510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k171247

B. Purpose for Submission:

Addition of blood urea nitrogen (BUN) and total carbon dioxide (TCO_2) tests to a previously cleared device

C. Measurand:

Blood urea nitrogen and total carbon dioxide

D. Type of Test:

Quantitative, electromechanical biosensor for TCO_2
Enzymatic potentiometric-based sensing for BUN

E. Applicant:

Epocal, Inc.

F. Proprietary and Established Names:

epoc Blood Urea Nitrogen Test
epoc Total Carbon Dioxide Test

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1770 Urea nitrogen test system
   21 CFR 862.1160 Bicarbonate/carbon dioxide test system

2. Classification:

   Class II

3. Product code:

   CDS - Electrode, Ion Specific, Urea Nitrogen
   JFL - pH Rate Measurement, Carbon-Dioxide

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indication for use below.

2. Indication(s) for use:

   The Blood Urea Nitrogen and Total Carbon Dioxide tests, as part of the epoc Blood Analysis System, is intended for use by trained medical professionals as an in vitro diagnostic device for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care.

   Blood Urea Nitrogen measurements from the epoc Blood Analysis System are used in the diagnosis and treatment of certain renal and metabolic diseases.

   Total Carbon Dioxide measurements from the epoc Blood Analysis System are used in the diagnosis and treatment of disorders associated with changes in body acid-base balance.

3. Special conditions for use statement(s):

   For prescription use and point-of-care use.
   For *in vitro* diagnostic use only.

4. Special instrument requirements:

   epoc Blood Analysis System

I. Device Description:

The epoc BUN test is being added as an additional sensor to the existing single use test card that is used with the epoc Blood Analysis System. The epoc TCO_2 test is being added based on the standard Henderson-Hasselbalch equation (using the measured pCO_2 and pH values); this test is metrologically traceable to the IFCC TCO_2 reference method. The test card is inserted into the epoc Reader and all analytical steps are performed automatically. The epoc Blood Analysis System is an *in vitro* diagnostic device system for the quantitative testing of blood gases, electrolytes, and metabolites in venous, arterial, and capillary whole blood samples. The epoc System is comprised of 3 major subsystems: epoc Host, epoc Reader and epoc BGEM Test Card. The main accessory used with the epoc System includes the epoc Care-Fill Capillary Tubes used to collect and introduce capillary blood samples into the epoc Test Card.

The epoc test card panel configuration currently includes sensors for the determination of pH, pCO_2, pO_2, Na, K, iCa, Cl, Glu, lactate, creatinine, and hematocrit in arterial, venous, and capillary blood samples cleared previously in k061597, k090109, k092849, k093297, and k113726. This premarket notification adds blood urea nitrogen (BUN) and total carbon dioxide (TCO_2) quantitation to the epoc BGEM Test Card and Blood Analysis System.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   i-STAT Chem8+ Cartridge (with i-STAT Portable Clinical Analyzer)

2. Predicate 510(k) number(s):

   k053110

3. Comparison with predicate:

Similarities		
Item	Candidate Device: epoc Blood Urea Nitrogen test and epoc Total Carbon Dioxide test (k171247)	Predicate Device: BUN and TCO_2 Tests using the i-STAT Chem8+ Cartridge (with i-STAT Portable Clinical Analyzer) (k053110)
Intended use	Intended for use by trained medical professionals as an *in vitro diagnostic device* for the quantitative testing of samples of heparinized or un-anticoagulated arterial, venous or capillary whole blood in the laboratory or at the point of care. BUN are used in the diagnosis and treatment of certain renal and metabolic diseases. TCO_2 measurements are used in the diagnosis and treatment of disorders associated with changes in body acid-base balance.	Same
Sample type	Venous, arterial and capillary whole blood	Same

Similarities		
Item	Candidate Device: epoc Blood Urea Nitrogen test and epoc Total Carbon Dioxide test (k171247)	Predicate Device: BUN and TCO_2 Tests using the i-STAT Chem8+ Cartridge (with i-STAT Portable Clinical Analyzer) (k053110)
Technology	An electrochemical multi-sensor array integrated into a single-use test that is interpreted by a handheld reader and associated software	Same
Reportable ranges (TCO_2)	5-50 mmol/L	Same

Differences		
Item	Candidate Device: epoc Blood Urea Nitrogen test and epoc Total Carbon Dioxide test (k171247)	Predicate Device: BUN and TCO_2 Tests using the i-STAT Chem8+ Cartridge (with i-STAT Portable Clinical Analyzer) (k053110)
Measured Parameter	pH; Carbon Dioxide, Partial Pressure (*p*CO2); Oxygen, Partial Pressure (*p*O2); Sodium (Na); Potassium (K); Ionized Calcium (iCa); Chloride (Cl); Glucose (Glu); Lactate (Lac); Creatinine (Crea); Hematocrit (Hct); **Blood Urea Nitrogen (BUN); Total CO2 (TCO2)**	Sodium (Na); Potassium (K); Ionized Calcium (iCa); Chloride (Cl); Glucose (Glu); Creatinine (Crea); Hematocrit (Hct); **Urea Nitrogen (BUN); Total CO2 (TCO2)**
Calculated Parameter	Bicarbonate (cHCO3-); Calculated Total Carbon Dioxide (cTCO2); (only available when measured TCO2 is not available) Base Excess (BE); Oxygen Saturation (cSO2); Alveolar Oxygen (A); Arterial Alveolar Oxygen Tension Gradient (A-a); Arterial Alveolar Oxygen Tension Ratio (a/A); Anion Gap (AGap, AGapK); Estimated Glomerular Filtration Rate (eGFR, eGRF-a); Hemoglobin (cHgb) BUN/Creatinine ratio (BUN/Crea)	Anion Gap (AnGap); Hemoglobin (Hgb)
Reportable ranges BUN	3-120 mg/dL	3-140 mg/dL

Differences		
Item	Candidate Device: epoc Blood Urea Nitrogen test and epoc Total Carbon Dioxide test (k171247)	Predicate Device: BUN and TCO_2 Tests using the i-STAT Chem8+ Cartridge (with i-STAT Portable Clinical Analyzer) (k053110)
Sample volume	At least 92 µL	95 µL

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition; 2014.

CLSI EP06-A, Evaluation of the linearity of Quantitative Measurement Procedures: a Statistical Approach; Approved Guideline—Second Edition; 2003.

CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition; 2002.

CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Third Edition; 2013.

CLSI EP17-A2, evaluation of detection capability for clinical laboratory measurement procedures; approved guideline - Second Edition.

IEC 61010-1, Safety requirements for electrical equipment for measurement, control and laboratory use – Part 1: General requirements; IECEE, 2010.

CLSI H11-A4, Procedures for the Collection of Arterial Blood Specimens; Approved Standard—Forth Edition; 2004.

L. Test Principle:

Urea Nitrogen (BUN) Sensor
The sensor module consists of an epoxy foil supporting array of foil electrode contacts on the outer side (or *contact surface*) and an array of sensor membranes on the inner side (or *sensor surface*). The epoc BUN electrode design is an enzymatic potentiometric-based sensing device. The BUN electrode uses the enzyme urease to hydrolyze urea to ammonium ions, as follows:

$$\text{Urea} + H_2O + 2H^+ + \text{Urease} \rightarrow 2NH_4^+ + CO_2$$

A potentiometric ion-selective electrode then detects the enzymatically-produced ammonium ion. The sensor is designed as a two-layer device, each layer providing the functions described above. The concentration of ammonium ions is obtained from the measured potential using the Nernst equation.

Total Carbon Dioxide
The epoc System calculates total carbon dioxide using the measured and reported values of pH and *p*CO2 according to the standard Henderson-Hasselbalch equation:

Calculated TCO_2 ($cTCO_2$) = $cHCO_3^-$ + 0.0307 x pCO_2
where: LOG $cHCO_3^-$ = pH + LOG pCO_2 – 7.608

This calculated TCO_2 ($cTCO_2$) value is metrologically traceable to the epoc pH and pCO_2 measurements, which are in turn traceable to primary standard reference materials for pH and pCO_2.

The measured TCO_2 is achieved by calibrating a function of pH and pCO_2 against the accepted IFCC Reference Measurement Procedure for Total Carbon Dioxide by mathematically modifying the calculated TCO_2 equation in order to match the IFCC reference values. Hence, the measured TCO_2 will be metrologically traceable to the IFCC TCO_2 reference method.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Internal Precision Study
The precision study was conducted following the CLSI EP5-A3 guideline. Two levels of aqueous controls were tested in duplicate on 2 separate runs per day over 20 days using 4 lots of test cards and 11 epoc Blood Analysis Systems. The total precision results are shown in the table below:

Total Precision: BUN				
Level	Mean (mg/dL)	N	SD	%CV
Low	7.1	320	0.32	4.5
High	51.7	320	1.16	2.3

Total Precision: TCO_2				
Level	Mean (mmol/L)	N	SD	%CV
L1	16.2	320	1.02	6.3
L3	30.7	320	0.92	3.0

External precision studies at POC sites:

Additional precision studies were performed at 3 point-of-care (POC) sites with multiple POC operators.

i. An external precision study was performed using three levels of commercially available controls. For each level of control, each operator ran a maximum 12 test cards from 3 lots. The results for within-run precision and total precision results are shown in the tables below:

BUN						
Level	Mean (mg/dL)	N	Within Run		Total Precision	
			SD	%CV	SD	%CV
L1	7.1	168	0.24	3.4	0.26	3.7
L2	17.7	171	0.45	2.5	1.11	6.3
L3	52.1	170	1.06	2.0	1.54	3.0

TCO_2						
Level	Mean (mmol/L)	N	Within Run		Total Precision	
			SD	%CV	SD	%CV
L1	15.9	172	0.44	2.8	0.50	3.1
L2	19.7	172	1.00	5.1	1.12	5.7
L3	30.4	169	0.58	1.9	1.05	3.4

ii. A whole blood precision study was performed using freshly collected lithium heparin venous whole blood samples. The 2 types of sample delivery methods were evaluated (syringe and capillary tubes) at all 3 POC sites. A total of 12 operators (4 operators per site) participated in the study. Within-run precision for each individual operator was calculated. The results of all sites and all operators are shown in the tables below:

BUN Whole Blood Precision: Syringe Delivery Mode					
Level	N	Range (mg/dL)	Mean (mg/dL)	SD	%CV
Lo	136	3.7 - 10.6	7.0	0.6	7.2%
Normal	136	12.5 – 35.5	17.3	0.7	4.1%
Hi	134	51.8 - 72.4	57.4	1.3	2.3%

BUN Whole Blood Precision: Capillary tube Delivery Mode					
Level	N	Range (mg/dL)	Mean (mg/dL)	SD	%CV
Lo	135	5.9 - 9.7	7.6	0.5	7.0%
Normal	135	11.9 – 20.8	15.6	0.6	3.9%
Hi	136	51.3 - 60.3	55.5	1.6	2.9%

TCO_2 Whole Blood Precision: Syringe Delivery Mode					
Level	n	Range (mmol/L)	Mean (mmol/L)	SD	%CV
Lo	136	5.0 - 15.9	10.5	0.4	3.7%
Normal	136	22.3 - 30.9	27.5	0.4	1.4%
Hi	134	33.8 - 40.0	36.5	0.6	1.5%

TCO_2 Whole Blood Precision: Capillary tube Delivery Mode					
Level	n	Range (mmol/L)	Mean (mmol/L)	SD	%CV
Lo	134	11.2 - 15.0	34.1	1.4	3.5%
Normal	137	22.4 - 28.3	25.6	0.7	2.9%
Hi	139	31.7 - 36.2	34.1	0.7	2.1%

b. Linearity/assay reportable range:

The linearity study was performed based on the CLSI EP6-A guideline. Lithium heparin whole blood samples with nine levels of analyte concentrations spanning the entire measuring range of each assay were prepared and tested. Regression analysis was performed as per CLSI EP6-A guideline; results are shown below.

BUN

Claimed Range	Test range	Slope	Intercept	R^2
3-120 mg/dL	4-120 mg/dL	1.0204	0.3996	0.9979

TCO_2

Claimed Range	Test range	Slope	Intercept	R^2
5-50 mmol/L	4-50 mmol/L	0.9032	3.3176	0.9994

The results of the linearity studies support the claimed measuring ranges described in the tables above.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability:
Calibration of the epoc system is performed using both primary and secondary NIST traceable standards.

The calibration fluid is prepared gravimetrically from pure materials and is handled anaerobically during the test card manufacturing process until it is sealed between metallized foils in each epoc test.

For TCO_2
The pCO2-pH (and hence the HCO^-) the stability in the calibration fluid as part of the epoc test card was previously cleared under k061597.

d. Detection limit:

The study was performed as per the CLSI EP17-A2 guideline. Test samples were prepared from whole blood using lithium heparin anticoagulant. 4 blank and 4 low concentration samples were each prepared separately for BUN and TCO_2. Each sample was tested using two epoc BGEM Test Cards lots over 3 days.

A minimum of 64 replicates of measurements (16 replicates x 4 samples) per lot were used to calculate the LoB, LoD, and LoQ of BUN. For TCO_2, a minimum of 60 replicates of measurements per lot were used (15 replicates x 4 samples). The LoB was calculated as the 95th percentile using the nonparametric method and a risk level, β, of 0.05. The LoD was evaluated from the lowest analyte level that had at least 95% of the replicates greater than the LoB. The limit of quantitation was determined according to accuracy goal based on total error (TE); for BUN the TE accuracy goal was 2 mg/dL and for TCO_2 of 4mmol/L. The results of the detection limits study are summarized below:

Analyte	LoB	LoD	LoQ	Claimed Range
BUN (mg/dL)	2	3	3	3 - 120
TCO_2 (mmol/L)	4	4.3	4.3	5 - 50

e. Analytical specificity:

An interferent testing of the BUN and TCO_2 measurements on the epoc Blood Analysis System was performed per the CLSI EP07-A2 guideline. Potential interferences were evaluated at BUN concentrations of 8 and 20 mg/dL and TCO_2 concentrations of 20 and 35 mmol/L. In each of these tests, human specimens were aliquoted into 2 samples. The test samples were spiked with interferent, while the control samples were spiked with the solvent of the interferent. The bias between the control sample and the test sample with added interferent was calculated. The concentration of interfering substance considered as causing no clinically significant interference is defined as a bias (difference between the test and the control sample) of: 1.77 mg/dL for BUN; 3.32 mmol/L for TCO_2 concentrations ≤20 mmol/L and 2.95 mmol/L for TCO_2 concentrations >20 mmol/L.

Summary of interference studies for BUN:
The interferences tested and found to be clinically non-significant are summarized below:

Substance tested	**Highest concentration tested showing no significant interference**
Acetaminophen	20 mg/dL

Substance tested	Highest concentration tested showing no significant interference
Acetoacetic Acid (Li salt)	21.6 mg/dL
Acetyl Salicylic Acid	65.2 mg/dL
Ammonium ions	5.35 mg/dL
Ascorbate (Na)	6.8 mg/dL
Benzalkonium Chloride	0.002%
Bilirubin Conjugated	28.8 mg/dL
Bilirubin Unconjugated	25 mg/dL
Bromide	386 mg/dL
Cefazolin (Na)	125.9 mg/dL
Ceftriaxone (Na)	96.6 mg/dL
CO2 High (NaHCO3)	630.6 mg/dL
Citrate (Na tribasic dihydrate)	588 mg/dL
Dopamine HCl	0.1 mg/dL
EDTA	744 mg/dL
Ethanol	400 mg/dL
Fluoride (Na)	399 mg/dL
Gallamine Triethiodide	4.46 mg/dL
Glucose	504 mg/dL
Glutathione oxidized	156 mg/dL
Glutathione reduced	156 mg/dL
Glycolic Acid	38 mg/dL
Hematocrit (High)	60% vs 45% (Spun)
Hematocrit (Low)	20% vs 45% (Spun)
Heparin (Na)	20 U/mL
β-Hydroxybutyrate (Na)	252 mg/dL
Hydroxyurea	15.2 mg/dL
Ibuprofen	50 mg/dL
Intralipid	500 mg/dL
Iodide (Na)	19.5 mg/dL
Lactate (Na)	74 mg/dL
L-Cysteine	12 mg/dL
L-dopa	0.5 mg/dL
Lithium (Cl)	13.5 mg/dL
Metamizole (Na)	210.8 mg/dL
Methotrexate	90 mg/dL
N-Acetyl Cysteine	163 mg/dL
Nithiodote (Na Thiosulfate)	264 mg/dL
Oxalate (K) Monohydrate	4 mg/dL
Pentothal (Na)	6.5 mg/dL
Perchlorate (Na)	12.2 mg/dL

Substance tested	Highest concentration tested showing no significant interference
pH – Low	pH <6.8
pH – High	pH>8
Protein – Low	3.5 g/dL
Protein – High	10 g/dL
Salicylic Acid (Na salicylate)	69.5 mg/dL
Thiocyanate (K)	16.7 mg/dL
Uric acid	23.5 mg/dL

Clinically significant interfering substances for BUN measurements are itemized below:

- Samples contaminated with benzalkonium salts used as coatings for in-dwelling lines may cause elevated BUN results. For proper line-flushing procedures refer to CLSI H11-A4.

- Citrate will have no significant effect up to 6.0 mmol/L (176.5 mg/dL) after which it will decrease the BUN concentration by up to 0.26 mg/dL BUN per mmol/L citrate.

- EDTA will have no significant effect up to 4.5 mmol/L (167 mg/dL) after which it will decrease the BUN concentration by up to 0.43 mg/dL BUN per mmol/L EDTA.

- Glutathione reduced will have no significant effect up to 1.7 mmol/L (52.2 mg/dL), after which it will increase the BUN concentration by up to 1.91 mg/dL BUN per mmol/L glutathione reduced. Blood glutathione (GSH) in human subjects is ~0.79-1.05 mmol/L. Long term oral glutathione reduced supplementation (250-1,000 mg/day administered for 6 months) increases glutathione plasma levels by ~0.2-8 µmol/L (~0.01-0.25 mg/dL). Short-term, oral intake of glutathione reduced does not affect plasma glutathione levels.

- β-Hydroxybutyrate will have no significant effect up to 17.2 mmol/L (216.9 mg/dL), after which it will decrease the BUN concentration by up to 0.11 mg/dL BUN per mmol/L hydroxybutyrate. The reference range for β-hydroxybutyrate in plasma is <0.4 to 0.5 mmol/L. β-hydroxybutyrate concentration over 3 mmol/L are indicative of ketoacidosis; in very severe diabetic ketoacidosis the concentration may exceed 25 mmol/L.

- Hydroxyurea will have no significant effect up to 1.3 mmol/L (9.9 mg/dL), after which it will increase the BUN concentration by up to 1.61 mg/dL BUN per mmol/L hydroxyurea. The recommended dose of hydroxyurea for patients range from 15 mg/kg/day to 30 mg/kg/day. A treatment dose of 2,000 mg/day (~30mg/kg) results in maximum plasma concentration of ~800µmol/L with oral administration and ~1 mmol/L with intravenous method.

- N-acetylcysteine will have no significant effect up to 9.2 mmol/L (150.1 mg/dL), after which it will increase the BUN concentration by up to 0.11 mg/dL BUN per mmol/L N-acetylcysteine. It has been reported that 1 mmol/L N-acetyl cysteine is therapeutically unattainable in plasma. The therapeutic level for N-acetyl cysteine is 0.3 mmol/L.

- Nithiodote will have no significant effect up to 4.1 mmol/L (64.8 mg/dL) after which it will decrease the BUN concentration by up to 0.41 mg/dL BUN per mmol/L Nithiodote. The expected peak sodium thiosulfate plasma concentration following a 12.5 g of Nithiodote is 16.7 mmol/L.

Summary of interference studies for TCO_2:
The interferences tested and found to be clinically non-significant are summarized below:

Substance tested	**Highest concentration tested showing no significant interference**
Acetaminophen	20 mg/dL
Acetoacetic Acid (Li salt)	21.6 mg/dL
Acetylsalicylic Acid	65.2 mg/dL
Ammonium ions	5.35 mg/dL
Ascorbate (Na)	6.8 mg/dL
Benzalkonium Chloride	0.001%
Bilirubin Conjugated	26.8 mg/dL
Bilirubin Unconjugated	25 mg/dL
Bromide	386 mg/dL
Cefazolin (Na)	125.9 mg/dL
Ceftriaxone (Na)	96.6 mg/dL
Citrate (Na tribasic dihydrate)	588 mg/dL
Dopamine HCl	0.1 mg/dL
EDTA	186mg/dL
Ethanol	400 mg/dL
Fluoride (Na)	399 mg/dL
Gallamine Triethiodide	4.46 mg/dL
Glucose	504mg/dL
Glutathione oxidized	156 mg/dL
Glutathione reduced	156 mg/dL
Glycolic Acid	38 mg/dL
Hematocrit (High)	60% vs 45% (Spun)
Hematocrit (Low)	20% vs 45% (Spun)
Heparin (Na)	20 U/mL
β-Hydroxybutyrate (Na)	252 mg/dL
Hydroxyurea	15.2 mg/dL

Substance tested	Highest concentration tested showing no significant interference
Ibuprofen	50 mg/dL
Intralipid	500 mg/dL
Iodide (Na)	19.5 mg/dL
Lactate (Na)	74 mg/dL
L-Cysteine	12 mg/dL
L-dopa	0.5 mg/dL
Lithium (Cl)	13.5 mg/dL
Metamizole (Na)	210.8 mg/dL
Methotrexate	90 mg/dL
N-Acetyl Cysteine	163 mg/dL
Nithiodote (Na Thiosulfate)	264 mg/dL
Oxalate (K) Monohydrate	4 mg/dL
Pentothal (Na)	6.5 mg/dL
Perchlorate (Na)	12.2 mg/dL
pH – Low	pH <6.8
Protein – Low	3.5 g/dL
Protein – High	10 g/dL
Salicylic Acid (Na salicylate)	69.5 mg/dL
Thiocyanate (K)	16.7 mg/dL
Uric acid	23.5 mg/dL

Clinically significant interfering substances for TCO_2 measurements are itemized below:

- Samples contaminated with benzalkonium salts used as coatings for in-dwelling lines may cause significant decrease in TCO_2 results. For proper line-flushing procedures refer to CLSI H11-A4.

- Citrate will have no significant effect up to 11.8 mmol/L (347.0 mg/dL) after which it will increase the TCO_2 concentration by up to 0.24 mmol/L TCO_2 per mmol/L citrate.

- EDTA will have no significant effect up to 4.8 mmol/L (178.7 mg/dL) after which it will increase the TCO_2 concentration by up to 0.57 mmol/L TCO_2 per mmol/L EDTA.

- N-acetyl cysteine will have no significant effect up to 9.6 mmol/L (156.7 mg/dL) after which it will increase the TCO_2 concentration by up to 0.54 mmol/L TCO_2 per mmol/L N-acetyl cysteine. It has been reported that 1 mmol/L N-acetyl cysteine is therapeutically unattainable in plasma. The therapeutic level for N-acetyl cysteine is 0.3 mmol/L.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were performed at 3 POC sites by POC operators. Lithium heparin venous and arterial whole blood samples and fresh capillary whole blood samples were analyzed for BUN using the epoc Blood Analysis System (candidate device) and compared to matched lithium heparin plasma samples analyzed using BUN assay on the Roche Cobas 8000 Modular Analyzer. Lithium heparin venous and arterial whole blood samples and fresh capillary whole blood samples were analyzed for TCO_2 using the epoc Blood Analysis System (candidate device) and the i-STAT CHEM8+/i-STAT system (predicate device). The results of the overall performance of the device at all the sites are summarized in the tables below.

BUN Regression Analysis Summary for epoc Blood Analysis System vs. Roche Cobas 8000 Modular Analyzer

Venous Samples - BUN					
	N	Intercept	Slope	R^2	Range (mg/dL)
Site 1	50	0.8	0.953	0.996	4-109
Site 2	49	0.8	0.962	0.996	4-118
Site 3	50	-0.6	1.035	0.997	4-118
All Sites	149	0.2	0.990	0.995	4-118

Arterial Samples - BUN					
	N	Intercept	Slope	R^2	Range (mg/dL)
Site 1	42	0.9	0.973	0.995	7-106
Site 2	49	0.9	0.943	0.996	8-118
Site 3	50	1.0	1.028	0.997	3-107
All Sites	141	0.9	0.977	0.994	3-118

Capillary Samples - BUN					
	N	Intercept	Slope	R^2	Range (mg/dL)
Site 1	48	0.4	1.001	0.995	5-117
Site 2	45	0.5	0.945	0.997	6-112
Site 3	50	0.0	0.995	0.998	6-118
All Sites	143	0.2	0.986	0.996	5-118

TCO_2 Regression Analysis Summary for epoc Blood Analysis System vs i-STAT-CHEM8+ Cartridges (Venous, Arterial, and Capillary Samples)

Venous Samples - TCO_2					
	N	Intercept	Slope	R^2	Range (mmol/L)
Site 1	54	-0.80	1.041	0.978	10-49
Site 2	60	-5.60	1.146	0.969	11-45
Site 3	50	-1.30	1.057	0.957	13-45
All Sites	164	-2.80	1.086	0.953	10-49

Arterial Samples - TCO_2					
	N	Intercept	Slope	R^2	Range (mmol/L)
Site 1	53	-2.5	1.125	0.965	11-41
Site 2	53	-2.3	1.098	0.972	7-44
Site 3	54	-0.8	1.024	0.974	19-41
All Sites	160	-1.8	1.079	0.966	7-44

Capillary Samples - TCO_2					
	N	Intercept	Slope	R^2	Range (mmol/L)
Site 1	103	1.7	0.947	0.949	8-49
Site 2	76	-0.12	1.029	0.946	9-49
Site 3	71	-0.36	1.053	0.954	9-47
All Sites	250	0.65	0.999	0.946	8-49

b. Matrix comparison:

A comparison was performed to demonstrate the equivalence between lithium heparin whole blood and un-anticoagulated venous whole blood and sodium heparin venous whole blood for testing BUN and TCO_2 levels. The results of linear regression for heparinized (Na heparin) vs. lithium heparin, and non-anticoagulated venous samples vs lithium heparin are shown below:

BUN				
Matrix	N	Intercept	Slope	R^2
No Additive	62	0.1	1.000	0.989
Sodium heparin	62	0.3	0.981	0.992

TCO_2				
Matrix	N	Intercept	Slope	R^2
No Additive	62	0.1	0.980	0.980
Sodium heparin	62	0.6	0.970	0.989

The results of the matrix comparison study support that lithium heparin, sodium heparin and non-anticoagulated whole blood specimens are suitable for use with the epoc Blood Urea Nitrogen Test and epoc Total Carbon Dioxide Test.

3. Clinical studies:

   a. Clinical Sensitivity:

   Not applicable.

   b. Clinical specificity:

   Not applicable.

   c. Other clinical supportive data (when a. and b. are not applicable):

   Not applicable.

4. Clinical cut-off:

   Not applicable.

5. Expected values/Reference range:

   The following expected values are provided in the product insert based on the literature:

Analyte	Reference Range
TCO_2	22-29 mmol/L (arterial)
	23-30 mmol/L (venous)
BUN	8-26 mg/dL

- Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, fourth edition, C.A. Burtis, E.R. Ashwood, and D.E. Bruns eds., Elsevier Saunders, St. Louis, 2006.
- E. Statland, Clinical Decision Levels for Lab Tests, Medical Economic Books, Oradell, Ni, 1987.
- Pruden E.L., Siggaard-Andersen 0., and Tietz N.W., Chapter 30 (Blood Gases and pH), of Tietz Textbook of Clinical Chemistry, Second Edition, ed. C.A. Burtis and E.R. Ashwood. W.B. Saunders Company, Philadelphia, 1994

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.