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

I Background Information:

A 510(k) Number

K200492

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	21 CFR 862.1450 - Lactic acid test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification of a previously cleared device - modification to the i-STAT CG4+ (blue) cartridge on the i-STAT 1 Analyzer.

B Measurand:

PO2, PCO2, pH 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, PO2, PCO2, and 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 disturbances and metabolic and respiratory-based 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

For Point-of-Care or clinical laboratory setting

D Special Instrument Requirements:

i-STAT 1 Analyzer

IV Device/System Characteristics:

A Device Description:

The i-STAT 1 System is comprised of the i-STAT 1 Analyzer, the i-STAT test cartridges and accessories (i-STAT 1 Downloader/Recharger, electronic simulator and portable printer). The system is designed for use by trained medical professionals at the patient point of care or in the clinical laboratory and is for prescription use only.

The i-STAT CG4+ test cartridge contains test reagents to analyze venous and arterial whole blood at the point of care or in the clinical laboratory for pH, PO2 (partial pressure of oxygen), PCO2 (partial pressure of carbon dioxide), and lactate. Each i-STAT CG4+ cartridge contains a reference and ground electrode, and potentiometric and amperometric sensors for the measurement of specific analytes. It also contains a buffered aqueous calibrant solution with known concentrations of analytes and preservatives. The test is contained in a single-use, disposable cartridge. Cartridges require two to three drops of whole blood which are typically applied to the cartridge using a transfer device.

The i-STAT 1 Analyzer (previously cleared under k103195 as the i-STAT 1 Wireless Analyzer) is a handheld, in vitro diagnostic analytical device designed to run only i-STAT test cartridges. The instrument interacts with the cartridge to move fluid across the sensors and generate a quantitative result.

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 as follows:

$$pH(T_p) = pH - 0.0147(T_p - 37) + 0.0065(7.4 - pH)(T_p - 37)$$

$$PO_2(T_p) = PO_2 \times 10^{\frac{5.49\times10^{-11}\,PO_2^{\,3.88} + 0.071}{9.72\times10^{-9}\,PO_2^{\,3.88} + 2.30}(T_p - 37)}$$

$$PCO_2(T_p) = PCO_2 \times 10^{0.019(T_p - 37)}$$

Calculated Results

The i-STAT 1 Analyzer can be customized to display calculated results. These results are derived using standard equations with inputs from the directly measured i-STAT sensor results. These calculations have no effect on the directly measured test results and are provided for the convenience of the end user who would otherwise perform the calculation manually.

HCO_3: HCO_3 (bicarbonate), the most abundant buffer in the blood plasma, is an indicator of the buffering capacity of blood. Regulated primarily by the kidneys, HCO_3 is the metabolic component of acid-base balance.

$$\log HCO_3 = pH + \log PCO_2 - 7.608$$

CO_2: TCO_2 is a measure of carbon dioxide which exists in several states: CO_2 in physical solution or loosely bound to proteins, bicarbonate (HCO_3) or carbonate (CO_3) anions, and carbonic acid (H_2CO_3). Measurement of TCO_2 as part of an electrolyte profile is useful chiefly to evaluate HCO_3 concentration. TCO_2 and HCO_3 are useful in the assessment of acid-base imbalance (along with pH and PCO_2) and electrolyte imbalance. The i-STAT CG4+ can report a calculated TCO_2 according to a simplified and standardized form of the Henderson-Hasselbalch equation.

$$TCO_2 = HCO_3 + 0.03PCO_2$$

BE: Base excess of the extracellular fluid (ECF) or standard base excess is defined as the concentration of titratable base minus the concentration of titratable acid when titrating the average ECF (plasma plus interstitial fluid) to an arterial plasma pH of 7.40 at PCO_2 of 40 mmHg at 37 °C. Excess concentration of base in the average ECF remains virtually constant during acute changes in the PCO_2 and reflects only the non-respiratory component of pH disturbances.

$$BE_{ecf} = HCO_3 - 24.8 + 16.2(pH-7.4)$$

$$BE_b = (1 - 0.014*Hb) * [HCO3 - 24.8 + (1.43 * Hb + 7.7) * (pH - 7.4)]$$

sO_2: sO_2 (oxygen saturation) is the amount of oxyhemoglobin expressed as a fraction of the total amount of hemoglobin able to bind oxygen (oxyhemoglobin plus deoxyhemoglobin).

sO_2 is calculated from measured PO_2 and pH and from HCO_3 calculated from measured PCO_2 and pH. However, this calculation assumes normal affinity of oxygen for hemoglobin. It does not take into account erythrocyte diphosphoglycerate (2,3-DPG) concentrations which affect the oxygen dissociation curve. The calculation also does not take into account the effects of fetal hemoglobin or dysfunctional hemoglobins (carboxy-, met-, and sulfhemoglobin). Clinically significant errors can result from incorporation of such an estimated sO_2 value for oxygen saturation in further calculations, such as shunt fraction, or by assuming the value obtained is equivalent to fractional oxyhemoglobin.

$$sO_2 = 100 \frac{(X^3 + 150X)}{X^3 + 150X + 23400}$$

$$\text{where } X = PO_2 \bullet 10^{(0.48(pH-7.4)-0.0013(HCO_3-25))}$$

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. Either lithium heparin tube or syringe may be used. Samples should be remixed thoroughly before testing.

4. Calibration:

The CG4+ cartridge includes 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 CG4+ cartridge with the i-STAT 1 System.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Epoc BGEM, Epoc Reader, Epoc Host
ABL800 Flex

B Predicate 510(k) Number(s):

K093297, K041874

C Comparison with Predicate(s):

Device & Predicate Device(s):	K200492	K041874
Device Trade Name	pH test in the i-STAT CG4+ cartridge with the i-STAT 1 System	ABL800 FLEX pH Test
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for use in the in vitro quantification of pH in arterial or venous whole blood in point of care or clinical laboratory settings.	Same

Device & Predicate Device(s):	K200492	K041874
	pH measurements are used in the diagnosis, monitoring, and treatment of respiratory disturbances and metabolic and respiratory-based acid-base disturbances.	
Principle of Measurement	Ion selective electrode	Same
General Device Characteristic Differences	K200492	K041874
Reportable Range	7.000 – 7.700	6.300 – 8.000
Sample Type	Arterial or venous whole blood	Arterial, venous or capillary whole blood
Sample Volume	95 µL	At least 50 – 70 µL
Reagent Format	Cartridge	Reagent handling system, stored within analyzer
Calibration	1-point on-board contained within the cartridge	1-point intervals 30 min, 1 hour, 2 hours

Device & Predicate Device(s):	K200492	K041874
Device Trade Name	PO2 test in the i-STAT CG4+ cartridge with the i-STAT 1 System	ABL800 FLEX PO2 Test
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for use in the in vitro quantification of PO2 in arterial or venous whole blood in point of care or clinical laboratory settings. PO2 measurements are used in the diagnosis, monitoring, and treatment of respiratory disturbances and	Same

Device & Predicate Device(s):	K200492	K041874
	metabolic and respiratory-based acid-base disturbances.	
Principle of Measurement	Amperometric measurement of oxygen reduction current	Same
General Device Characteristic Differences	K200492	K041874
Reportable Range	15 – 530 mmHg 2.00 – 70.49 kPa	0.0 – 800 mmHg 0.00 – 107 kPa
Sample Type	Arterial or venous whole blood	Arterial, venous or capillary whole blood
Sample Volume	95 µL	At least 50 – 70 µL
Reagent Format	Cartridge	Reagent handling system, stored within analyzer
Calibration	1-point on-board contained within the cartridge	1-point intervals 30 min, 1 hour, 2 hours

Device & Predicate Device(s):	K200492	K041874
Device Trade Name	PCO2 test in the i-STAT CG4+ cartridge with the i-STAT 1 System	ABL800 FLEX PCO2 Test
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for use in the in vitro quantification of PCO2 in arterial or venous whole blood in point of care or clinical laboratory settings. pCO2 measurements are used in the diagnosis, monitoring, and treatment of respiratory disturbances and metabolic and respiratory-based acid-base disturbances.	Same

Device & Predicate Device(s):	K200492	K041874
Principle of Measurement	Ion selective electrode	Same
General Device Characteristic Differences	K200492	K041874
Reportable Range	15.0 – 130.0 mmHg 2.00 –17.29 kPa	5.0 – 250 mmHg 0.67 – 33.3 kPa
Sample Type	Arterial or venous whole blood	Arterial, venous or capillary whole blood
Sample Volume	95 µL	At least 50 – 70 µL
Reagent Format	Cartridge	Reagent handling system, stored within analyzer
Calibration	1-point on-board contained within the cartridge	1-point intervals 30 min, 1 hour, 2 hours

Device & Predicate Device(s):	K200492	K093297
Device Trade Name	Lactate test in the i-STAT CG4+ cartridge with the i-STAT 1 System	epoc BGEM, epoc READER, epoc HOST
General Device Characteristic Similarities		
Intended Use/Indications For Use	Lactate measurements are used in the diagnosis and treatment of lactic acidosis in conjunction with measurements of blood acid/base status.	Same
Principle of Measurement	Amperometric measurement of oxidized hydrogen peroxide produced by lactate oxidase activity	Same
Reportable Range	0.30 – 20.00 mmol/L 2.7 – 180.2 mg/dL	Same
General Device Characteristic Differences	K200492	K093297
Sample Type	Arterial or venous whole blood	Arterial, venous or capillary whole blood
Sample Volume	95 µL	At least 50 – 70 µL

Device & Predicate Device(s):	K200492	K093297
Reagent Format	Cartridge	Reagent handling system, stored within analyzer
Calibration	1-point on-board contained within the cartridge	1-point on-board contained within the card

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures

CLSI EP07-A3: Interference Testing in Clinical Chemistry; Approved Guideline –Third Edition

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

CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry, First Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Internal within-site precision (aqueous control material)
A single site precision study for the i-STAT pH, PO2, PCO2, and Lactate assays 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 CG4+ (blue) 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.

pH

Level	Mean	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	6.5215	0.00347	0.05	0.00228	0.03	0.00129	0.02	0.00435	0.07
L2	7.0199	0.00252	0.04	0.00040	0.01	0.00132	0.02	0.00287	0.04
L3	7.4758	0.00250	0.03	0.00098	0.01	0.00075	0.01	0.00279	0.04
L4	7.7551	0.00209	0.03	0.00071	0.01	0.00097	0.01	0.00241	0.03
L5	7.9862	0.00322	0.04	0.00118	0.01	0.00135	0.02	0.00369	0.05

PO2

Level	Mean (mmHg)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	70.2	2.08	3.0	0.70	1.0	1.08	1.5	2.45	3.5
L2	85.7	2.40	2.8	0.76	0.9	0.93	1.1	2.69	3.1
L3	120.4	2.25	1.9	1.18	1.0	0.81	0.7	2.66	2.2
L4	152.9	1.88	1.2	1.78	1.2	1.55	1.0	3.02	2.0
L5	363.4	4.15	1.1	5.07	1.4	2.40	0.7	6.98	1.9

PCO2

Level	Mean (mmHg)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	87.08	0.916	1.1	0.872	1.0	0.470	0.5	1.349	1.5
L2	59.48	0.872	1.5	0.228	0.4	0.190	0.3	0.921	1.5
L3	29.24	0.617	2.1	0.227	0.8	0.151	0.5	0.675	2.3
L4	21.14	0.521	2.5	0.141	0.7	0.118	0.6	0.552	2.6
L5	15.05	0.473	3.1	0.138	0.9	0.114	0.8	0.506	3.4

Lactate

Level	Mean (mmol/L)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	18.448	0.1505	0.8	0.0266	0.1	0.0634	0.3	0.1655	0.9
L2	7.967	0.0459	0.6	0.0132	0.2	0.0128	0.2	0.0495	0.6
L3	2.251	0.0073	0.3	0.0030	0.1	0.0021	0.1	0.0082	0.4
L4	0.924	0.0108	1.2	0.0038	0.4	0.0041	0.4	0.0122	1.3
L5	0.497	0.0123	2.5	0.0033	0.7	0.0037	0.7	0.0133	2.7

Internal within-site precision (whole blood)

A single site precision study was conducted for PO2, PCO2, pH, and Lactate using samples targeted to three levels within the test reportable range of each test. Venous whole blood collected in lithium heparinized tubes from a healthy subject was altered via tonometry and/or acid/base spiking for PO2, PCO2 and pH and via spiking or plasma replacement for lactate to prepare the different sample levels. The samples were tested using one lot of i-STAT CG4+ (blue) cartridges and 60 i-STAT 1 Analyzers. The results of the whole blood precision are shown below.

pH

Sample ID	N	Mean (pH units)	SD	%CV
S1	30	7.5465	0.00285	0.04
S2	30	7.2259	0.00511	0.07
S3	45	7.3657	0.00344	0.05

PO2

Sample ID	N	Mean (mmHg)	SD	%CV
S1	30	31.0	0.58	1.9
S2	30	239.2	3.38	1.4
S3	45	84.8	2.63	3.1

PCO2

Sample ID	N	Mean (mmHg)	SD	%CV
S1	30	21.52	0.293	1.4
S2	30	73.12	0.705	1.0
S3	45	42.69	0.762	1.8

Lactate

Sample ID	N	Mean (mmol/L)	SD	%CV
S1	10	0.578	0.0210	3.6
S2	10	3.718	0.0325	0.9
S3	12	15.809	0.0679	0.4

Point of Care precision – aqueous control material

A three 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 point of care site, testing was performed a minimum of once per day for five (5) days on six (6) i-STAT 1 Analyzers using six lots of i-STAT CG4+ (blue) cartridges. 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. Within-day, between-day and total variance components were calculated by site. These components were also calculated for all sites combined and provided in the tables below:

pH

Level	N	Mean (pH units)	Within-Day		Between-Day		Within-Site Total		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	96	6.5291	0.0042	0.07	0.0000	0.00	0.0042	0.07	0.0028	0.04	0.0051	0.08
L2	96	7.0312	0.0026	0.04	0.0005	0.01	0.0027	0.04	0.0021	0.03	0.0034	0.05
L3	98	74918	0.0019	0.02	0.0000	0.00	0.0019	0.02	0.0011	0.01	0.0022	0.03
L4	96	7.7455	0.0018	0.02	0.0001	0.00	0.0018	0.02	0.0005	0.01	0.0019	0.02
L5	96	7.9676	0.0023	0.03	0.0013	0.02	0.0026	0.03	0.0002	0.00	0.0026	0.03

PO2

Level	N	Mean (mmHg)	Within-Day		Between-Day		Within-Site Total		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	96	76.8	2.42	3.2	0.5	0.7	2.47	3.2	0.91	1.2	2.63	3.4
L2	96	89.0	2.12	2.4	0.64	0.7	2.22	2.5	0.71	0.8	2.33	2.6
L3	98	121.8	1.70	1.4	1.27	1.0	2.12	1.7	1.12	0.9	2.40	2.0
L4	96	151.4	1.48	1.0	1.66	1.1	2.22	1.5	2.20	1.5	3.13	2.1
L5	96	344.5	6.18	1.8	4.96	1.4	7.92	2.3	6.44	1.9	10.21	3.0

PCO2

Level	N	Mean (mmHg)	Within-Day		Between-Day		Within-Site Total		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	96	82.05	1.335	1.6	0.000	0.0	1.335	1.6	0.571	0.7	1.453	1.8
L2	96	57.36	0.770	1.3	0.000	0.0	0.770	1.3	0.280	0.5	0.819	1.4

Level	N	Mean (mmHg)	Within-Day		Between-Day		Within-Site Total		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L3	98	28.02	0.411	1.5	0.128	0.5	0.431	1.5	0.210	0.7	0.479	1.7
L4	96	21.43	0.346	1.6	0.210	1.0	0.405	1.9	0.132	0.6	0.426	2.0
L5	96	15.29	0.356	2.3	0.146	1.0	0.385	2.5	0.211	1.4	0.439	2.9

Lactate

Level	N	Mean (mmol/L)	Within-Day		Between-Day		Within-Site Total		Between-Site		Overall	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	96	17.74	0.238	1.3	0.104	0.6	0.260	1.5	0.204	1.1	0.330	1.9
L2	96	7.77	0.085	1.1	0.055	0.7	0.101	1.3	0.042	0.5	0.109	1.4
L3	98	2.22	0.008	0.4	0.004	0.2	0.009	0.4	0.004	0.2	0.010	0.5
L4	96	0.98	0.013	1.4	0.021	2.1	0.025	2.5	0.015	1.5	0.029	2.9
L5	96	0.58	0.018	3.0	0.027	4.7	0.032	5.6	0.021	3.7	0.039	6.7

Point of Care Precision (Whole Blood)

Whole blood precision was evaluated using venous and arterial whole blood specimens collected with lithium heparin. The repeatability analysis was conducted using the data collected across multiple point of care sites. The mean values for each sample were divided into subintervals for each sample type. The results are provided below:

Precision for venous and arterial whole blood

Analyte	Units	Sample Type	Sample Range	N	Mean	SD	CV (%)
pH	pH units	Venous Whole Blood	<7.30	20	7.202	0.0064	0.09
			7.30 – 7.45	77	7.374	0.0060	0.08
			>7.45	7	7.585	0.0030	0.04
		Arterial Whole Blood	<7.30	22	7.259	0.0059	0.08
			7.30 – 7.45	119	7.389	0.0060	0.08
			>7.45	36	7.494	0.0047	0.06
PO_2	mmHg	Venous Whole Blood	<50	59	28.8	0.9	3.0
			50 - 100	27	58.2	2.0	3.4
			100 - 250	4	188.6	1.4	0.7
			>250	6	450.0	12.4	2.8
		Arterial Whole Blood	<50	2	40.3	0.5	1.2
			50 - 100	65	77.5	3.4	4.4
			100 - 250	78	156.6	3.7	2.4
			>250	33	355.6	8.5	2.4
PCO_2	mmHg	Venous Whole Blood	<35	6	16.83	0.29	1.7
			35 - 62.5	83	46.23	0.77	1.7
			>62.5	26	91.61	0.73	0.8
		Arterial Whole Blood	<35	33	31.23	0.51	1.6
			35 - 62.5	140	42.65	0.90	2.1
			>62.5	4	74.36	0.37	0.5
Lactate	mmol/L	Venous Whole Blood	<1.0	50	0.70	0.016	2.26
			1.0 – 5.0	62	1.83	0.021	1.14
			>5.0	11	12.88	0.200	1.55
		Arterial Whole Blood	<1.0	57	0.72	0.018	2.49
			1.0 – 5.0	42	1.87	0.020	1.08
			>5.0	8	8.55	0.036	0.42

2. Linearity:

The linearity study was designed based on CLSI EP06-A. The linearity of the i-STAT pH, PO2, PCO2, and Lactate tests in the i-STAT CG4+ (blue) 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. The number of i-STAT 1 Analyzers used varied; 45 for PO2, 60 for PCO2 and 31 for pH. The total number of cartridge lots used was 13, each i-STAT test utilized at least 5 of the 13 cartridge lots. Each test sample was tested in replicates of 3 per cartridge lot for a total of 15 results per level. For lactate, 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 on 100 i-STAT 1 Analyzers 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	7.0 – 7.7
PO2	5 – 530 mmHg
PCO2	15 – 130 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+ (blue) cartridge using the i-STAT 1 system was established by conducting interference testing following the recommendations in CLSI EP07-A3. 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 two concentrations of low and high for lactate (1.00 ± 0.30 mmol/L and 1.67 ± 0.30 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 at least 10 using six lots of the i-STAT CG4+ (blue) cartridges. The number of i-STAT 1 Analyzers used varied; 68 for PO2, 67 for PCO2, 80 for pH and 112 for lactate. 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	0.0287 mmol/L
Calcium	20 mg/dL
Ethanol	130 mmol/L
Ibuprofen	1.06 mmol/L
Morphine	0.0273 mmol/L
Potassium	8 mmol/L
Sodium	170 mmol/L
Bilirubin	40 mg/dL
Hemoglobin	10 g/L
Triglyceride**	1500 mg/dL
Intralipid**	2493 mg/dL
Thiopental	1660 mmol/L

**Intralipid 20% and Triglyceride were assessed using the same data set.

Lactate

Substance	Highest concentration at which no significant interference was observed
Acetaldehyde*	45 µmol/L
Acetaminophen	1.03 mmol/L
N-Acetyl-Cysteine	0.92 mmol/L
Ascorbic Acid	0.298 mmol/L
β-Hydroxybutyric Acid	6 mmol/L
Bilirubin	40 mg/dL
Dopamine	4.06 mmol/L
Formaldehyde*	0.133 mmol/L
Hemoglobin	10.0g/L
Hydroxyurea	0.405 mmol/L
Pyruvate	0.570 mmol/L
Salicylate	0.207 mmol/L
Thiocyanate	0.898 mmol/L
Triglyceride**	1500 mg/dL
Intralipid**	3423 mg/dL
Uric Acid	1.4 mmol/L

* The molecular weight of the substance tested was used to convert the test concentration from mmol/L to mg/dL. The molecular weight of each substance could vary depending on the form chosen.

**Intralipid 20% and Triglyceride were assessed using the same data set.

For those substances that on initial screening were found to interfere with lactate 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
Glycolic Acid	≥ 1.18 mmol/L	Increased lactate results
Lithium bromide	≥ 40.7 mmol/L	Decreased lactate results

The sponsor includes the following statements in the labeling for the device:

Bromide at 2.5 mmol/L is the peak plasma concentration associated with halothane anesthesia, in which bromide is released.

Glycolic acid at ≥ 1.18 mmol/L showed increased results. Glycolic acid is a product of ethylene glycol metabolism. Glycolic acid at a concentration of 10.0 mmol/L can cause increased i-STAT lactate results. At this level another method should be used to measure lactate. Unexpected increased lactate concentrations caused by glycolic acid may be a clue 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 0.97-30.6 mmol/L.

4. Assay Reportable Range:

See section A.2 Linearity.

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

Traceability
pH values assigned to the i-STAT System controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference materials SRMs 186-I, 186-II, 185, and 187.

PO2 values assigned to the i-STAT controls and calibration verification materials are traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

PCO2 values assigned to the i-STAT controls and calibration verification materials are traceable to U.S. National Institute of Standards and Technology (NIST) standard reference materials via commercially available certified specialty medical gas standards.

Lactate values assigned to the i-STAT System controls and calibration verification materials are 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 PO2, PCO2, pH, and Lactate tests using the i-STAT CG4+

(blue) cartridge on the i-STAT 1 Analyzer. The results support the sponsor's sample stability claims. The sample stability claims for PO2, PCO2, and pH are 10 minutes for samples with lithium heparin anticoagulant. The sample stability claim for lactate samples with lithium heparin anticoagulant is testing the sample immediately after collection.

6. Detection Limit:

The LoB and LoD of the i-STAT Lactate test in the i-STAT CG4+ (blue) cartridge were evaluated on the i-STAT 1 Analyzer based on CLSI EP17-A2, using whole blood that was altered to a "blank" lactate concentration for LoB testing and two "low" lactate concentrations for LoD testing. The studies were conducted across four days by four operators using two lots of i-STAT CG4+ cartridges and 60 i-STAT 1 Analyzers. 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 determined LoB and LoD for the i-STAT Lactate test on the i-STAT 1 Analyzer is shown below.

Analyte	LoB	LoD
Lactate	0.15 mmol/L	0.19 mmol/L

Linearity studies were used to support the lower end of the measuring range for pH, PO2 and PCO2 (see section M.1.b above).

The LoQ of the i-STAT pH, PO2, PCO2, and Lactate tests in the i-STAT CG4+ (blue) cartridge were evaluated on the i-STAT 1 Analyzer using whole blood that was altered using tonometry to low pH (< 7 pH units), PO2 (< 15 mmHg), PCO2 (< 15 mmHg), and by plasma replacement to low lactate (0.22 – 0.29 mmol/L) concentrations. The number of i-STAT 1 Analyzers used varied; 30 for PO2, 30 for PCO2, 31 for pH and 60 for lactate. The testing was conducted in replicates of fifteen per sample by five (5) operators for PO2 and pH, six (6) operators for PCO2, and four (4) operators for lactate using two cartridge lots for each test over three (3) days. 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
PO_2	≤ 5.00 mmHg
PCO_2	≤ 5.000 mmHg
pH	≤ 0.04000 pH units
Lactate	≤ 0.6000 mmol/L

The LoQ for each of the i-STAT pH, PO2, PCO2, and Lactate tests was determined to be below the lower limit of the reportable range for each of the i-STAT tests as shown below.

Analyte	Reportable range	LoQ
pH (pH units)	7.0 – 7.7	6.716
PO_2 (mmHg)	15 – 530	10
PCO_2 (mmHg)	15 – 130	9.7
Lactate (mmol/L)	0.30 – 20.00	0.27

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:

pH

A total of 316 whole blood specimens (111 lithium heparin venous whole blood specimens and 205 lithium heparin arterial whole blood specimens) collected at two point of care sites were tested using three lots of i-STAT CG4+ (blue) cartridges. Fourteen specimens were contrived. The data were analyzed by Passing-Bablok regression analysis comparing the first replicate of the candidate device results to the singlicate result of the predicate device. The data from combined sites is shown below.

Analyte	N	Sample Range Tested (pH units)	Slope	Intercept	r
pH	316	7.001 – 7.661	1.05	-0.34	0.97

PO2

A total of 308 whole blood specimens (103 lithium heparin venous whole blood specimens and 205 lithium heparin arterial whole blood specimens) collected at two point of care sites were tested using three lots of i-STAT CG4+ (blue) cartridges. Nine specimens were contrived. The data were analyzed by Passing-Bablok regression analysis comparing the first replicate of the candidate device results to the singlicate result of the predicate device. The data from combined sites is shown below.

Analyte	N	Sample Range Tested (pH units)	Slope	Intercept	r
PO2	308	15.4 – 480.0	1.03	-3.96	0.99

PCO2

A total of 327 whole blood specimens (122 lithium heparin venous whole blood specimens and 205 lithium heparin arterial whole blood specimens) collected at two point of care sites were tested using three lots of i-STAT CG4+ (blue) cartridges. Twenty-five specimens were contrived. The data were analyzed by Passing-Bablok regression analysis comparing the first

replicate of the candidate device results to the singlicate result of the predicate device. The data from combined sites is shown below.

Analyte	N	Sample Range Tested (pH units)	Slope	Intercept	r
PCO2	327	15.1 – 128.0	1.01	-1.29	0.99

Lactate
A total of 246 whole blood specimens (133 lithium heparin venous whole blood specimens and 113 lithium heparin arterial whole blood specimens) collected at three point of care sites were tested using two lots of i-STAT CG4+ (blue) cartridges. Twelve specimens were contrived. The data were analyzed by Passing-Bablok regression analysis comparing the first replicate of the candidate device results to the mean result of the predicate device. The data from combined sites is shown below.

Analyte	N	Sample Range Tested (pH units)	Slope	Intercept	r
Lactate	246	0.320 – 19.980	0.96	0.08	1.00

2. Matrix Comparison:

Not applicable. For use with lithium heparinized whole blood only.

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

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

***** The i-STAT System can be configured with the preferred units. Not applicable for pH test.
****** Calculated from Siggard-Andersen nomogram (1).
******* 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) 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).
(2) 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).
(3) B.E. Statland, Clinical Decision Levels for Lab Tests (Oradell, NJ: Medical Economics Books, 1987).

F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

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.