0 mmHg
PCO2	≤ 5.0 mmHg
Lactate	≤ 0.6 mmol/L

The LoQ for each test is shown below.

Analyte	Reportable range	LoQ
pH (pH units)	6.5 – 7.8	6.471
PO_2 (mmHg)	5.0 - 700	5
PCO_2 (mmHg)	5.0 – 130.0	3.0
Lactate (mmol/L)	0.30 -20.00	0.18

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Method comparison studies for arterial, venous, and capillary whole blood specimens were conducted on the i-STAT CG4+ (white) cartridge with the i-STAT 1 System based on the recommendations in CLSI EP09c-Ed3. Heparinized arterial and venous whole blood specimens collected across multiple point of care sites were evaluated using i-STAT CG4+ (white) cartridges on the i-STAT 1 analyzer against whole blood specimens tested on a comparative method.

pH, PO2, and PCO2

For pH, PO2, and PCO2 a Passing-Bablok linear regression analysis was performed using the first replicate result from the i-STAT 1 analyzer versus the results from the comparative method. Two (2) capillary specimens collected from skin puncture with balanced heparin capillary tubes from each study subject across multiple point of care sites. One (1) tube was used to test in singlicate on the i-STAT 1 analyzer and the other tube was used to test in singlicate on the comparative method. The arterial, venous, and capillary data were pooled, and a Passing-Bablok linear regression analysis for pH, PO2, and PCO2 was performed using the singlicate result from the i-STAT CG4+ cartridge versus the result from the comparative method. The method comparison results for arterial, venous, and capillary whole blood specimens are shown below.

Test (units)	Comparative Method Arterial/Venous/Capillary	N	Slope	Intercept	r
pH (pH units)	RAPIDPoint 500/500e	551	1.00	-0.01	0.98
PO2 (mmHg)	RAPIDPoint 500/500e	557	1.01	-1.29	0.99
PCO2 (mmHg)	i-STAT G3+	475	1.03	-0.30	0.99

The method comparison results for capillary whole blood specimens only for pH, PO2, and PCO2 are shown below.

Test (units)	N	Slope	Intercept	r
pH (pH units)	193	1.01	-0.08	0.97
PO2 (mmHg)	192	1.08	-5.47	0.99
PCO2 (mmHg)	184	1.05	-0.54	0.98

Lactate

The arterial and venous data were pooled, and a Passing-Bablok linear regression analysis for Lactate was performed using the singlicate result from the i-STAT CG4+ cartridge versus the result from the comparative method. The method comparison results for arterial and venous whole blood specimens are shown below.

Test (units)	Comparative Method	N	Slope	Intercept	r
Lactate (mmol/L)	i-STAT CG4+ (K200492)	544	0.98	-0.03	0.99

Additionally, the systematic bias and predicted bias at medical decision levels for each analyte (pH, pO2, pCO2, and lactate) per sample type were evaluated and considered.

2. Matrix Comparison:

A matrix comparison study was conducted following the recommendations in CLSI EP35 to evaluate the performance of the i-STAT pH, PO2, PCO2 and lactate tests in the i-STAT CG4+ (white) cartridge on the i-STAT 1 System comparing arterial or venous whole blood specimens collected without anticoagulant (candidate specimen) to samples collected with balanced heparin or lithium heparin anticoagulant (primary specimen). For pH, PO2, and

PCO2, a total of 228 matched whole blood samples were tested which included native arterial (n=114) and native venous (n=114) specimens. For lactate, a total of 289 matched whole blood samples were tested which included native arterial (n=108) and native venous (n=167) specimens. Each specimen was tested in duplicate using two i-STAT CG4+ (white) cartridges with two i-STAT 1 analyzers. A Passing-Bablok linear regression analysis was performed using the first replicate results from the candidate (y-axis) versus the first replicate result from the primary specimen (x-axis). Venous and arterial samples performed similarly and were combined in the analysis. The regression analysis results for these samples are summarized below.

Test (units)	N	Candidate Specimen Range	Primary Specimen Range	r	Slope	Intercept
pH (pH units)	228	7.176-7.567	7.192-7.549	0.96	1.00	0.00
PO2 (mmHg)	228	15-197	15-197	0.99	1.01	-0.53
PCO2 (mmHg)	228	26.3-77.4	26.8-77.0	0.97	1.03	-1.58
Lactate (mmol/L)	289*	0.31-19.42	0.30-19.43	1.00	1.00	-0.02

*Includes 14 contrived venous specimens tested at Abbott Point of Care

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 pH, PCO2, PO2 and lactate assays on the i-STAT CG4+ (white) cartridge are cited from literature:

Analyte	Units*	Reference Range	
		arterial	venous
Measured			
pH	pH units	7.35 - 7.45 (1)	7.31 – 7.41*
PO2	mmHg kPa	80 – 105 (2)** 10.7 - 14.0 (2)**	N/A
PCO2	mmHg kPa	35 - 45 (1) 4.67 - 6.00	41 – 51(1) 5.47 - 6.80
lactate	mmol/L mg/dL	0.36 - 1.25 (3)*** 3.2 - 11.3 (3)***	0.90 - 1.70 (3)*** 8.1 - 15.3 (3)***

***** Calculated from Siggard-Andersen nomogram

****** The reference ranges shown are for a healthy population. Interpretation of blood gas measurements depend on the underlying condition (e.g., patient temperature, ventilation, posture and circulatory status).

******* The i-STAT reference ranges for venous whole blood listed above are similar to reference ranges derived from serum or plasma measurements with standard laboratory methods.

(1) 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).

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

(3) D.B. Sacks, Carbohydrates, in Tietz Textbook of Clinical Chemistry, Second Edition, ed. C.A. Burtis and E.R. Ashwood, (Philadelphia: W.B. Saunders Company, 1994).

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.