

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

A. 510(k) Number:

k132418

B. Purpose for Submission:

Modification of a previously cleared device (k053165)

C. Measurand:

Sodium, Potassium, Chloride

D. Type of Test:

Ion Selective Electrode Potentiometry

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

cobas c 501 ISE Indirect Na, K, Cl for Gen. 2

G. Regulatory Information:

1. Regulation section:

21CFR 862.1665, Ion Specific Electrode, Sodium

21CFR 862.1600, Ion Specific Electrode, Potassium

21CFR 862.1170, Ion Specific Electrode, Chloride

2. Classification:

Class II

3. Product code:

JGS

CEM

CGZ

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indication(s) for use below

2. Indication(s) for use:

The ISE module of the Roche/Hitachi systems is intended for the quantitative determination of sodium, potassium, and chloride in serum, plasma, or urine using ion-selective electrodes.

Sodium measurements are used in the diagnosis and treatment of aldosteronism (excessive secretion of hormone aldosterone), diabetes insipidus (chronic excretion of large amounts of dilute urine, accompanied by extreme thirst), adrenal hypertension, Addison's disease (caused by destruction of the adrenal glands), dehydration, inappropriate antidiuretic hormone secretion, or other diseases involving electrolyte imbalance. Potassium measurements are used to monitor electrolyte balance in the diagnosis and treatment of disease conditions characterized by low or high blood potassium levels. Chloride measurements are used in the diagnosis and treatment of electrolyte and metabolic disorders such as cystic fibrosis and diabetic acidosis.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

cobas c 501

I. Device Description:

The main modification of the device is the ISE calibrator 3 (S3) was changed from serum based to aqueous based and the concentrations of the Na, K, and Cl were made to be the same as ISE calibrator 2 (S2). The following ISE calibrators, auxiliary reagents, and electrodes are required to calibrate and calculate results for the ISE module and were used in the performance studies of the cobas c 501 ISE system.

ISE Calibrators S1, S2, and S3:

- S1: ISE Standard Low (120 mmol/L Na⁺, 3 mmol/L K⁺, 80 mmol/L Cl⁻)
- S2: ISE Standard High (160 mmol/L Na⁺, 7 mmol/L K⁺, 120 mmol/L Cl⁻)

- S3: ISE Standard High (160 mmol/L Na⁺, 7 mmol/L K⁺, 120 mmol/L Cl⁻)

Auxiliary Reagents:

- ISE Reference Electrolyte (1 mol/L potassium chloride) provides a strong stable ion reference potential in the reference electrode necessary for each ISE measurement.
- ISE Diluent (HEPES buffer: 10mmol/L, Triethanolamine: 7 mmol/L, preservative) is used for sample dilution.
- ISE Internal Standard (HEPES buffer: 10mmol/L, Triethanolamine: 7 mmol/L, Sodium Chloride: 3.06 mmol/L, Sodium acetate: 1.45 mmol/L, Potassium Chloride: 0.16 mmol/L, preservative) is used for a baseline calibration which is performed once every ISE cycle.
- ISE Cleaning Solution: Sodium hydroxide solution (12%) is intended to clean the ion-selective electrodes, vessel and tubing.

ISE Electrodes: Sodium Electrode, Potassium Electrode, Chloride Electrode, and Reference Electrode

J. Substantial Equivalence Information:

1. Predicate device name(s):
cobas c 501 analyzer ISE
2. Predicate 510(k) number(s):
k053165
3. Comparison with predicate:

Similarities		
Item	Candidate device cobas c 501 ISE Indirect Na, K, Cl for Gen. 2	Predicate device cobas c 501 analyzer ISE (k053165)
Intended Use	The ISE module of the Roche/Hitachi cobas c system is intended for the quantitative determination of sodium, potassium and chloride in serum, plasma or urine using ion-selective electrodes.	Same
Measurement Principle	ISE Potentiometry	Same
Onboard storage temperature	5-12°C	Same
Ion Selective Electrodes	Potentiometric chloride, potassium, sodium and reference electrodes.	Same

Similarities		
Item	Candidate device cobas c 501 ISE Indirect Na, K, Cl for Gen. 2	Predicate device cobas c 501 analyzer ISE (k053165)
Sample Dilution	1:31	Same
Reportable Range for Serum and Plasma	Sodium: 80-180 mmol/L Potassium: 1.5-10 mmol/L Chloride: 60-140 mmol/L	Same

Differences		
Item	Candidate device	Predicate device
Standard 3 (High) Calibrator	ISE standard high (aqueous)	S3 (serum based compensator)
Reportable Range for Urine	Sodium: 20-250 mmol/L Potassium: 3-100 mmol/L Chloride: 20-250 mmol/L	Sodium: 10-250 mmol/L Potassium: 1-100 mmol/L Chloride: 10-250 mmol/L

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

CLSI EP5-A2: Evaluation of Precision of Clinical Chemistry Devices, Approved Guideline-2nd Edition

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

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

L. Test Principle:

The cobas c 501 with an ISE module is an Ion-Selective Electrode (ISE) system for the determination of sodium, potassium, and chloride in serum, plasma, and urine. An ISE makes use of the unique properties of certain membrane materials to develop an electrical potential (electromotive force, EMF) for the measurements of ions in solution. The electrode has a selective membrane in contact with both the test solution and an internal filling solution. The internal filling solution contains the test ion at a fixed concentration. Because of the particular nature of the membrane, the test ions will closely associate with the membrane on each side. The membrane EMF is determined by the difference in concentration of the test ion in the test solution and the internal filling solution. The EMF develops according to the Nernst equation for a specific ion in solution.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies for serum and urine applications of the cobasc501 ISE electrodes for the measurement of Na, K, and Cl were performed using 1 analyzer, 1 site, 1 lot of reagent, and 6 samples. The 6 samples used for the serum precision testing were comprised of 4 human serum sample pools of varying concentrations (low, mid, mid-low, and high) for each analyte; and Precinorm U and Precipath U controls. The 6 samples used for the urine precision testing were comprised of 4 human urine sample pools of varying concentrations (low, mid, mid-low, and high) for each analyte; and Liquichek Level 1 and Liquichek Level 2 controls. The within run precision study was performed with 21 single determinations for each analyte. The intermediate precision was performed over a period of 21 days, 2 runs per day, and 2 aliquots per run for a total of 84 samples per analyte. The result summaries for the precision studies are presented in the tables below:

Within Run Precision

Sodium (Serum)

Sample	PNU	PPU	HS low	HS med	HS MDL	HS high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	21	21	21	21	21	21
Mean	125.6	147.5	84.4	121.3	131.7	177.2
SD	0.3	0.4	0.2	0.2	0.3	0.4
%CV	0.2	0.3	0.3	0.2	0.2	0.2

Sodium (Urine)

Sample	Liq 1	Liq 2	HU low	HU med	HU MDL	HU high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	21	21	21	21	21	21
Mean	80.2	169.2	29.9	131.3	22.7	236.1
SD	0.2	0.2	0.3	0.2	0.3	0.2
%CV	0.2	0.2	0.3	0.2	0.3	0.2

Potassium (Serum)

Sample	PNU	PPU	HS low	HS med	HS MDL	HS high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	21	21	21	21	21	21
Mean	3.58	6.78	1.62	4.99	2.64	9.49
SD	0.02	0.04	0.01	0.02	0.01	0.05
%CV	0.6	0.6	0.6	0.4	0.4	0.5

Potassium (Urine)

Sample	Liq 1	Liq 2	HU low	HU med	HU MDL	HU high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	21	21	21	21	21	21
Mean	31.7	70.6	5.25	51.90	15.3	89.80
SD	0.2	0.3	0.03	0.2	0.1	0.4
%CV	0.6	0.4	0.6	0.4	0.7	0.5

Chloride (Serum)

Sample	PNU	PPU	HS low	HS med	HS MDL	HS high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	21	21	21	21	21	21
Mean	85.2	117.4	67.6	128.6	91.6	139.0
SD	0.3	0.4	0.2	0.3	0.3	0.4
%CV	0.4	0.3	0.2	0.2	0.4	0.3

Chloride (Urine)

Sample	Liq 1	Liq 2	HU low	HU med	HU MDL	HU high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	21	21	21	21	21	21
Mean	95.2	195.4	25.0	130.6	23.4	242.9
SD	0.3	0.5	0.1	0.4	0.1	0.7
%CV	0.3	0.2	0.4	0.3	0.3	0.3

Total (Intermediate) Precision

Sodium (Serum)

Sample	PNU	PPU	HS low	HS med	HS MDL	HS high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	84	84	84	84	84	84
Mean	126.0	148.2	84.8	121.4	131.6	176.7
SD	0.7	0.5	1.0	0.8	0.7	0.6
%CV	0.5	0.4	1.1	0.6	0.5	0.4

Sodium (Urine)

Sample	Liq 1	Liq 2	HU low	HU med	HU MDL	HU high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	84	84	84	84	84	84
Mean	81.6	172.3	30.6	131.7	23.3	236.7
SD	1.3	2.6	0.9	0.6	0.9	1.3
%CV	1.6	1.5	3.0	0.5	3.8	0.6

Potassium (Serum)

Sample	PNU	PPU	HS low	HS med	HS MDL	HS high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	84	84	84	84	84	84
Mean	3.57	6.59	1.62	4.97	2.63	9.46
SD	0.04	0.05	0.03	0.04	0.07	0.07
%CV	1.0	0.7	1.6	0.8	0.7	1.0

Potassium (Urine)

Sample	Liq 1	Liq 2	HU low	HU med	HU MDL	HU high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	84	84	84	84	84	84
Mean	31.5	70.6	5.2	52.1	15.4	90.3
SD	0.5	1.17	0.04	0.7	0.1	1.4
%CV	1.7	1.7	0.7	1.3	0.9	1.5

Chloride (Serum)

Sample	PNU	PPU	HS low	HS med	HS MDL	HS high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	84	84	84	84	84	84
Mean	86.2	119.2	68.5	129.0	92.3	139.0
SD	0.5	0.5	0.6	0.6	0.5	0.6
%CV	0.6	0.4	0.8	0.5	0.6	0.4

Chloride (Urine)

Sample	Liq 1	Liq 2	HU low	HU med	HU MDL	HU high
Unit	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	mmol/L
n	84	84	84	84	84	84
Mean	97.5	198.2	25.8	131.4	24.3	243.4
SD	1.6	2.3	0.6	0.7	0.6	1.8
%CV	1.6	1.2	2.3	0.5	2.4	0.7

b. Linearity/assay reportable range:

Linearity studies were performed according to CLSI EP6-A. Dilution series of 11 concentrations were prepared using low and high human serum, plasma, and urine sample pools for each of the analytes and tested in triplicate. Linear regression analysis was done according to EP6-A. Linear regression summary results of the study are presented in the table below:

Analyte	Matrix	Slope	Intercept	Range Tested (mmol/L)
Sodium	Serum	0.9804	2.7508	70-190
Sodium	Plasma	1.0076	0.8378	70-185
Sodium	Urine	1.0100	2.1287	15-250
Potassium	Serum	0.9978	0.0437	1.5-11.0
Potassium	Urine	0.9781	0.3260	3.0-110
Chloride	Serum	1.0690	1.1321	60-145
Chloride	Plasma	0.9788	3.4818	60-140
Chloride	Urine	0.9918	2.4216	15-250

The plasma potassium linearity study resulted in a polynomial regression in which the 3rd order polynomial regression was considered significant. Therefore, the deviation of the results from the 3rd order linear regression were compared against the best fit line. The plasma potassium polynomial regression results are summarized in the following table:

Sample	Best line regression mmol/L	Predicted 3 rd order mmol/L	Absolute difference	Relative % difference
1	0.948	0.993	0.045	4.7418
2	2.1783	2.1786	0.0003	0.0158
3	3.4086	3.386	-0.0226	-0.6628
4	4.6388	4.6101	-0.0288	-0.62
5	5.8691	5.8461	-0.0231	-0.3928
6	7.0994	7.089	-0.0104	-0.1461
7	8.3297	8.334	0.0044	0.0526
8	9.5599	9.5763	0.0163	0.1706
9	10.7902	10.8107	0.0205	0.902
10	12.0205	12.0326	0.0121	0.1007
11	13.2508	13.2369	-0.0138	-.1044

Urine auto-rerun dilution validation study:

An auto-rerun validation study was performed to evaluate the accuracy of the analyzer's auto dilution function to obtain results for urine samples with analyte concentrations above the measuring range. Three samples (low, middle, and high) of the extended range were used for the study. Each sample was manually diluted with 1:1.5 ratio using a sample volume of 9.7 µL. Each sample was measured in triplicate on one cobas c 501 analyzer which uses a decreased sample volume dilution method. The results from the manually diluted urine samples were compared to the results from the auto-rerun dilution samples. The study protocol and pre-determined acceptance criteria were reviewed and found to be adequate. The results of the auto-rerun study support the sponsor's extended measuring range claims for urine sodium (250 to 375 mmol/L), urine potassium (100 to 150 mmol/L) and urine chloride (100 to 150 mmol/L) samples.

The results of the linearity studies and the auto-rerun validation for urine samples support the sponsor's following claimed measuring ranges:

Serum Sodium: 80-180 mmol/L
Serum Potassium: 1.5-10.0 mmol/L
Serum Chloride: 60-140 mmol/L

Urine Sodium: 20-250 mmol/L (auto-dilution extended range: 251-375 mmol/L)
Urine Potassium: 3-100 mmol/L (auto-dilution extended range: 101-150 mmol/L)
Urine Chloride: 20-250 mmol/L (auto-dilution extended range: 251-375 mmol/L)

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

Traceability:

The ISE Standard Low (S1) and ISE Standard High (S2 and S3) are standardized against primary calibrators prepared gravimetrically from purified salts. The Sodium Chloride, Potassium Dihydrogenphosphate and Sodium Hydrogencarbonate salts with a minimum of 99.5% purity and USP grade were used.

Stability:

Shelf life: The ISE Standard Low (S1) and ISE Standard High (S2 and S3) are stable at 15-25° C for 60 months or until the expiration date listed on the labeling.
Open vial: The ISE standards are intended to be used immediately after opening and are intended to be used for one calibration only.

Value assignment:

The ISE standard low is prepared by dissolving 1870.32 g of Sodium Chloride, 163.30 g of Potassium dihydrogenphosphate, and 1344.00 g of Sodium hydrogencarbonate in 400.00 kg of water.

The ISE standard high is prepared by dissolving 2805.50 g of Sodium Chloride, 381.05 g of Potassium dihydrogenphosphate, and 1344.00 g of Sodium hydrogencarbonate in 400.00 kg of water.

All standard solutions are checked against the reference methods and must meet the internal specifications before released. The expected values are as follows:

- S1: ISE Standard Low (120 mmol/L Na⁺, 3 mmol/L K⁺, 80 mmol/L Cl⁻)
- S2: ISE Standard High (160 mmol/L Na⁺, 7 mmol/L K⁺, 120 mmol/L Cl⁻)
- S3: ISE Standard High (160 mmol/L Na⁺, 7 mmol/L K⁺, 120 mmol/L Cl⁻)

All 3 standards are used for the full calibration, S3 is considered as a compensator. The slope of the calibration curve is calculated from Standards 1 and 2; the ISE compensation will affect the intercept, not the slope.

d. Detection limit:

Studies were carried out in accordance with CLSI Guidance Document EP17-A for Sodium, Potassium and Chloride analytes. For determination of LoB one analyte free sample was measured in 5 replicates, 6 runs, 3 days, on 2 cobas c 501 analyzers. Total of 60 measurements were obtained per analyzer. For determination of LoD, five samples (one replicate) with low-analyte concentration were measured in 6 runs for 3 days on 2 cobas c 501 analyzer modules. In total 60 measurements were obtained per analyzer. For LoQ studies a low level sample set was prepared by diluting 3 human urine and serum samples with an analyte free diluent (ISE Diluent). The low level sample set was tested in single replicate for 3 days in 2 runs per day on two cobas c 501 analyzers. LoQ is defined as the concentration where total error is less than 20%. Results from the detection limit studies are summarized in the table below:

	LoB (mmol/L)	LoD (mmol/L)	LOQ (mmol/L)	Claimed measuring range (mmol/L)
Sodium (serum)	3.9	5.7	9.7	80-180
Potassium (serum)	0.17	0.2	0.3	1.5-10
Chloride (serum)	3.4	4.7	6.7	60-140
Sodium (urine)	3.9	5.7	11.4	20-375

Potassium (urine)	0.17	0.2	0.2	3-150
Chloride (urine)	3.4	4.7	8.8	20-375

e. Analytical specificity:

Drug interference: Serum and urine sample pools with low and high concentrations of each analyte were spiked with drugs and concentrations listed below. The analyte concentrations of the spiked aliquots were tested in triplicate and the mean of the triplicate determinations is compared to the analyte concentration of the reference sample which contains no drugs. The sponsor's definition of significant interference is $\geq \pm 10\%$ of the initial value.

Approximate Concentration of Analytes tested for drug interference

Analyte	Matrix	Low (mmol/L)	High (mmol/L)
Sodium	Serum	123	150
Sodium	Urine	60	215
Potassium	Serum	3.80	6.50
Potassium	Urine	20	95
Chloride	Serum	95	105
Chloride	Urine	105	225

There was no significant interference for serum sodium, potassium, and chloride when these analytes and interferents were tested in the concentrations indicated below.

Drug Interference for Serum Sodium, Potassium and Chloride

Drug	Concentration at which no significant interference was observed (mg/dL)
Acetylcystein	150
Ampicillin-Na	1000
Ascorbic acid	300
Cyclosporin	5
Na-Cefoxitin	2500
Heparin	5000 U
Intralipid	10000
Levodopa	20
Methyldopa	20
Metronidazole	200
Phenylbutazone	400

Doxycyclin	50
Acetysalicylic acid	1000
Rifampicin	60
Acetaminophen	200
Ibuprofen	500
Theophylline	100

There was no significant interference for urine sodium, potassium, and chloride when these analytes and interferents were tested in the concentrations indicated below.

Drug Interference for Urine Sodium, Potassium and Chloride

Drug	Concentration at which no significant interference was observed (mg/dL)
Acetaminophen	3000
N-Acetyl cystein	10
Salicyurlic acid	6000
Ascorbic acid	4000
Na-Cefoxitin	120000
Gentamycin Sulfate	400
Ibuprofen	4000
Levodopa	1000
Methyldopa	2000
Metronidazole	200
Ofloxacin	900
Phenylbutazone	300
Tetracycline	300
Rifampicin	60

Endogenous Interference

Serum sample pools with low and high concentrations of each analyte were spiked with conjugated and unconjugated bilirubin, hemoglobin, and intralipids in the concentrations listed below. Urine sample pools with low and high concentrations of each analyte were spiked with conjugated bilirubin and hemoglobin. The analyte concentrations of the spiked aliquots were tested in triplicate and the mean of the triplicate determinations is compared to the analyte concentration of the reference sample which contains no endogenous substances. The sponsor's definition of significant interference is $\geq \pm 10\%$ of the initial value.

Serum and Urine Sodium, Potassium and Chloride Concentrations Tested

	Analyte	Analyte Concentration Low (mmol/L)	Analyte Concentration High (mmol/L)
Interferent	Serum		
Unconjugated bilirubin	Sodium	126	147
	Potassium	2.83	5.99
	Chloride	92	111
Conjugated bilirubin	Sodium	125	148
	Potassium	2.98	6.29
	Chloride	95	115
Hemoglobin	Sodium	120	141
	Potassium	2.78	5.89
	Chloride	93	111
Lipemia	Sodium	113	133
	Potassium	2.65	6.62
	Chloride	84	101
Interferent	Urine		
Conjugated bilirubin	Sodium	39	210
	Potassium	18.8	65.6
	Chloride	46	96
Hemoglobin	Sodium	35	198
	Potassium	18	63
	Chloride	47	190

Results Summary:

Serum: Concentration of interferent at which no significant interference was observed.

Interferent	Sodium	Potassium	Chloride
Hemoglobin	1000 mg/dL	Avoid hemolyzed specimens*	1000 mg/dL
Conjugated Bilirubin	60 mg/dL	60 mg/dL	60 mg/dL
Unconjugated Bilirubin	60 mg/dL	60 mg/dL	60 mg/dL
Lipemia	2000 mg/dL	2000 mg/dL	2000 mg/dL

* Hemolysis interferes with potassium determinations.

Sponsor has the following limitation in the labeling:

“Hemoglobin levels higher than 90 mg/dL increase the apparent potassium concentrations significantly (appropriately H index 90). Potassium concentration in

erythrocytes is 25 times higher than in normal plasma. The level of interference may be variable depending on the exact content of erythrocytes. Avoid hemolyzed specimens”

Urine: Concentration of interferent at which no significant interference was observed.

Interferent	Sodium	Potassium	Chloride
Hemoglobin	1000 mg/dL	100 mg/dL	1000 mg/dL
Conjugated Bilirubin	60 mg/dL	60 mg/dL	60 mg/dL

f. Assay cut-off:
Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Sodium, potassium and chloride values for human plasma and urine samples were obtained on the Roche/Hitachi cobas c 501 analyzers and were compared to those determined on the corresponding reference method and with the Roche/Hitachi 912. The reference methods used were: Flame Photometer IL 943 for Sodium and Potassium and the Chloride Analyzer 926S for Chloride. No more than 20% of the samples were either spiked or diluted to cover the measuring range. In addition, the samples were tested in singlicate on one cobas 501 with the candidate device and one c 501 with the predicate device. The results were calculated using Passing/Bablok Linear regression. The method comparison result summary is shown in the tables below:

Serum Sodium Method Comparison:
Flame Photometer vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
103	87-178	$y=1.000x+0.300$	0.999

Serum Sodium Method Comparison:
Predicate device vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
103	87-176	$y=1.014x-1.176$	1.000

Urine Sodium Method Comparison:
Flame Photometer vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
100	24-250	$y=0.964+4.032$	1.000

Urine Sodium Method Comparison:
Predicate device vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
100	25-245	$y=0.995x+0.687$	1.000

Serum Potassium Method Comparison:
Flame Photometer vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
106	1.59-9.56	$y=1.007x-0.190$	1.00

Serum Potassium Method Comparison:
Predicate device vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
106	1.52-9.49	$y=1.006x+0.024$	1.00

Urine Potassium Method Comparison:
Flame Photometer vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
105	4.00-97.2	$y=1.018x-0.397$	1.00

Urine Potassium Method Comparison:
Predicate device vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
105	4.05-97.4	$y=0.997x+0.062$	0.999

Serum Chloride Method Comparison:
Coulmetry vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
105	62-136	$y=1.033x-1.800$	0.998

Serum Chloride Method Comparison:
Predicate device vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
105	61-138	$y=1.000x +0.50$	0.999

Urine Chloride Method Comparison:
Coulometry vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
105	22-248	$y=1.020x -1.70$	0.999

Urine Chloride Method Comparison:
Predicate device vs candidate device

n	Range mmol/L	Regression Passing-Bablok	r
105	21-250	$y=0.989x+0.669$	1.000

b. *Matrix comparison:*

A matrix comparison study was performed to compare the recovery of the proposed anticoagulated sample type, lithium heparin, to the recovery of serum sample type. Thirty matched serum (SST) and lithium heparin samples were run in singlet on one cobas c 501 analyzer, at one site, with one lot of ISE diluent. Testing was performed during one day. Passing/Bablok linear regression analysis was used to evaluate the mean data and the result summary is shown below:

Serum vs. Lithium Heparin Plasma

Analyte	n	Range mmol/L	Slope	Intercept	Correlation Coefficient (r)
Sodium	30	80-174	1.003	-0.659	1.000
Potassium	30	1.77-8.98	0.9960	0.023	0.995
Chloride	30	64-136	1.009	-0.754	0.999

Sponsor concluded that lithium heparin is an acceptable anti-coagulant to be used with the candidate device.

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 expected values for adult based serum, plasma and 24-hour urine out put are cited from the literature¹:

Serum (Adults)

Sodium: 136-145 mmol/L

Potassium: 3.5-5.1 mmol/L

Chloride: 98-107 mmol/L

Plasma (Adults)

Sodium: 136-145 mmol/L

Potassium: 3.4-4.5 mmol/L

Chloride: 98-107 mmol/L

Urine, 24 hour (Adults)

Sodium: 40-220 mmol/24h

Potassium: 25-125 mmol/24h

Chloride: 110-250 mmol/24h

References:

1. Tietz Fundamentals of Clinical Chemistry, Fifth Edition, Edited by Carl A. Burlis and Edward R. Ashwood, W.B. Saunders Company, 2001:970, 1004,1009 (ISBN 0-7216-8634-6).

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.