510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K261039

B Applicant

Abbott Point of Care, Inc.

C Proprietary and Established Names

i-STAT Crea cartridge with the i-STAT 1 System

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device

B Measurand:

Creatinine

C Type of Test:

Quantitative amperometric assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

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

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 settings

D Special Instrument Requirements:

i-STAT 1 Analyzer

IV Device/System Characteristics:

A Device Description:

The single-use, white disposable i-STAT Crea cartridge is used with the i-STAT 1 analyzer as part of the i-STAT 1 System to measure creatinine in arterial, venous, or capillary whole blood. The i-STAT Crea cartridges contain the required sensors, a fluid pack (calibrant pouch), a sample entry well and closure, fluid channels, waste chamber, and the necessary mechanical features for controlled fluid movement within the cartridge. The i-STAT 1 analyzer interacts with the i-STAT Crea cartridge to move fluid across the sensors and generate a quantitative result, provided as a direct readout of numerical values. Cartridges require two to three drops of whole blood applied to the cartridge.

Reagents
Each i-STAT Crea cartridge contains a ground electrode and amperometric sensor for the measurement of specific analytes. It also contains a buffered aqueous calibrant solution with known concentrations of analytes. A list of reactive ingredients relevant for the i-STAT Crea cartridge is shown below:

Sensor	Reactive Ingredient	Biological Source	Minimum Quantity
Crea	Creatinine	NA	158.4 umol/L
	Creatine Amidinohydrolase	microbial	0.01 IU
	Creatinine Amidohydrolase	microbial	0.02 IU
	Sarcosine Oxidase	microbial	0.001 IU

B Principle of Operation:

The enabling technology for the i-STAT 1 System is in the microfabricated electrochemical sensors located in the single-use disposable i-STAT cartridges. Creatinine on the i-STAT cartridge is measured amperometrically. Creatinine in the sample is hydrolyzed to creatine in a reaction catalyzed by the enzyme creatinine amidohydrolase. Creatine is then hydrolyzed to

sarcosine in a reaction catalyzed by the enzyme creatine amidinohydrolase. The oxidation of sarcosine, catalyzed by the enzyme sarcosine oxidase, produces hydrogen peroxide (H_2O_2). The liberated hydrogen peroxide is oxidized at the platinum electrode to produce a current which is proportional to the sample creatinine concentration.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Nova StatSensor Creatinine Hospital Meter System

B Predicate 510(k) Number(s):
K171059

C Comparison with Predicate(s):

Device & Predicate Device(s):	K261039	K171059
Device Trade Name	Creatinine test in the i-STAT Crea cartridge with the i-STAT 1 System	Nova StatSensor Creatinine Hospital Meter System
General Device Characteristic Similarities		
Intended Use/Indications For Use	In vitro quantification of creatinine in arterial, venous, or capillary whole blood in point of care or clinical laboratory settings.	Same
Principle of Measurement	Amperometric measurement of oxidized hydrogen peroxide	Same
Traceability	Traceable to NIST SRM967	Same
General Device Characteristic Differences		
Reportable Range	0.2 – 20.0 mg/dL	0.3 – 12.0 mg/dL
Sample Volume	65 µL	1.2 µL

VI Standards/Guidance Documents Referenced:

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

CLSI EP06-Ed2: Evaluation of Linearity of Quantitative Measurement Procedures – Second Edition.

CLSI EP07-ED3: Interference Testing in Clinical Chemistry – Third Edition.

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

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition.

CLSI EP35: Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures. 2nd Edition.

CLSI EP37: Supplemental Tables for Interference Testing in Clinical Chemistry. 2nd Edition.

CLSI EP39: A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of In Vitro Medical Laboratory Tests. 1st Edition.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
Precision studies were conducted following the recommendations in CLSI EP05-A3

Internal Precision Study (Aqueous Control Materials)
The precision of the i-STAT Creatinine test in the *i-STAT Crea* cartridge with the *i-STAT 1 System* was evaluated using five (5) levels of aqueous control materials. The study was conducted using thirteen (13) analyzers and one (1) test cartridge lot over at least 20 days at one (1) site. Repeatability, between-run, between-day, and within-laboratory precision were estimated for each level. The results are shown below.

20-day precision of the i-STAT Crea cartridge on the i-STAT 1 analyzer

Test (units)	Fluid Level	N	Mean	Repeatability		Between-Run		Between-Day		Within-Laboratory	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV
Crea (mg/dL)	L1	82	16.46	0.363	2.20	0.005	0.03	0.245	1.49	0.438	2.66
	L2	83	4.38	0.101	2.31	0.033	0.74	0.039	0.88	0.113	2.58
	L3	83	1.67	0.034	2.06	0.000	0.00	0.015	0.88	0.037	2.24
	L4	82	0.46	0.019	4.22	0.004	0.89	0.007	1.49	0.021	4.57
	L5	81	0.23	0.020	8.31	0.009	3.80	0.003	1.46	0.022	9.25

Levels tested for creatinine have more than 80 replicates due to additional cartridges run.

Lot-to-Lot Precision

The precision of the i-STAT Creatinine test in the *i-STAT Crea* cartridge with the *i-STAT 1 System* across multiple cartridge lots was evaluated at one site. The study was conducted using three (3) lots of *i-STAT Crea* cartridges, each lot tested in five (5) replicates over five (5) non-consecutive days with aqueous control materials using 15 i-STAT 1 analyzers. The results of the lot-to-lot precision study for the *i-STAT Crea* cartridge on the *i-STAT 1 System* are shown below.

Lot-to-Lot Precision of i-STAT Crea Cartridge on the i-STAT 1 Analyzer											
Test (units)	**Level**	**N**	**Mean**	**Repeatability**		**Between-Lot**		**Between-Day**		**Within-Laboratory**	
				SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Crea (mg/dL)	L1	75	16.74	0.285	1.7	0.217	1.3	0.148	0.9	0.388	2.3
	L2	75	4.44	0.067	1.5	0.061	1.4	0.023	0.5	0.094	2.1
	L3	75	1.66	0.028	1.7	0.030	1.8	0.006	0.4	0.042	2.5
	L4	75	0.44	0.019	4.3	0.013	2.9	0.004	0.9	0.023	5.3

Instrument-to-Instrument Precision

The precision of the i-STAT Creatinine test in the *i-STAT Crea* cartridge with the *i-STAT 1 System* across multiple *i-STAT 1* analyzers was evaluated. The study was conducted using three (3) *i-STAT 1* analyzers and one (1) lot of *i-STAT Crea* cartridges tested in five (5) replicates over five (5) non-consecutive days with aqueous control materials. The results of the instrument-to-instrument precision study for the *i-STAT Crea* cartridge on the *i-STAT 1 System* are shown below.

Instrument-to-Instrument Precision of i-STAT Crea Cartridge on the i-STAT 1 Analyzer											
Test (units)	**Level**	**N†**	**Mean**	**Repeatability**		**Between-Instrument**		**Between-day**		**Within-Laboratory**	
				SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Crea (mg/dL)	L1	77	16.39	0.370	2.26	0.000	0.0	0.198	1.21	0.420	2.56
	L2	75	4.37	0.070	1.6	0.017	0.4	0.038	0.9	0.081	1.90
	L3	75	1.67	0.030	1.78	0.000	0.0	0.015	0.92	0.033	2.01
	L4	75	0.46	0.023	5.0	0.007	1.5	0.000	0.0	0.024	5.22
	L5	76	0.23	0.026	11.6	0.003	1.3	0.003	1.3	0.027	11.70

†The N for some levels tested have more than 75 replicates due to additional cartridges run.

Multi-site, multi-day precision (aqueous materials)

Multi-site, multi-day precision testing was performed at three (3) point of care sites using a panel of aqueous material containing five levels of creatinine. At each site, each level was tested once per day by two (2) operators for five (5) days on six (6) i-STAT 1 analyzers (per site) using one (1) lot of i-STAT Crea cartridges. Repeatability, between-day, between-operator, within-site, between-site variance components, and reproducibility were calculated for all sites combined and are provided below.

Multi-site multi-day precision of the i-STAT Crea cartridge on the i-STAT 1 analyzer														
Level	N	Mean	Repeatability		Between-Day		Between-Operator		Within-Site		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	90	16.33	0.415	2.5	0.263	1.6	0.000	0.0	0.492	3.0	0.520	3.2	0.715	4.4
L2	90	3.71	0.081	2.2	0.045	1.2	0.029	0.8	0.097	2.6	0.084	2.3	0.128	3.5
L3	90	1.02	0.037	3.6	0.023	2.2	0.000	0.0	0.043	4.2	0.020	2.0	0.047	4.6
L4	90	0.49	0.025	5.1	0.014	2.9	0.000	0.0	0.029	5.8	0.003	0.6	0.029	5.9
L5	90	0.37	0.043	11.6	0.007	1.9	0.000	0.0	0.043	11.7	0.021	5.7	0.048	13.0

Precision (whole blood) at Point of Care Sites

The precision of the i-STAT Creatinine test in the i-STAT Crea cartridge on the i-STAT 1 System was evaluated using whole blood specimens in point-of-care settings at multiple clinical sites. At each site, anticoagulated arterial, venous, or capillary whole blood specimens were tested in duplicate. For each sample type, the specimens were grouped into subintervals of the creatinine test reportable range for analysis. The results are summarized below.

Whole blood precision of venous, arterial, and capillary whole blood for the i-STAT Crea cartridge on the i-STAT 1 analyzer						
Test (units)	Sample Type	Sample Range	N	Mean	SD	%CV
Crea (mg/dL)	Venous Whole Blood	0.2-1.0	66	0.76	0.040	5.23
		>1.0-2.0	25	1.38	0.040	2.89
		>2.0-7.5	32	3.92	0.070	1.78
		>7.5-12.0	16	9.68	0.108	1.11
		>12.0-20.0	27	15.76	0.292	1.85
	Arterial Whole Blood	0.2-1.0	146	0.73	0.037	5.00
		>1.0-2.0	105	1.35	0.045	3.31
		>2.0-7.5	82	3.68	0.067	1.83
		>7.5-12.0	14	9.25	0.154	1.66
		>12.0-20.0	14	15.07	0.280	1.86
	Capillary Whole Blood	0.2-1.0	94	0.72	0.048	6.69
		>1.0-2.0	24	1.32	0.054	4.10
		>2.0-7.5	26	4.07	0.105	2.57
		>7.5-12.0	10	9.26	0.297	3.20
		>12.0-20.0	7	15.30	0.245	1.60

2. Linearity:

The linearity study was conducted following the recommendations in CLSI EP06-Ed2. The linearity of the i-STAT Creatinine test in the i-STAT Crea cartridge with the i-STAT 1 System was evaluated using five lots of i-STAT CREA cartridges, 30 i-STAT 1 analyzers, and venous whole blood collected with lithium heparin from one healthy donor, altered to 11 creatinine levels ranging from <0.2 mg/dL to > 20.0 mg/dL. Each sample level was tested in replicates of three for each of the five i-STAT CREA cartridge lots (for a total of 15 results per level) on i-STAT 1 analyzers. The data was analyzed using weighted least square linear regression. The observed non-linearity within the reportable range did not exceed ±7.23%.

Regression summary for the creatinine test in the i-STAT Crea cartridge on the i-STAT 1 analyzer						
Test	**Units**	**Reportable Range**	**Range Tested**	**Slope**	**Intercept**	**R^2**
Creatinine	mg/dL	0.2 – 20.0	0.14 – 22.92	0.999	0.024	0.999

The results support the linearity of the i-STAT Creatinine test in the i-STAT Crea cartridge on the i-STAT 1 System over the reportable range of 0.2 – 20.0 mg/dL.

3. Analytical Specificity/Interference:

Interference

The analytical specificity of the i-STAT Creatinine test in the *i-STAT Crea c*artridge with the *i-STAT 1 System* was evaluated by conducting interference testing following the recommendations in CLSI EP07 ED3. Interference from potentially interfering substances was assessed using lithium heparin venous whole blood samples spiked to two concentrations of low (0.5 – 1.1 mg/dL) and high (1.5 – 2.5 mg/dL) creatinine. 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 approximately 10 using four lots of the i-STAT Crea cartridge. 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: ± greater of 0.2 mg/dL, or 10% of the control mean or median (mg/dL).

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

Substance[1]	Highest concentration at which no interference was observed
Acetaldehyde[2]	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[2]	62.46 mg/dL
Bicarbonate[2]	294 mg/dL
Bilirubin, Conjugated	40 mg/dL
Bilirubin, Unconjugated	40 mg/dL
Calcium Chloride	20 mg/dL
Cefoxitin	697 mg/dL
Creatine[2]	5.01 mg/dL
Dopamine Hydrochloride	0.0621 mg/dL
Formaldehyde	0.399 mg/dL
Intralipid 20%	3527 mg/dL
Lactate (Lithium Lactate)	90 mg/dL
Methyldopa	2.25 mg/dL
pH	8.0 pH units
Pyruvate (Lithium Pyruvate)	5 mg/dL
Salicylate (Lithium Salicylate)	2.86 mg/dL
Triglyceride	1500 mg/dL

Substance[1]	Highest concentration at which no interference was observed
Uric Acid	23.5 mg/dL

[1] The compound tested to evaluate the interfering substance is presented in parenthesis.
[2] The test concentration for this substance is not included in CLSI guideline EP37 1st edition

Interfering Substance	Interferent Testing Concentration mmol/L	Interferent Testing Concentration mg/dL	Interference	Comment
Bromide (Lithium Bromide)	2.5	21.7	No	Refer to comment below.
	37.5	325.7	Yes	Use another method. Refer to comment below.

Labeling includes the following comment:

- Bromide has been tested at two levels: a toxic level of 37.5 mmol/L and a therapeutic plasma concentration level of 2.5 mmol/L. The latter is the peak plasma concentration associated with halothane anesthesia, in which bromide is released. Abbott has not identified a therapeutic condition that would lead to levels consistent with 37.5 mmol/L. Bromide increases variability in the i-STAT Crea cartridge which leads to inconsistent results, Abbott recommends using another method for bromide concentration greater than 2.5 mmol/L.

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

Interfering Substance	Creatinine Level	Interferent Testing Concentration	Highest Concentration Tested without Interference	Interference Results
Glycolic Acid	High	10.0 mmol/L	4.9 mmol/L	Decreased results at > 4.9 mmol/L
Hemoglobin[3]	High	10 g/L	8 g/L	Decreased results at > 8 g/L
Hydroxyurea	High	0.405 mmol/L	0.02 mmol/L	Increased results > 0.02 mmol/L
	Low		0.02 mmol/L	
Nithiodote (Sodium Thiosulfate)	Low	16.7 mmol/L	14.5 mmol/L	Increased results at > 14.5 mmol/L

[3] The test concentration denotes the quantity of free hemoglobin added to the whole blood test sample.

Labeling includes the following comments:

- Glycolic acid may be present in patient samples as the primary toxic metabolite of ethylene glycol ingestion. Glycolic acid concentrations of approximately 3–10

mmol/L are consistent with clinically significant ethylene glycol exposure and may be associated with evolving 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.[1]

[1.] Porter, W. H., Crellin, M., Rutter, P. W., and Oeltgen, P. (2000) Interference by glycolic acid in the Beckman synchron method for lactate: a useful clue for unsuspected ethylene glycol intoxication. Clin Chem. 46, 874-875

- Hydroxyurea is a DNA synthesis inhibitor used in the treatment of sickle cell anemia, HIV infection, and various types of cancer. The malignancies that it is used to treat include melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera, thrombocythemia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in a patient's blood may be sustained at approximately 100 to 500 µmol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.
- Nithiodote (Sodium Thiosulfate) is indicated for the treatment of acute cyanide poisoning. The journal article titled "Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate" indicated that sodium thiosulfate could be used in the treatment of calciphylaxis indicating that "the highest concentration likely to be seen in plasma [is] after infusion of a 12.5 g dose of sodium thiosulfate pentahydrate. Assuming that the 12.5 g dose of sodium thiosulfate pentahydrate is distributed in a typical blood volume of 5 L with a hematocrit of 40%, the peak sodium thiosulfate plasma concentration expected is 16.7 mmol/L.[15]

  [15] Wendroth, S. M., Heady, T. N., Haverstick, D. M., Bachmann, L. M., Scott, M. G., Boyd, J. C., and Bruns, D. E. (2014) Falsely increased chloride and missed anion gap elevation during treatment with sodium thiosulfate. Clin Chim Acta. 431, 77-79

- The sponsor provided information to support the labeling limitation that pCO2 is a factor that may affect creatinine results. The labeling states;
  "The following manual calculation should be applied for creatinine results >2.0 mg/dL if the pCO2 value is suspected to be abnormal (i.e. <20 or >60 mmHg):
  $Creatinine_{corrected} = creatinine * (1 + 0.0025 * (PCO2 - 40))$, where pCO2 is measured in mmHg.
  No correction is required for creatinine results ≤2.0 mg/dL."

Altitude Study

Studies were conducted to evaluate the effect of altitude on the i-STAT Creatinine test in the i-STAT Crea cartridge. Evaluation of the study data showed the predicted bias observed at the medical decision levels (0.6, 1.6, and 6.0 mg/dL) between the creatinine results obtained from the i-STAT Crea cartridges tested at a simulated altitude of 10,000 feet above sea level and at sea level were between 0.5 and 3.5%. The results of the study support the claim of equivalent performance between sea level (control condition) and at an altitude of approximately 10,000 feet (ft) above sea level (test condition) when using the i-STAT Creatinine test.

Oxygen Sensitivity

Studies were conducted to evaluate the effect of oxygen on the i-STAT Creatinine test in the i-STAT Crea cartridge. Evaluation of the study data showed the difference in creatinine results at the oxygen levels evaluated were within 0.2 mg/dL or 10%. The results of the study support the claim that no impact on performance was found at oxygen levels within 24 - 605 mmHg when using the i-STAT Creatinine test.

4. Assay Reportable Range:

The claimed reportable range for the i-STAT Crea cartridge is 0.2 – 20.0 mg/dL.

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

Traceability

The creatinine assay on the i-STAT Crea cartridge with the i-STAT 1 System 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.

Sample Stability

The sponsor has provided information to support the following sample stability claims in their labeling:

- Balanced heparin anticoagulant or lithium heparin anticoagulant whole blood: 30 minutes
- Non-anticoagulant whole blood: 3 minutes at room temperature (18-30°C).

6. Detection Limit:

Detection limit studies were based on CLSI EP17-A2.

Limit of Blank and Detection (LoB/LoD)

The LoB and LoD of the i-STAT Creatinine test in the i-STAT Crea cartridge were evaluated on the i-STAT 1 analyzer. The study was conducted across four days using two lots of i-STAT CREA cartridges and whole blood samples altered to achieve a blank creatinine level for LoB testing and two low creatinine levels for LoD testing. As whole blood is not stable over multiple days, it was not possible to run the same low-level sample across multiple test events. Consequently, fresh samples were prepared for each day of testing, and the analysis was performed after all days of testing were completed.

The LoB (Cr0) sample was tested using 20 i-STAT CREA cartridges from each of the two cartridge lots on i-STAT 1 analyzers for a total of 40 test results per test event. The higher of the two LoB values from each lot is reported in the labeling as the LoB.

The LoD (Cr1, Cr2) samples were tested using 20 i-STAT CREA cartridges from each of the two cartridge lots on i-STAT 1 analyzers for a total of 40 test results per sample level per test event. 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.

Summary of LoB and LoD results for the creatinine test in the i-STAT Crea cartridge on the i-STAT 1 analyzer			
Test	**Units**	**LoB**	**LoD**
Creatinine	mg/dL	0.07	0.12

Limit of Quantitation (LoQ)

The LoQ of the i-STAT Creatinine test in the i-STAT Crea cartridge was evaluated on the i-STAT 1 analyzer using two cartridge lots and whole blood that was altered to four low creatinine levels (< 0.2 mg/dL). The study was conducted across four days. Whole blood samples from four healthy donors were altered to a low creatinine level. As whole blood is not stable over multiple days, it was not possible to run the same low-level sample across multiple test events. Consequently, fresh samples were prepared for each day of testing, and the analysis was performed after all days of testing were completed. The TE estimates for each sample and cartridge lot were calculated, and the highest result obtained was 0.0725 mg/dL. The lowest level of creatinine that met the TE goal (set as 0.3 mg/dL) for each individual cartridge lot is the LoQ value for each individual lot. The determined LoQ is the highest LoQ value from the two lots.

The LoQ for the i-STAT Creatinine test was determined to be 0.13 mg/dL, which is below the lower limit of the reportable range for the i-STAT Creatinine test as shown in the table below.

Summary of LoQ result for the creatinine test in the i-STAT Crea cartridge on the i-STAT 1 analyzer			
Test	**Units**	**Lower limit of the reportable range**	**LoQ**
Creatinine	mg/dL	0.2	0.13

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison

The method comparison study for arterial, venous, and capillary whole blood specimens on the i-STAT Crea cartridge with the i-STAT 1 System was conducted following the recommendations in CLSI EP09c-ED3. Three method comparison studies were conducted under multiple clinical study protocols.

- Heparinized arterial and venous whole blood specimens collected across multiple point of care sites and collection locations were evaluated using i-STAT Crea cartridges on the i-STAT 1 analyzer against whole blood specimens tested on a comparative method. A Passing-Bablok linear regression analysis was performed using the first replicate result from the i-STAT 1 analyzer versus the mean result from the comparative method.
- Two (2) capillary specimens collected from skin puncture with balanced heparin capillary tubes from subjects 18 years or older across multiple point of care sites were

evaluated and analyzed in singlicate on the i-STAT Crea cartridge on the i-STAT 1 analyzer against a venous whole blood specimen from the same subject on the comparative method.

- Two (2) capillary specimens collected from heelstick puncture with balanced heparin capillary tubes from neonate subjects across multiple point of care sites were evaluated and analyzed in singlicate on the i-STAT Crea cartridge on the i-STAT 1 analyzer and on the comparative method.

A Passing-Bablok linear regression analysis was performed using the results of each sample type from the *i-STAT Crea* cartridge versus the comparative method results. Method comparison results for 364 arterial, 168 venous, and 168 capillary whole blood specimens are shown below.

Method comparison results for arterial, venous, and capillary specimens						
Test	**Sample Type**	**Comparative Method**	**N**	**Slope**	**Intercept**	**r**
Creatinine (mg/dL)	Arterial	i-STAT CHEM8+	364	0.98	0.01	1.00
	Venous	i-STAT CHEM8+	168	0.99	0.01	1.00
	Capillary	epoc Blood Analysis System (capillary) or i-STAT CHEM8+ (venous)	168	1.00	0.00	1.00

The predicted bias at the medical decision levels, 0.6, 1.6, and 6.0 mg/dL, was reviewed and found to be acceptable.

2. Matrix Comparison:

The matrix comparison studies were conducted following the recommendations in CLSI EP35.

To evaluate the performance of the i-STAT Creatinine test in the i-STAT Crea cartridge on the i-STAT 1 System comparing whole blood specimens collected without anticoagulant (candidate specimen) to samples collected with balanced heparin or lithium heparin anticoagulant (primary specimen), a total of 354 matched whole blood samples were tested which included native arterial (n=182) and native venous (n=155) specimens.

Two (2) native whole blood specimens (venous or arterial) were collected from each subject using one of the following sets of collection devices:

Venous or arterial specimens were collected in one (1) non-anticoagulated syringe (candidate specimen collection device) and one (1) heparin syringe (primary specimen collection device).

For some subjects, venous specimens were collected in one (1) non-anticoagulated tube (candidate specimen collection device) and one (1) evacuated heparin tube (primary specimen collection device).

Non-anticoagulated whole blood specimens were collected from 17 subjects to prepare contrived specimen pairs (candidate and primary specimens) for testing. Specimens were contrived to achieve adequate distribution of creatinine levels across the reportable range of 0.2–20.0 mg/dL. Specimens with high creatinine

concentrations were contrived by adding an appropriate amount of creatinine spike solution (720 mg/dL in deionized water) to the plasma layer of the non-anticoagulated blood samples. No specimens were contrived to represent low creatinine concentrations. The contrived whole blood specimens were aliquoted into two (2) collection devices as follows: A non-anticoagulated syringe was used as candidate collection device. A heparin syringe was used as primary collection device.

Candidate specimens were tested in duplicate using two (2) i-STAT Crea cartridges on two (2) i-STAT 1 analyzers within three (3) minutes of sample collection. Primary specimens were tested in duplicate using two (2) i-STAT Crea cartridges on two (2) i-STAT 1 analyzers within 30 minutes of sample collection.

A Passing-Bablok linear regression analysis was performed using the first replicate result from the candidate (y-axis) versus the first replicate result from the primary specimen (x-axis). The regression analysis results are summarized below.

Matrix comparison results Arterial samples All sites						
Test (units)	**N***	**Candidate Specimen Range (mg/dL)**	**Primary Specimen Range (mg/dL)**	**r**	**Slope**	**Intercept**
Creatinine (mg/dL)	191	0.3-18.2	0.3-17.9	1.00	1.00	0.00

*Includes nine (9) contrived arterial specimens

Matrix comparison results Venous samples All sites						
Test (units)	**N***	**Candidate Specimen Range (mg/dL)**	**Primary Specimen Range (mg/dL)**	**r**	**Slope**	**Intercept**
Creatinine (mg/dL)	163	0.4-19.2	0.4-18.6	1.00	1.00	0.00

*Includes eight (8) contrived venous specimens

The results of non-anticoagulated venous and arterial whole blood specimens when tested using the i-STAT Crea cartridge on the i-STAT 1 analyzer supports the claim that the performance is equivalent to anticoagulated (balanced heparin or lithium heparin) venous and arterial whole blood specimens.

C Clinical Evidence:

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:

The reference range for the i-STAT Creatinine test in the *i-STAT Crea* cartridge is based on literature reference and is listed below.

Reference range				
Test	**Units**	**Reportable Range**	**Reference Range**	
			Arterial	**Venous**
Creatinine	mg/dL	0.2 – 20.0	0.6 – 1.3 [1]	
	µmol/L	18-1768	53-115	

[1] Burtis, C. A., Ashwood, E. R., and Bruns, D. E. (2006) *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*, 4th Ed. St. Louis, MO: Elsevier Saunders.

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.