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

A. 510(k) Number:

K052724

B. Purpose for Submission:

This is a new submission for the clearance of an ISE reagent set.

C. Measurand:

Sodium, Potassium, Chloride, and Carbon Dioxide

D. Type of Test:

Ion specific electrode

E. Applicant:

Teco Diagnostics

F. Proprietary and Established Names:

Teco ISE Reagent Set for CS system

G. Regulatory Information:

1. Regulation section:
   21 CFR Sec. 862.1170: Chloride test system
   21 CFR Sec. 862.1600: Potassium test system
   21 CFR Sec. 862.1665: Sodium test system
   21 CFR Sec. 862.1120: Blood gases (PO2) and blood pH test system
   21 CFR Sec. 862.1150: Calibrator

2. Classification:

   Class II

3. Product code:
   CGZ - Electrode, Ion-Specific, Chloride
   CEM - Electrode, Ion-Specific, Potassium
   JGS - Electrode, Ion-Specific, Sodium

CHL – Electrode, Blood gas ($p(CO_2)$)
JIX - Calibrator

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended use(s):

   The ISE Electrolyte Buffer, Electrolyte Reference, CO2 Acid Reagent and CO_2 Alkaline Buffer are intended for use in the determination of sodium, potassium, chloride and carbon dioxide in serum on Beckman SYNCHRON® analyzers.

2. Indication(s) for use:

   Teco ISE Reagent Set is intended for quantitative measurement of Sodium, Potassium; Chloride and Carbon Dioxide in human serum samples on the Beckman CX System.

   ISE Buffer reagent is intended for quantitative measurement of Sodium, Potassium, and Chloride.

   ISE Reference Reagent is to provide reference points for Sodium, Potassium, and Chloride.

   The CO2 Acid Reagent is to release Carbon Dioxide from serum samples.

   The CO2 Buffer Reagent is to provide a reference point for Carbon Dioxide.

3. Special conditions for use statement(s):

   For Prescription Use Only

4. Special instrument requirements:

   Beckman CX System

I. Device Description:

The ISE Electrolyte buffer and ISE Electrolyte Reference maintain a constant ion activity on the glass electrode surface for sodium and the validamycin electrode surface for potassium. The addition of sample to the ISE electrolyte buffer will cause the change of ion activity and develop a potential on the ion selective electrode. The magnitude of potential change will be proportional to the concentration of sodium or

potassium.

The addition of the CO_2 Acid Reagent to the ISE Electrolyte Buffer and sample mixture acidifies the solution and releases CO_2 into solution. The CO_2 passes through the membrane, lowering the pH of CO_2 Alkaline Buffer. The decrease of pH in the alkaline buffer is proportional to the CO_2 concentration.

The ISE electrolyte buffer, ISE electrolyte reference, and CO_2 Acid Reagent are supplied in 2 liter bottles. The CO_2 Alkaline Buffer is supplied in a 500 ml bottle.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Phoenix ISE Reagents for Beckman CX systems

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

   k020364

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Chemical Principle	Measures electrolyte activity by use of ion specific electrode	Measures electrolyte activity by use of ion specific electrode
Intended Use	For the quantitative determination of Na, K, Cl, and CO_2 in serum.	For the quantitative determination of Na, K, Cl, and CO_2 in serum.
Format	Liquid, ready to use	Liquid, ready to use
Storage	Room Temperature	Room Temperature

Differences		
Item	Device	Predicate
Linearity	Na: 30 - 190 mM K: 2 - 9 mM Cl: 30 - 150 mM	Na: 30 - 200 mM K: 2 - 15 mM Cl: 30 - 200 mM

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

EP05-A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline-Second Edition

EP06-A: Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline

EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition

EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

The sample is mixed with the high ionic strength ISE Electrolyte Buffer. This dilution minimizes the variation in the activity coefficients of the analytes to be measured. As the sample passes through the flow cell, a potential is generated at the surface of the ion selective electrodes. The chloride, potassium and sodium concentrations of the sample can then be determined from these potentials using the Nerst equation.

Before the sample leaves the flow cell, it is further diluted with the CO_2 Acid Reagent. On acidification, the serum sample releases carbon dioxide. Some of this carbon dioxide diffuses through the silicone membrane of the CO_2 electrode and, as an acid anhydride, lowers the pH of the CO_2 Alkaline Buffer. The decrease of pH in alkaline buffer change is proportional to the CO_2 concentration.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Within Run precision for Teco ISE CX Reagents was determined following a modification of NCCLS EP5-A. Three commercial human serum controls were assayed on Beckman CX Systems 20 times following calibration of the instrument.

   For sodium, the within run precision studies on the low level control yielded a mean of 115 mM with a standard deviation of 0.88 mM and a %CV of 1.0. At an intermediate concentration of sodium, the within run precision studies yielded a mean of 140 mM with a standard deviation of 1.21 mM and a %CV of 1.0. At the highest level studied, the within run precision studies yielded a mean of 159 mM, a standard deviation of 1.52 mM and a %CV of 1.0.

   For potassium, the within run precision studies on the low level control yielded a mean of 2.1 mM with a standard deviation of 0.07 mM and a %CV of 3.0. At an intermediate concentration of potassium, the within run precision studies yielded a mean of 4.1 mM with a standard deviation of 0.07 mM and a %CV of 2.0. At the highest level studied, the within run precision

studies yielded a mean of 7.5 mM, a standard deviation of 0.08 mM and a %CV of 1.0.

For chloride, the within run precision studies on the low level control yielded a mean of 82 mM with a standard deviation of 1.03 mM and a %CV of 1.0. At an intermediate concentration of chloride, the within run precision studies yielded a mean of 105 mM with a standard deviation of 1.27 mM and a %CV of 1.0. At the highest level studied, the within run precision studies yielded a mean of 125 mM, a standard deviation of 1.25 mM and a %CV of 1.0.

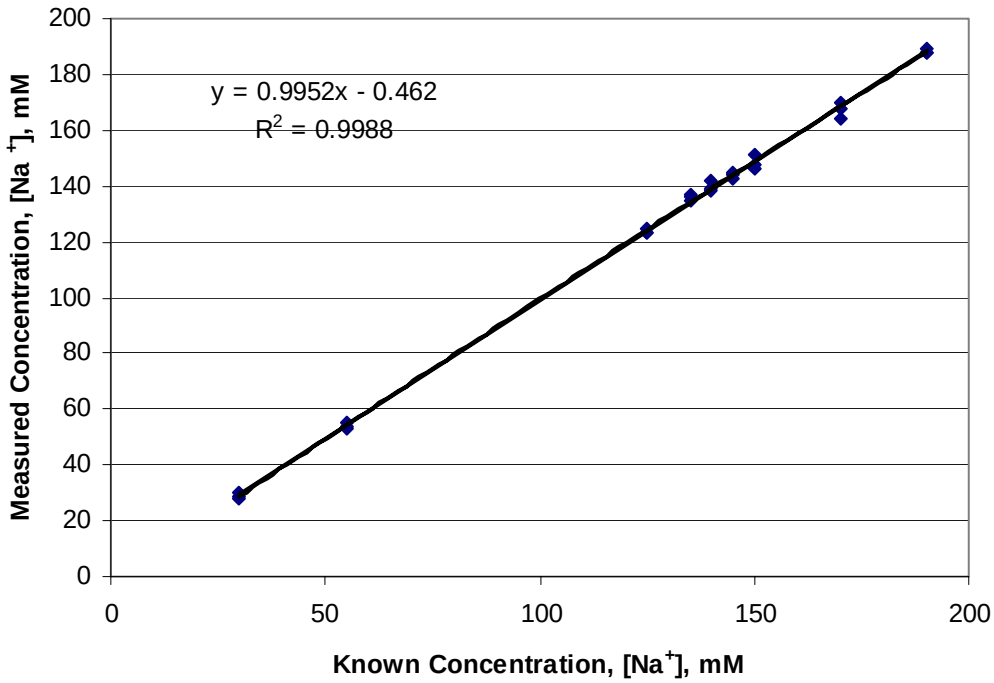
For carbon dioxide, the within run precision studies on the low level control yielded a mean of 15.7 mM with a standard deviation of 0.66 mM and a %CV of 4.0. At an intermediate concentration of carbon dioxide, the within run precision studies yielded a mean of 19.25 mM with a standard deviation of 1.02 mM and a %CV of 5.0. At the highest level studied, the within run precision studies yielded a mean of 24.75 mM, a standard deviation of 0.91 mM and a %CV of 4.0.

The run-to-run precision for Teco ISE CX Reagents was determined following a modification of NCCLS EP5-A. Three commercial human serum controls were assayed on Beckman CX Systems five times per day for five days for the total of 25 values per analyte.

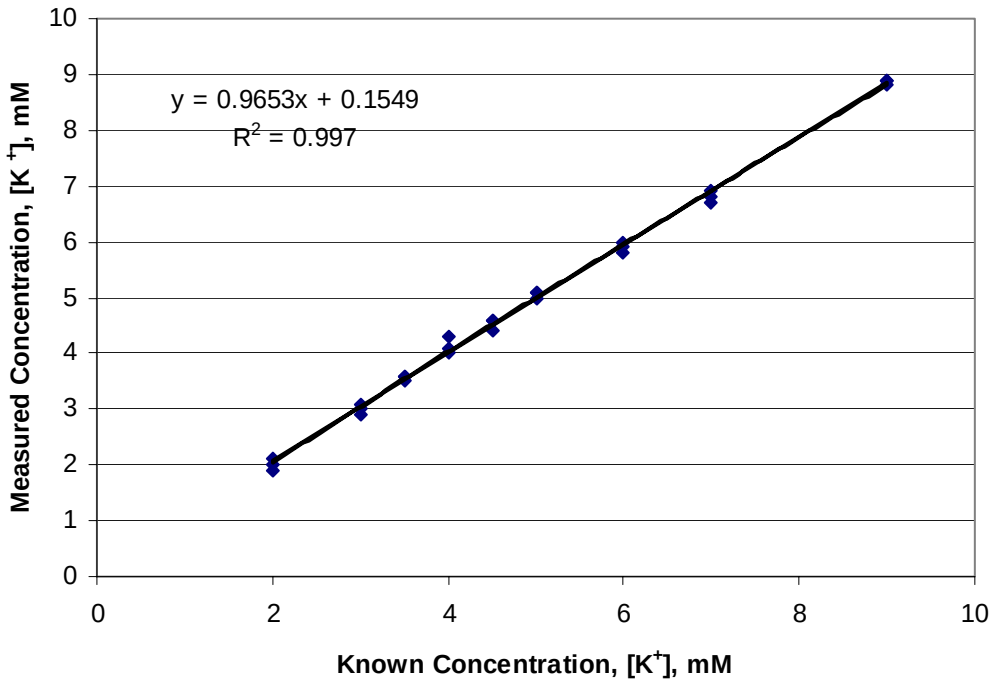
b. Linearity/assay reportable range:

Linearity studies were designed using NCCLS EP6-P. These tests were performed on Beckman CX Systems. Linearity was assessed using a commercially available kit developed to aid in the determination of linearity. Nine different concentrations spanning the range of each analyte were measured in triplicate.

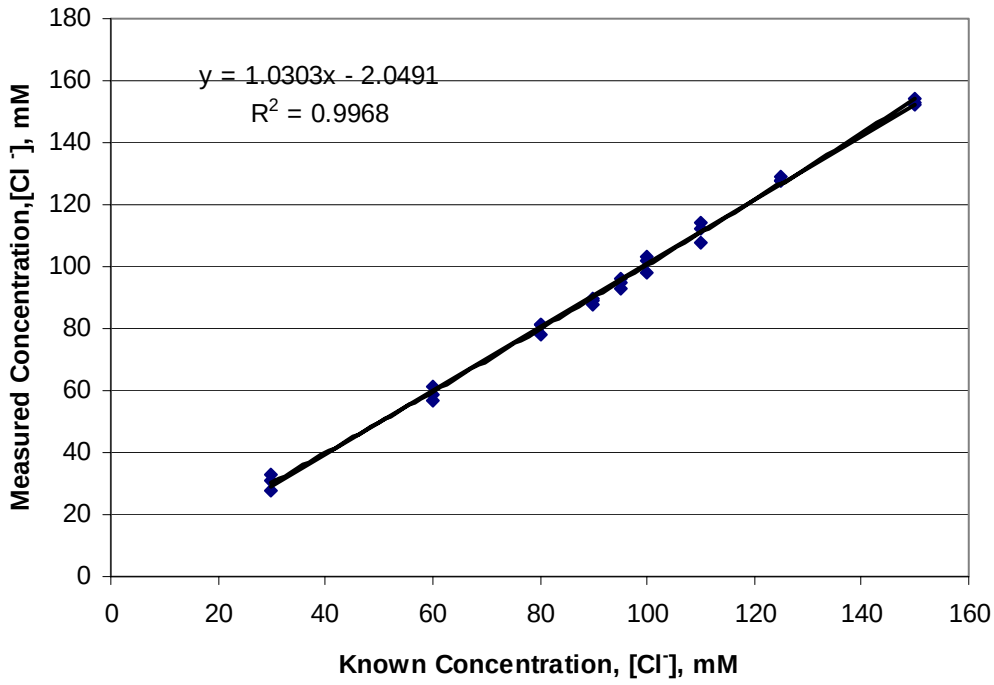
As seen in the following figure, the submitted device demonstrated a linear response to a known series of sodium concentrations ranging from 30 to 190 mM, the range claimed by the assay. There were no outliers. While fitting a 2nd order polynomial to the series did result in a slight but significant improvement to the fit, this improvement was not clinically significant.



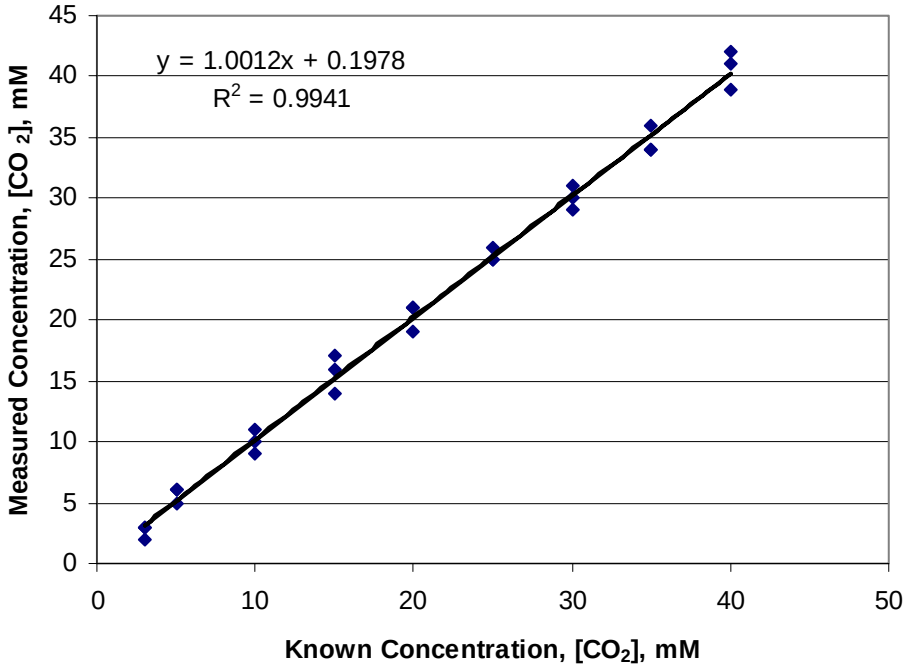
The following figure demonstrates the response of the submitted device to a series of known series of potassium concentrations, concentrations ranging from 2 to 9 mM, the range claimed by the assay. There were no outliers. Since fitting a 2nd order polynomial to the series did not result in a statistically significant improvement to the model, the company determined that the device's response over the claimed range for potassium was linear.



The following figure demonstrates the response of the submitted device to a series of known series of chloride concentrations, concentrations ranging from 30 to 150 mM, the range claimed by the assay. Using a 2nd order polynomial to model the performance of the device did not improve the clinical utility of the device. The company determined that the device's response over the claimed range for chloride was linear.



The following figure demonstrates the response of the submitted device to a series of known series of carbon dioxide concentrations, concentrations ranging from 3 to 40 mM, the range claimed by the assay. Since fitting a 2nd order polynomial to the series did not result in a statistically significant improvement to the model, the company determined that the device's response over the claimed range for carbon dioxide was linear.



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

The company assessed the stability of their reagents and controls through a combination of real-time and accelerating studies. Real-time studies were used to asses their "reagent on board" stability claim of 30 days. Their reagent set did not show a statistically significant change in performance over the 35 day span tested.

The company substantiated their estimate of the product shelf life using a combination of accelerated aging studies. Accelerated aging at 50 °C for 70 days without a clinically significant change in performance supported their claim for an 18 month shelf life at room temperature. Aging studies 37 °C for 10 days without a clinically significant change in performance supported their claim for an 18 month shelf life in refrigerated (2-8 °C) storage.

The concentration of the calibrators was determined gravimetrically using analytic grade material traceable to commercial laboratory sources.

d. *Detection limit:*

The company followed CLSI EP-17A in determining the lower limit of detection for their device. While repeated measurements on sodium-free blanks would have supported a lower detection limit, the company opted for a conservative lower limit of 2 mmol/L for sodium. Primarily because of the clinical relevance of this value, the company further limited their claim to 30

mmol/L as the lower limit of linearity for sodium for the assay. Using the CLSI guideline of 2 standard deviations from repeated measurements of their blank, the company arrived at a lower limit of detection of 0.2 mmol/L for potassium. Primarily because of the clinical relevance of this value, the company further limited their claim to 3.5 mmol/L as the lower limit of linearity for potassium. Similarly, the company found a conservative lower limit of 2 mmol/L for chloride but choose a clinically more accessible value of 30 mmol/L as their lower limit of linearity. Finally, the company determined that the lower detection limit for carbon dioxide was 0.5 mmol/L using their device. The company opted for a more clinically accessible value of 3 mmol/L as the lower limit of linearity for their assay.

e. Analytical specificity:

The company followed CLSI EP07-A2: "Interference Testing in Clinical Chemistry" in determining the number of sample to measure when evaluating interference.

Following this CLSI guideline, they determined that at the stated concentrations, the following species:

Species	**Concentration**
Hemoglobin	100 mg/dL
Bilirubin	30 mg/dL
Triglyceride	1800 mg/dL

did not statistically interfere with the performance of the device.

f. Assay cut-off:

Not applicable**.**

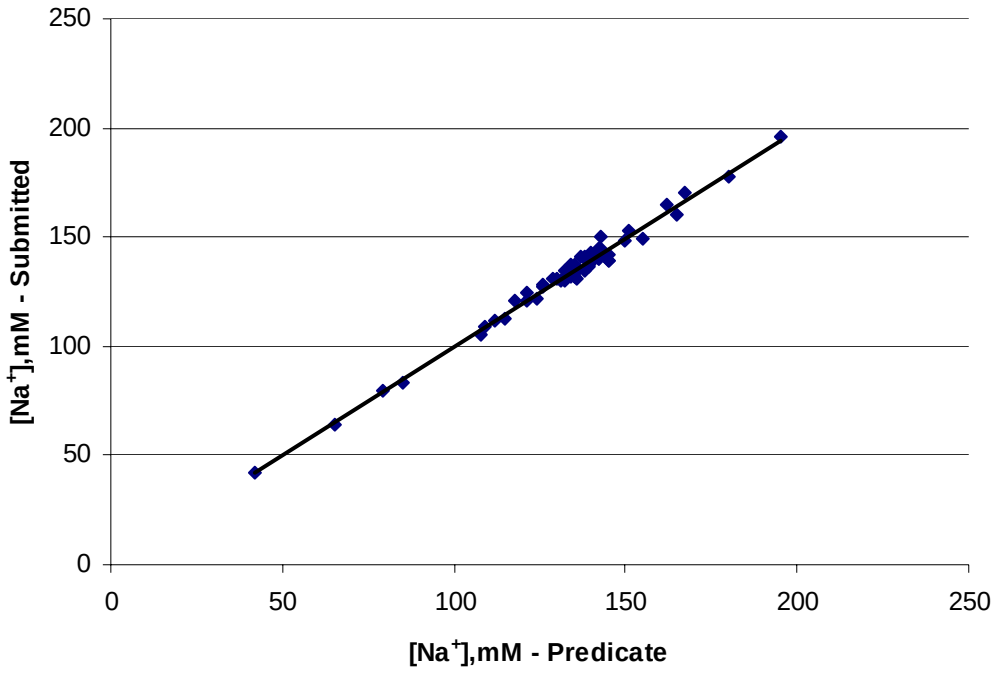
2. Comparison studies:

a. Method comparison with predicate device:

The company compared their submitted device to their predicate using 60 clinical samples spanning the concentration ranges claimed for the analytes.

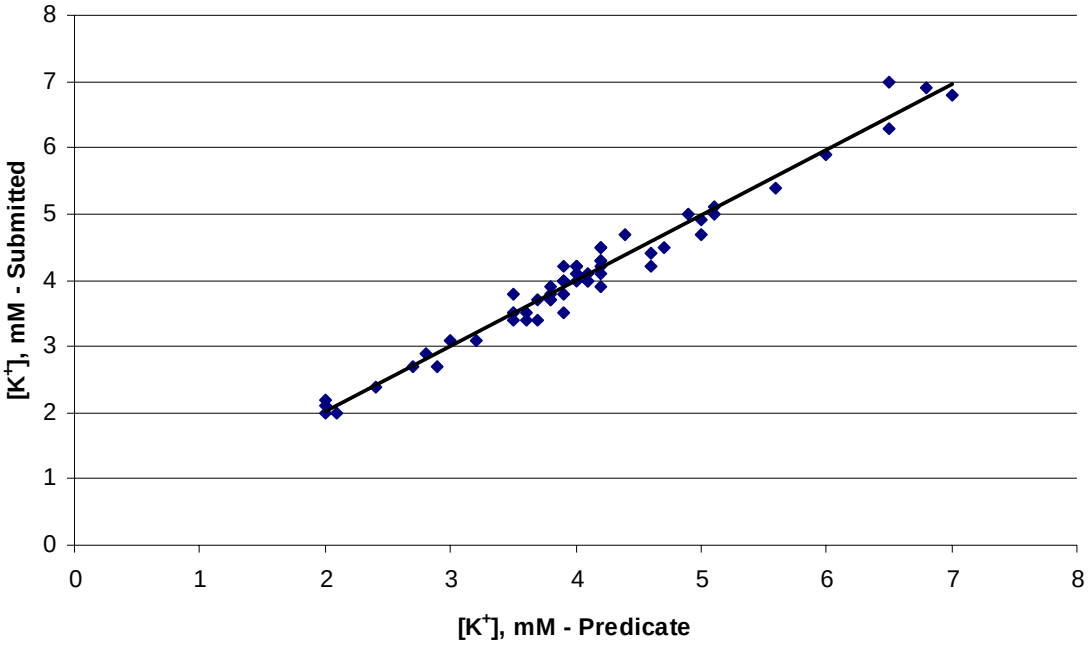
For sodium, the company discarded two samples because the measured concentration exceeded their claimed upper limit. A linear regression on the remaining 58 clinical samples yielded a slope of 1.01, an intercept of 0.4, and an r-squared value of 0.99 for the submitted vs. predicate fit.

The following chart graphically depicts the relation between the predicate and submitted device for sodium:



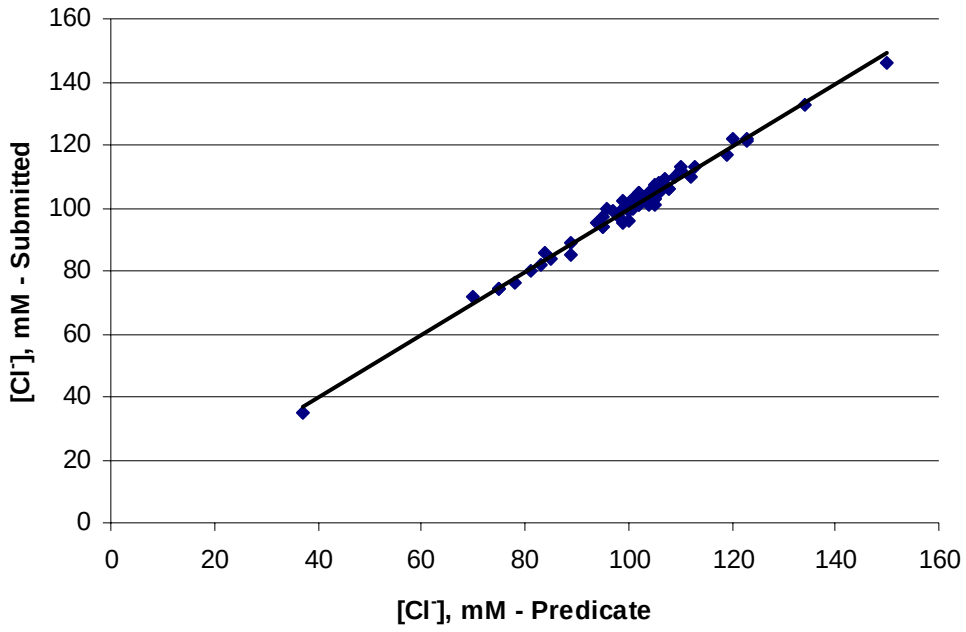
For potassium, a linear regression on 60 clinical samples yielded a slope of 1.0, an intercept of 0.01, and an r-squared value or 0.99 for the submitted vs. predicate fit.

The following chart graphically depicts the relation between the predicate and submitted device for potassium:



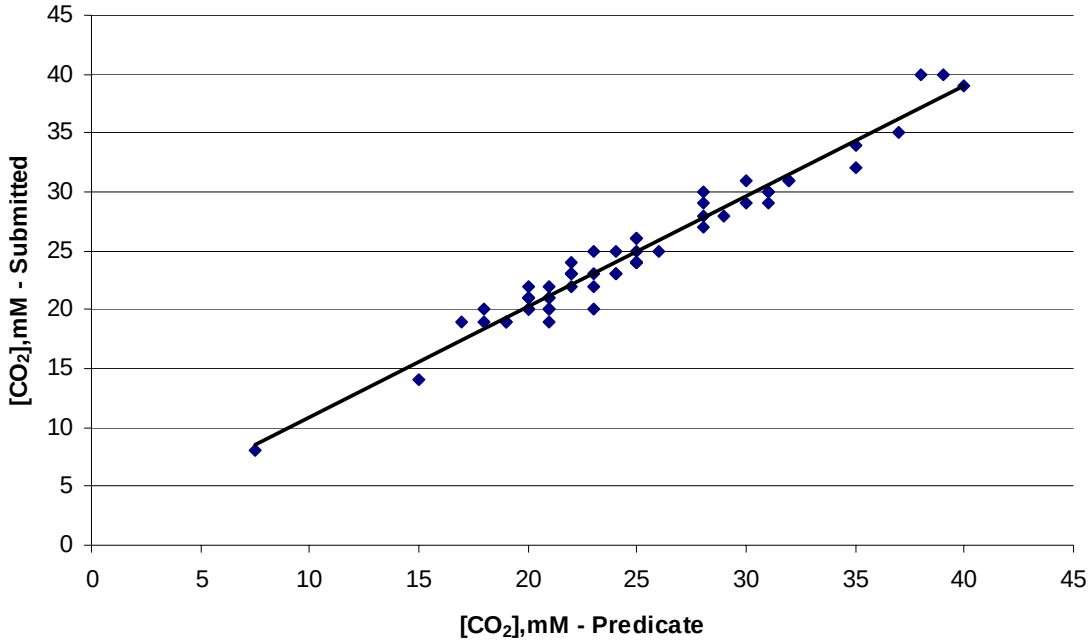
For chloride, a linear regression on 60 clinical samples yielded a slope of 0.99, an intercept of 1.34, and an r-squared value or 0.99 for the submitted vs. predicate fit.

The following chart graphically depicts the relation between the predicate and submitted device for chloride:



For carbon dioxide the company discarded one sample because the measured concentration exceeded their claimed upper limit. A linear regression on the remaining 59 clinical samples yielded a slope of 1.02, an intercept of -0.5554, and an r-squared value or 0.98 for the submitted vs. predicate fit.

The following chart graphically depicts the relation between the predicate and submitted device for carbon dioxide:



b. Matrix comparison:

Not applicable

3. <u>Clinical studies</u>:

a. Clinical Sensitivity:

Not applicable for a device of this type.

b. Clinical specificity:

Not applicable for a device of this type.

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

Not applicable for a device of this type.

4. <u>Clinical cut-off:</u>

Not applicable for a device of this type.

5. Expected values/Reference range[†]:

K	:	3.5 – 5.1	mmol/L	or 13.75 – 19.9 mg/dL
Na	:	136-145	mmol/L	or 312 – 334 mg/dL
Cl	:	98-107	mmol/L	or 350 – 379 mg/dL
CO_2	:	22-28	mmol/L	or 96.8 – 123.2 mg/dL

[†]Tietz,N.W., ed., Fundamentals of Clinical Chemistry, 3rd Edition, W.B. Saunders, Philadelphia, PA (1987)

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.