Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

k183678

B Applicant

Abbott Point of Care Inc.

C Proprietary and Established Names

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

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CGA	Class II	21 CFR 862.1345 - Glucose Test System	CH - Clinical Chemistry
CGL	Class II	21 CFR 862.1225 - Creatinine test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:
Modification of a previously cleared device — modification to the i-STAT CHEM8+ (blue) cartridge run on the i-STAT 1 Analyzer

B Measurand:
Glucose and creatinine

C Type of Test:
Quantitative amperometric assays

III Intended Use/Indications for Use:

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

B Indication(s) for Use:
The i-STAT CHEM8+ cartridge with the i-STAT 1 System is intended for use in the in vitro quantification of glucose and creatinine in arterial or venous 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.

Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

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 consists of the i-STAT 1 Analyzer and the i-STAT CHEM8+ (blue) cartridges. 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 1 Analyzer (previously cleared under k103195 as the i-STAT 1 Wireless Analyzer) is a handheld analytical device designed to run i-STAT test cartridges. The instrument interacts with the cartridge to move fluid across the sensors and generate a quantitative result.

The single-use, disposable i-STAT CHEM8+ (blue) cartridge contains test reagents to analyze whole blood at the point of care or in the clinical laboratory for glucose, creatinine, and other analytes. The cartridge format allows all the tests in the cartridge to be performed simultaneously. The cartridges contain the required sensors, a fluid pouch, a sample entry well and closure, fluid channels, waste chamber, and the necessary mechanical features for controlled fluid movement within the 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:

Creatinine on the i-STAT CHEM8+ (blue) cartridge is measured amperometrically. Creatinine (in the sample) is hydrolyzed to creatine by the enzyme creatinine amidohydrolase. Creatine is then hydrolyzed to sarcosine by the enzyme creatine amidinohydrolase. The oxidation of sarcosine, catalyzed by the enzyme sarcosine oxidase, produces hydrogen peroxide. A voltage is applied to the cartridge electrodes with current generated by the reduction of hydrogen peroxide. The current is directly proportional to the concentration of the creatinine.

Glucose on the i-STAT CHEM8+ (blue) 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.

V Substantial Equivalence Information:

A Predicate Device Name(s):
SYNCHRON Systems Glucose Reagent on UniCel DxC 600/800 SYNCHRON Clinical System; SYNCHRON Systems Creatinine Reagent on UniCel DxC 600/800 SYNCHRON Clinical System

B Predicate 510(k) Number(s):
k042291

C Comparison with Predicate(s):

Device & Predicate Device(s):	k183678	k042291
Device Trade Name	i-STAT CHEM8+ Cartridge with the i-STAT 1 System (Glucose)	SYNCHRON Systems Glucose Reagent on UniCel DxC 600/800 SYNCHRON Clinical System
General Device Characteristic Similarities	k183678	k042291
Intended Use/Indications For Use	Intended for *in vitro* quantification of glucose. Glucose measurements are used in the diagnosis, monitoring, and treatment of carbohydrate metabolism disorders including, but not limited to, diabetes	Same

	mellitus, neonatal hypoglycemia, idiopathic hypoglycemia, and pancreatic islet cell carcinoma.	
General Device Characteristic Differences	k183678	k042291
Reportable Range	20 - 700 mg/dL	0 - 600 mg/dL; (serum, plasma) up to 1200 mg/dL by sample dilution
Sample Type	Arterial or venous whole blood	Serum, plasma, urine, CSF
Sample Volume	95 µL	0.5 mL
Principle of Measurement	Amperometric	Colorimetric
Reagent Format	Cartridge	Reagent handling system, stored within analyzer

Device & Predicate Device(s):	k183678	k042291
Device Trade Name	i-STAT CHEM8+ Cartridge with the i-STAT 1 System (Creatinine)	SYNCHRON Systems Creatinine Reagent on UniCel DxC 600/800 SYNCHRON Clinical System
General Device Characteristic Similarities	k183678	k042291
Intended Use/Indications For Use	Intended for in vitro quantification of creatinine. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.	Same

General Device Characteristic Differences	k183678	k042291
Reportable Range	0.2 - 20.0 mg/dL	0.1 - 25.0 mg/dL (Serum)
Sample Type	Arterial or venous whole blood	Serum, urine
Sample Volume	95 µL	0.5 mL
Principle of Measurement	Amperometric	Colorimetric
Reagent Format	Cartridge	Reagent handling system, stored within analyzer

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP07 Interference Testing in Clinical Chemistry, 3rd Edition

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Internal site precision
A single site precision study for the creatinine and glucose assays was conducted following the recommendations in CLSI EP05. Five concentration levels of commercially available calibration verification samples were tested using one lot of i-STAT CHEM8+ (blue) cartridges and twelve i-STAT 1 Analyzers. Each sample was measured in duplicates per run, with two runs per day for 20-days resulting in a total of 80 test results per level. The results are summarized below.

Creatinine:

Level	Mean (mg/dL)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L5	0.18	0.026	14.4	0.007	3.9	0.007	0.2	0.028	15.6
L4	0.51	0.027	5.3	0.008	1.6	0.006	1.2	0.029	5.7
L3	1.69	0.033	2.0	0.008	0.5	0.007	0.4	0.035	2.1

Level	Mean (mg/dL)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L2	4.23	0.093	2.2	0.029	0.7	0.027	0.6	0.101	2.4
L1	15.90	0.321	2.0	0.096	0.6	0.030	0.2	0.337	2.1

Glucose:

Level	Mean (mg/dL)	Within-run		Between Run		Between Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	26.7	0.47	1.8	0.13	0.5	0.10	0.4	0.49	1.8
L2	40.9	0.46	1.1	0.16	0.4	0.18	0.4	0.52	1.3
L3	123.0	0.43	0.3	0.13	0.1	0.12	0.1	0.47	0.4
L4	286.5	1.25	0.4	0.55	0.2	0.33	0.1	1.40	0.5
L5	608.1	5.21	0.9	1.46	0.2	1.31	0.2	5.56	0.9

Point of Care precision – aqueous control material

A three site precision study was performed using a panel of five aqueous control solutions containing different levels of creatinine and glucose. Each sample was assayed at each site once per day for five days across each of six i-STAT 1 Analyzers for a total of 90 measurements. At each site, all testing was conducted by a different operator per site using six lots of i-STAT CHEM8+ (blue) cartridges. The results were analyzed for within-day (between-analyzer), within-site, and overall (summation of between-site, between-day and between-analyzer) variance components and provided in the tables below:

Creatinine:

Sample	Mean (mg/dL)	Within-day		Within-site		Overall	
		SD	%CV	SD	%CV	SD	%CV
Level 1	16.16	0.362	2.2	0.390	2.4	0.422	2.6
Level 2	4.21	0.085	2.0	0.088	2.1	0.091	2.2
Level 3	1.61	0.039	2.4	0.040	2.5	0.041	2.5
Level 4	0.60	0.020	3.3	0.021	3.5	0.021	3.5
Level 5	0.20	0.024	12.0	0.024	12.0	0.024	12.0

Glucose:

Sample	Mean (mg/dL)	Within-day		Within-site		Overall	
		SD	%CV	SD	%CV	SD	%CV
Level 1	27.0	0.55	2.0	0.81	3.0	1.01	3.7
Level 2	40.5	0.68	1.7	0.82	2.0	0.91	2.2
Level 3	124.4	0.58	0.5	0.64	0.5	0.64	0.5
Level 4	291.0	1.34	0.5	1.91	0.7	2.19	0.8
Level 5	609.6	11.30	1.9	11.85	1.9	11.85	1.9

Point of Care precision – whole blood

A three site precision study was performed using lithium heparin venous whole blood samples targeted to four different concentration levels of creatinine or glucose. For creatinine, a total of 14 native and nine contrived samples were tested using one cartridge lot common to all sites. For glucose, a total of 14 native and four contrived samples were tested using one cartridge lot common to all sites. Each sample was tested three times on each of

seven analyzers on one day for a total of 21 results. Certain samples had fewer replicates due to non-reportable errors, identified by the test system as quality check codes (QCCs) or star outs. A total of 14 i-STAT 1 Analyzers were used per site, and all testing was completed by the same operator at each site for a total of three operators. The results were analyzed for variance from within-analyzer (repeatability) and total (combined within-analyzer and between-analyzer variance components). Results are summarized in the tables below.

Creatinine:

				Within-analyzer		Total	
Concentration (mg/dL)	Site	N	Mean (mg/dL)	SD	%CV	SD	%CV
< 1	01	21	0.82	0.038	4.6	0.044	5.4
	01	21	0.60	0.038	6.3	0.038	6.3
	01	21	0.52	0.049	9.4	0.049	9.4
	02	20	0.96	0.049	5.1	0.051	5.3
	02	21	0.96	0.053	5.5	0.053	5.5
	02	21	0.56	0.058	10.4	0.058	10.4
	02	21	0.87	0.044	5.1	0.049	5.6
	03	21	0.81	0.031	3.8	0.031	3.8
	03	21	0.70	0.031	4.4	0.032	4.6
	03	21	0.59	0.031	5.3	0.031	5.3
1-15	03	21	1.23	0.049	4.0	0.049	4.0
	03	21	1.17	0.049	4.2	0.049	4.2
1.5-2.0	01	21	1.53	0.049	3.2	0.049	3.2
	02	14	1.83	0.053	2.9	0.053	2.9
	02	21	1.97	0.062	3.1	0.062	3.1
	03	21	1.70	0.058	3.4	0.058	3.4
5.0-7.0	01	21	5.62	0.172	3.1	0.172	3.1
	02	21	6.31	0.246	3.9	0.246	3.9
	03	21	5.30	0.072	1.4	0.072	1.4
7.0-12	02	21	9.47	0.127	1.3	0.155	1.6
>12	01	21	14.37	0.388	2.7	0.388	2.7
	02	21	14.90	0.515	3.5	0.515	3.5
	03	21	14.30	0.558	3.9	0.558	3.9

Glucose

				Within-analyzer		Total	
Concentration (mg/dL)	Site	N	Mean (mg/dL)	SD	%CV	SD	%CV
30-110	01	21	95.3	0.98	1.0	0.98	1.0
	01	21	72.3	1.23	1.7	1.23	1.7
	02	21	95.1	0.90	0.9	0.90	0.9
	02	21	95.5	0.69	0.7	0.69	0.7
	02	21	80.0	0.38	0.5	0.38	0.5
	03	21	101.3	0.76	0.8	0.76	0.8
	03	21	87.8	0.58	0.7	0.58	0.7

				Within-analyzer		Total	
Concentration (mg/dL)	Site	N	Mean (mg/dL)	SD	%CV	SD	%CV
	03	21	98.9	0.58	0.6	0.63	0.6
111-150	01	21	148.2	0.62	0.4	0.62	0.4
	02	20	143.0	0.85	0.6	0.85	0.6
	02	14	143.3	1.25	0.9	1.25	0.9
	03	21	142.2	0.79	0.6	0.79	0.6
151-400	01	21	385.7	2.38	0.6	2.98	0.8
	02	21	318.0	3.25	1.0	3.25	1.0
	03	21	151.8	1.02	0.7	1.02	0.7
401-700	01	21	618.4	7.95	1.3	7.95	1.3
	02	21	444.2	2.23	0.5	2.23	0.5
	03	21	582.0	2.82	0.5	2.93	0.5

2. Linearity:

The linearity of the creatinine and glucose assays on the i-STAT CHEM8+ (blue) cartridge was evaluated following the recommendations in CLSI EP06-A. Lithium heparin venous whole blood was obtained from a healthy subject and 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. Each sample was measured in replicates of 15 using five lots of i-STAT CHEM8+ (blue) cartridges. An assessment of linearity was performed using polynomial regression analysis.

For creatinine, regression analysis found that at each level, the deviation from linearity was less than 0.15 mg/dL or 7.5%.

For glucose, regression analysis found that at each level, the deviation from linearity was less than 3 mg/dL or 5%.

Linear regression analysis results for all five lots combined are presented in the tables below.

Creatinine:

Range tested (mg/dL)	Slope	Intercept	R^2
0.13 – 21.32	0.97	0.11	1.00

Glucose:

Range tested (mg/dL)	Slope	Intercept	R^2
16.5 – 821	1.00	-2.14	1.00

The observed proportional response supports the claim that the creatinine and glucose assays on the i-STAT CHEM8+ (blue) are linear across the measurement ranges of:

Creatinine: 0.2 - 20.0 mg/dL
Glucose: 20 - 700 mg/dL

3. Analytical Specificity/Interference:

The analytical specificity of the creatinine and glucose assays on the i-STAT CHEM8+ (blue) cartridge was established by conducting interference testing following the recommendations in CLSI EP07 ED3. Interference from certain exogenous and endogenous substances was assessed using lithium heparin venous whole blood samples spiked to two concentrations of low and high: creatinine (0.6 mg/dL, 2.0 mg/dL) and glucose (40 mg/dL, 220 mg/dL). 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 one lot of the i-STAT CHEM8+ (blue) cartridges. 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 Creatinine: ± 0.3 mg/dL up to 2 mg/dL and ± 15% above 2 mg/dL

For Glucose: greater of ± 6 mg/dL or ± 10%

For any substances identified as an interferent, a dose response analysis was performed to assess the highest concentration without significant error, as defined above.

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

Creatinine:

Substance	Highest concentration at which no interference was observed
Acetaldehyde	0.2 mg/dL
Acetaminophen	15.6 mg/dL
N-Acetyl-L-Cysteine	15.0 mg/dL
L-Ascorbic Acid	5.25 mg/dL
β-Hydroxybutyric Acid	62.5 mg/dL
Bicarbonate	294 mg/dL
Bilirubin	40 mg/dL
Calcium Chloride	20 mg/dL
Creatine	5.01 mg/dL
Dopamine Hydrochloride	0.0621 mg/dL
Formaldehyde	0.399 mg/dL
Glycolic Acid	76.0 mg/dL
Hemoglobin	1000 mg/dL
Lithium Lactate	90 mg/dL
Methyldopa	2.25 mg/dL
pH	8.0 pH units
Lithium Pyruvate	5 mg/dL
Lithium Salicylate	2.86 mg/dL
Sodium Thiosulfate	264 mg/dL
Triglyceride	1500 mg/dL
Uric Acid	23.5 mg/dL

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

Substance	Concentration	Interference
Lithium bromide	≥ 159 mg/dL (18.3 mmol/L)	Increased creatinine results
Hydroxyurea	≥ 0.23 mg/dL (0.03 mmol/L)	Increased creatinine results

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

Lithium Bromide at ≥ 18.3 mmol/L showed increased creatinine results. 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 at ≥ 0.03 mmol/L showed increased creatinine results. Hydroxyurea is a DNA synthesis inhibitor used in the treatment 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 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

Glucose:
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
Lithium Acetoacetate	20 mg/dL
N-Acetyl-L-Cysteine	15.0 mg/dL
Ammonium Chloride	10.7 mg/dL
L-Ascorbic Acid	5.25 mg/dL
Bilirubin	40 mg/dL
Cholesterol	400 mg/dL
Creatinine	15 mg/dL
Dopamine Hydrochloride	0.0621 mg/dL
Ethanol	600 mg/dL
Lithium Fluoride	0.12 mg/dL
Formaldehyde	0.399 mg/dL
Fructose	18 mg/dL
Galactose	60 mg/dL
Gentamicin Sulfate	3 mg/dL
Glucosamine Hydrochloride	0.647 mg/dL
Glutathione, reduced	3 mEq/L

Substance	Highest concentration at which no interference was observed
Acetaldehyde	0.2 mg/dL
Acetaminophen	15.6 mg/dL
Lithium Acetoacetate	20 mg/dL
N-Acetyl-L-Cysteine	15.0 mg/dL
Glycolic Acid	76.0 mg/dL
Guaifenesin	0.45 mg/dL
Hemoglobin	1000 mg/dL
Sodium Heparin	330 U/dL
β-Hydroxybutyric Acid	62.5 mg/dL
Ibuprofen	21.9 mg/dL
Isoniazid	6 mg/dL
Lithium Lactate	90 mg/dL
Mannose	18.0 mg/dL
Maltose	360 mg/dL
pH	8.0 pH units
Lithium Pyruvate	5 mg/dL
Lithium Salicylate	2.86 mg/dL
Lithium Thiocyanate	5.22 mg/dL
Sodium Thiosulfate	264 mg/dL
Triglyceride	1500 mg/dL
Uric Acid	23.5 mg/dL
Xylose	45.0 mg/dL
Gentisic Acid	1.50 mg/dL

For those substances that on initial screening where 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:

Substance	Concentration	Interference
Lithium bromide	≥ 102 mg/dL (11.8 mmol/L)	Decreased glucose results
Hydroxyurea	≥ 0.61 mg/dL (0.08 mmol/L)	Increased glucose results

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

Lithium Bromide at ≥ 11.8 mmol/L showed decreased results. 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 at ≥ 0.08 mmol/L showed increased results. Hydroxyurea is a DNA synthesis inhibitor used in the treatment 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 100 to

500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

Hematocrit (glucose only):
A study was performed with the i-STAT CHEM8+ (blue) cartridge glucose assay to assess the effect of hematocrit on the reported result. Lithium heparin venous whole blood samples were collected from 8 donors. Across the donors, eight samples were prepared with 4 glucose levels (32-40, 110-118, 255-268, 644-674 mg/dL). Each of samples was further altered to three hematocrit levels of low, mid, and high (15-17%, 43-45%, and 71-75%) for a total of 24 samples. Each sample was measured in replicates of 20 using one lot of i-STAT CHEM8+ (blue) cartridges and one i-STAT Analyzer. The hematocrit effect was assessed per donor by comparing the mean glucose at low hematocrit or high hematocrit to the reference glucose result - which was at the mid-level hematocrit. The results of the study demonstrated that there was no significant difference in glucose results at the extremes of the hematocrit range compared to a mid-level hematocrit.

Altitude effects
A study was conducted to assess the effect of high altitude on the i-STAT CHEM8+ (blue) cartridge creatinine and glucose assays. The study was performed inside a barometric chamber with pressure set to simulate altitudes of:

2000 m (6562 ft.) for creatinine
3000 m (9842 ft.) for glucose

Six lithium heparin venous whole blood samples (one native and five contrived) were used for creatinine testing and seven heparin whole blood samples (one native and six contrived) were used for glucose testing. For creatinine each sample was run on seven analyzers using one lot cartridges for total of 42 measurements. For glucose each sample was run on six analyzers using one lot of i-STAT CHEM8+ (blue) cartridges for total of 42 measurements. The 42 individual creatinine and glucose measurements were compared to results obtained by running the samples on comparator methods established to be insensitive to effects of altitude. The impact on the performance of the tests at altitude was assessed by Passing-Bablok regression analysis:

Analyte	Range (mg/dL)	Slope	Intercept	r
Creatinine	0.56 – 13.6	1.13	-0.25	1.00
Glucose	21.5 – 683	1.00	-2.26	1.00

Oxygen sensitivity
A study was conducted to assess the effect of blood oxygen on the i-STAT CHEM8+ (blue) cartridge for the creatinine and glucose assays. Lithium heparin venous whole blood samples from two donors per analyte were altered to achieve four analyte levels (creatinine: 0.6, 2.5, 8.8, and 15 mg/dL and glucose: 30, 100, 260, and 550 mg/dL). The samples were further divided to two oxygen levels prepared by tonometry; high (>500 mmHg) and low (creatinine: 20-30 mmHg and glucose: 24-26 mmHg). For creatinine, each sample was measured in replicates of 12 on 12 i-STAT 1 Analyzers using one lot of i-STAT CHEM8+ (blue) cartridges. For glucose, each sample was measured in replicates of 12 on 12 i-STAT 1

Analyzers using one lot of i-STAT CHEM8+ (blue) cartridges. The results of the study demonstrated no significant differences in creatinine or glucose results between the high and low oxygen concentrations.

4. Assay Reportable Range:

   See section A.2 Linearity

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

   The creatinine assay on the i-STAT CHEM8+ (blue) cartridges and creatinine 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 NIST SRM 967.

   The glucose assay on the i-STAT CHEM8+ (blue) cartridges and 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 .

6. Detection Limit:

   Detection capability studies of limit of blank (LoB), limit f detection (LoD), and limit of quantitation (LoQ) for creatinine and glucose assays on the i-STAT CHEM8+ Cartridge with the i-STAT 1 Analyzer were conducted following the recommendations in CLSI EP17-A2.

   LoB
   The LoB for the i-STAT CHEM8+ (blue) cartridge for the creatinine and glucose assays was evaluated using lithium heparin venous whole blood samples that were collected from a healthy subject, and altered to create a blank sample. The sample was measured in 80 replicates across each of two i-STAT CHEM8+ (blue) cartridge lots for a total of 160 cartridges. The samples were tested over three days for creatinine and four days for glucose. The LoB was calculated using a parametric data analysis for each of the two lots. The higher of the two LoB values from each lot is reported in the labeling as the LoB.

   LoD
   The LoD for creatinine and glucose was evaluated using lithium heparin venous whole blood samples that were collected from four healthy subjects, and altered to two low concentrations of creatinine and glucose for each donor. Each of the eight samples was measured in 20 replicates per day for three days across each of two i-STAT CHEM8+ (blue) cartridge lots for a total of 320 cartridges. The samples were tested over three days for creatinine and four days for glucose. The LoD was calculated using a parametric data analysis for each of the two lots. The higher of the two LoD values from each lot is reported in the labeling as the LoD.

   LoQ
   The LoQ for creatinine and glucose was evaluated using lithium heparin venous whole blood samples that were collected on each day from a unique healthy subject. The whole blood sample was altered to four low concentrations for both creatinine and glucose. Each of the four samples was measured in 15 replicates per day for four days across each of two i-STAT

CHEM8+ (blue) cartridge lots for a total of 120 cartridges. 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 goals; given in the following table.

Analyte	Total Error goals
Creatinine	< 0.30 mg/dL
Glucose	< 6.00 mg/dL

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

Analyte	Reportable Range	LoB	LoD	LoQ
Creatinine	0.2 - 20.0 mg/dL	0.05 mg/dL	0.10 mg/dL	0.1 mg/dL
Glucose	20 - 700 mg/dL	1 mg/dL	2 mg/dL	12 mg/dL

7. Assay Cut-Off:
Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The accuracy of the creatinine and glucose assays on the i-STAT CHEM8+ (blue) cartridge on the i-STAT 1 Analyzer was evaluated by a method comparison study for agreement with the predicate devices. The study was conducted across two point of care sites.

Creatinine:
A total of 145 lithium heparin venous whole blood specimens and 32 lithium heparin arterial whole blood specimens were tested using one lot of i-STAT CHEM8+ (blue) cartridges. Eight 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:

Site	N	Sample Range Tested (mg/dL)	Regression Equation	r
1	138	0.50 - 16.10	y = 1.050x - 0.060	1.000
2	42	0.36 - 4.64	y = 1.000x - 0.055	0.990
combined	180	0.36 - 16.10	y = 1.043x - 0.062	1.000

Glucose:
A total of 145 lithium heparin venous whole blood specimens and 32 lithium heparin arterial whole blood specimens were tested using one lot of i-STAT CHEM8+ (blue) cartridges. Eight specimens were contrived. Passing-Bablok regression analysis of the total of 185 samples comparing the first replicate of the candidate device results to the singlicate result of the predicate device:

Site	N	Sample Range Tested (mg/dL)	Regression Equation	r
1	139	30 - 617	y = 0.993x - 2.18	1.000
2	46	26 - 312	y = 0.968 + 5.79	0.990
combined	185	26 - 617	y = 0.98x + 0.00	1.000

2. Matrix Comparison:
   Not applicable. Lithium heparin whole blood is the only acceptable sample type for this device.

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 and creatinine assays on the i-STAT CHEM8+ (blue) cartridge are cited from literature*:

Analyte	Reference Range
Creatinine	0.6 - 1.3 mg/dL
Glucose (fasting)	70 - 105 mg/dL

* Tietz Textbook of Clinical Chemistry and Molecular Diagnostics 4th Edition. CA Burtis, ER Ashwood, DE Bruns, ed., Elsevier Saunders Inc., 2006, page 2264.

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.