510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K253491

B Applicant

Roche Diagnostics

C Proprietary and Established Names

ISE indirect K for Gen.2; ISE indirect Na for Gen.2; ISE indirect Cl for Gen.2; cobas pro integrated solutions

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CEM	II	21 CFR 862.1600 - Potassium Test System	CH - Clinical Chemistry
JGS	II	21 CFR 862.1665 - Sodium Test System	CH - Clinical Chemistry
CGZ	II	21 CFR 862.1170 - Chloride Test System	CH - Clinical Chemistry
JJE	I	21 CFR 862.2160 - Discrete photometric chemistry analyzer for clinical use	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Addition of previously cleared assays to a modified instrument platform

B Measurand:

Potassium, Sodium, Chloride

C Type of Test:

Quantitative, ion selective electrode

III Intended Use/Indications for Use:

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

B Indication(s) for Use:
cobas pro integrated solutions is an automated analyzer, intended for running qualitative, semiquantitative, and quantitative clinical chemistry and immunochemistry assays as well as ion-selective measurements.

The ISE analytical unit of the cobas c 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 the 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.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

cobas pro integrated solutions

IV Device/System Characteristics:

A Device Description:

cobas pro integrated solutions
The cobas pro integrated solutions is a fully automated, random-access, software-controlled system intended for in vitro quantitative and qualitative analysis of analytes in body fluids. The quantitative analysis also includes semi-quantitative. The cobas ISE neo, with a throughput of up to 900 tests per hour, is being added to the cobas pro integrated solutions.

ISE indirect Na for Gen.2, ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2
ISE auxiliary reagents include:

- ISE Reference Electrolyte: 1 mol/L potassium chloride
- ISE Diluent: HEPES buffer: 10 mmol/L; Triethanolamine: 7 mmol/L; Preservative
- ISE Internal Standard: HEPES buffer: 10 mmol/L; Triethanolamine: 7 mmol/L; Sodium chloride: 3.06 mmol/L; Sodium acetate: 1.45 mmol/L; Potassium chloride: 0.16 mmol/L; Preservatives
- ISE Cleaning Solution: Sodium hydroxide solution: 3 mol/L with sodium hypochlorite solution < 2 % active Cl
- Deproteinizer and ISE Deproteinizer: The Deproteinizer and ISE Deproteinizer are aqueous sodium hypochlorite solutions.
- Electrodes: Sodium, Potassium, Chloride, Reference

B Principle of Operation:

An Ion-Selective Electrode (ISE) makes use of the unique properties of an ion-selective membrane to develop an electrical potential (electromotive force, EMF) for the measurements of ions in solution. The selective membrane is in contact with both the test solution and an internal filling solution. Due to the selectivity of the membrane, only the ions to be measured contribute to the EMF. 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 and ion concentration is determined according to the Nernst equation.

C Instrument Description Information:

1. Instrument Name:

   cobas pro integrated solutions

2. Specimen Identification:

   The specimen is in a tube with a barcode label. The system identifies specimens by scanning the barcode. This is the primary use case for sample identification. The system also supports manual entry of sample IDs to support the needs of the customer.

3. Specimen Sampling and Handling:

   Specimen sampling and handling procedures are analyte specific and documented in the respective reagent method sheets.

4. Calibration:

   The software automatically recommends calibration for all tests requiring calibration. Calibration may also be ordered manually at any time. Calibration methods and procedures are analyte specific and documented in the respective reagent method sheets.

5. Quality Control:

   The method sheet for each assay used on the system contains QC recommendations for the specific application.

V Substantial Equivalence Information:

A Predicate Device Name(s):
ISE indirect K for Gen.2; ISE indirect Cl for Gen.2; cobas 6000 Series System
ISE indirect Na for Gen.2; cobas pro integrated solutions

B Predicate 510(k) Number(s):
K060373, K191899

C Comparison with Predicate(s):

Comparison of ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2

Device & Predicate Device(s):	K253491	K060373
Device Trade Name	ISE indirect K for Gen.2; ISE indirect Cl for Gen.2	ISE indirect K for Gen.2; ISE indirect Cl for Gen.2
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for quantitative determination of potassium and chloride in serum, plasma or urine using ion-selective electrodes.	Same
General Device Characteristic Differences		
Analyzer Units	cobas ISE neo	cobas c 501 module (comprises a photometric unit and an ISE unit)

Comparison of ISE indirect Na for Gen.2

Device & Predicate Device(s):	K253491	K191899
Device Trade Name	ISE indirect Na for Gen.2	ISE indirect Na for Gen.2
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for quantitative determination of sodium in serum, plasma or urine using ion-selective electrodes.	Same

General Device Characteristic Differences		
Analyzer Units	cobas ISE neo	cobas ISE

Comparison of the cobas pro integrated solution and cobas 6000 Series system

Device & Predicate Device(s):	K253491	K060373
Device Trade Name	cobas pro integrated solutions	cobas 6000 Series System
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended for automated running of quantitative ion-selective measurements	Same
General Device Characteristic Differences		
Analyzer Units	cobas ISE neo	cobas c 501 module (comprises a photometric unit and an ISE unit)

VI Standards/Guidance Documents Referenced:

- Clinical and Laboratory Standards Institute (CLSI EP05-A3). Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.
- CLSI EP06 2nd Edition. Evaluation of the Linearity of Quantitative Measurement Procedures.
- CLSI EP17-A2. Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition.
- IEC 61010-1 Edition 3.1 2017-01 consolidated version. Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 1: General Requirements (including: Corrigendum 1).

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were performed in accordance with CLSI guideline EP05-A3. The protocol consisted of testing two sample replicates per run, two runs per day for ≥ 21 days on the candidate device. The protocol was repeated for each application in serum, plasma and urine. Repeatability and within-laboratory precision estimates were calculated. The samples were randomized in each run separately. Pooled samples were used for each level. Samples 1 and

5 were diluted or spiked, samples 2-4 were native. The results are summarized in the tables below.

Summary of Precision Results – ISE Indirect Na for Gen.2

Sample	N	Mean (mmol/L)	Repeatability		Mean (mmol/L)	Within-Laboratory Precision	
			SD (mmol/L)	CV (%)		SD (mmol/L)	CV (%)
Serum Control 1	84	116	0.714	0.6	116	1.40	1.2
Serum Control 1	84	140	0.658	0.5	140	1.41	1.0
Serum 1	84	87.0	0.404	0.5	87.0	0.947	1.1
Serum 2	84	133	0.609	0.5	133	1.05	0.8
Serum 3	84	137	0.675	0.5	137	0.984	0.7
Serum 4	84	159	0.797	0.5	159	1.24	0.8
Serum 5	84	176	0.811	0.5	176	1.29	0.7
Plasma Control 1	84	115	0.529	0.5	115	1.11	1.0
Plasma Control 1	84	139	0.543	0.4	139	1.34	1.0
Plasma 1	84	87.3	0.367	0.4	87.3	1.05	1.2
Plasma 2	84	131	0.815	0.6	131	0.999	0.8
Plasma 3	84	136	0.734	0.5	136	1.01	0.7
Plasma 4	84	156	0.742	0.5	156	1.09	0.7
Plasma 5	84	173	0.818	0.5	173	1.13	0.7
Urine Control 1	84	81.1	0.380	0.5	81.1	1.17	1.4
Urine Control 2	84	171	0.947	0.6	171	1.72	1.0
Urine 1	84	27.0	0.295	1.1	26.1	1.20	4.6
Urine 2	84	135	0.492	0.4	135	1.33	1.0
Urine 3	84	111	0.432	0.4	111	1.02	0.9
Urine 4	84	198	0.847	0.4	198	2.04	1.0
Urine 5	84	237	1.02	0.4	237	2.84	1.2

Summary of Precision Results – ISE Indirect K for Gen.2

Sample	N	Mean (mmol/L)	Repeatability		Mean (mmol/L)	Within-Laboratory Precision	
			SD (mmol/L)	CV (%)		SD (mmol/L)	CV (%)
Serum Control 1	84	3.65	0.0240	0.7	3.65	0.0553	1.5
Serum Control 1	84	7.44	0.0405	0.5	7.48	0.0942	1.3
Serum 1	84	1.76	0.0105	0.6	1.76	0.0556	3.2
Serum 2	84	5.08	0.0279	0.6	5.12	0.0674	1.3
Serum 3	84	3.64	0.0187	0.5	3.64	0.0432	1.2
Serum 4	84	5.65	0.0286	0.5	5.65	0.0583	1.0
Serum 5	84	9.70	0.0505	0.5	9.76	0.0815	0.8
Plasma Control 1	84	3.62	0.0194	0.5	3.65	0.0556	1.5
Plasma Control 1	84	7.44	0.0327	0.4	7.49	0.0947	1.3
Plasma 1	84	1.69	0.0126	0.7	1.69	0.0592	3.5
Plasma 2	84	5.56	0.0253	0.5	5.06	0.0561	1.1

Sample	N	Mean (mmol/L)	Repeatability		Mean (mmol/L)	Within-Laboratory Precision	
			SD (mmol/L)	CV (%)		SD (mmol/L)	CV (%)
Plasma 3	84	3.50	0.0221	0.6	3.52	0.0485	1.4
Plasma 4	84	5.56	0.0253	0.5	5.56	0.0579	1.0
Plasma 5	84	9.70	0.0527	0.5	9.77	0.0866	0.9
Urine Control 1	84	30.3	0.208	0.7	30.3	0.597	2.0
Urine Control 2	84	71.7	0.673	0.9	71.7	2.00	2.8
Urine 1	84	3.51	0.0611	1.7	3.51	0.0611	1.7
Urine 2	84	48.5	0.394	0.8	48.5	1.22	2.5
Urine 3	84	29.3	0.239	0.8	29.3	0.510	1.7
Urine 4	84	75.2	0.609	0.8	75.2	2.09	2.8
Urine 5	84	88.3	0.772	0.9	88.3	2.67	3.0

Summary of Precision Results – ISE Indirect Cl for Gen.2

Sample	N	Mean (mmol/L)	Repeatability		Mean (mmol/L)	Within-Laboratory Precision	
			SD (mmol/L)	CV (%)		SD (mmol/L)	CV (%)
Serum Control 1	84	85.9	0.560	0.7	85.9	1.21	1.4
Serum Control 1	84	107	0.652	0.6	107	1.27	1.2
Serum 1	84	68.0	0.322	0.5	68.0	1.07	1.6
Serum 2	84	104	0.463	0.4	104	0.938	0.9
Serum 3	84	97.8	0.461	0.5	97.8	0.935	1.0
Serum 4	84	114	0.613	0.5	114	1.05	0.9
Serum 5	84	138	0.651	0.5	138	1.11	0.8
Plasma Control 1	84	86.2	0.454	0.5	85.9	1.20	1.4
Plasma Control 1	84	107	0.455	0.4	107	1.34	1.3
Plasma 1	84	65.0	0.301	0.5	65.2	1.20	1.8
Plasma 2	84	101	0.632	0.6	101	1.07	1.1
Plasma 3	84	94.5	0.541	0.6	94.4	1.02	1.1
Plasma 4	84	110	0.497	0.5	110	1.14	1.0
Plasma 5	84	135	0.735	0.5	135	1.28	0.9
Urine Control 1	84	82.3	0.402	0.5	82.0	0.985	1.2
Urine Control 2	84	193	1.14	0.6	193	2.12	1.1
Urine 1	84	23.5	0.535	2.3	23.5	1.63	7.0
Urine 2	84	132	0.571	0.4	132	1.33	1.0
Urine 3	84	105	0.656	0.6	106	1.10	1.0
Urine 4	84	201	0.925	0.5	202	2.01	1.0
Urine 5	84	247	1.02	0.4	247	3.51	1.4

2. Linearity:

The linearity studies were conducted to demonstrate that measurements across the claimed measuring range for each parameter are linear. The studies were performed according to

CLSI guideline EP06-Ed2. Testing for each sample type was completed with three reagent lots, in one run each, 4 replicates per sample on the candidate device. Dilution series (12 concentrations for each sample type) were prepared using human sample pools with analyte concentration above the upper limit of the linearity interval and human sample pools with analyte concentration below the lower limit of the linearity interval.

ISE Indirect Na for Gen.2

The results demonstrated that the deviation from linearity did not exceed 0.4% for serum and plasma samples, and 0.6% for urine samples within the measuring range. Linear regression results are summarized in the table below.

Sample	Linear Regression	Correlation Coefficient (r2)
Serum	y = 1.0017x – 0.0971	1.0000
Plasma	y = 1.0044x – 0.4425	1.0000
Urine	y = 1.0013x + 0.0028	0.9999

ISE Indirect K for Gen.2

The results demonstrated that the deviation from linearity did not exceed 1.5% for serum and plasma samples, and 10% for urine samples within the measuring range. Linear regression results are summarized in the table below.

Sample	Linear Regression	Correlation Coefficient (r2)
Serum	y = 0.9966x + 0.0146	0.9999
Plasma	y = 1.0008x – 0.0118	1.0000
Urine	y = 1.0429x + 0.2021	0.9991

ISE Indirect Cl for Gen.2

The results demonstrated that the deviation from linearity did not exceed 0.4% for serum and plasma samples, and 2% for urine samples within the measuring range.

Sample	Linear Regression	Correlation Coefficient (r2)
Serum	y = 1.0009x – 0.3864	0.9999
Plasma	y = 1.0032x – 0.6441	1.0000
Urine	y = 0.9752x – 0.9047	0.9999

Results support the following measuring ranges:

- Serum/Plasma:
  - Sodium: 80 - 180 mmol/L
  - Potassium: 1.5 - 10.0 mmol/L
  - Chloride: 60 - 140 mmol/L
- Urine:
  - Sodium: 20 - 250 mmol/L
  - Potassium: 3 - 100 mmol/L

- Chloride: 20 - 250 mmol/L

Dilution Recovery Studies

ISE indirect K for Gen. 2, ISE indirect Na for Gen. 2, and ISE indirect Cl for Gen. 2:
A dilution study was performed by diluting five high concentration urine samples with water in a 1:46 ratio. The data support the 1:46 dilution claim in the Method Sheet.

3. Analytical Specificity/Interference:

Endogenous Interference
The effects on quantitation of analyte in the presence of potentially interfering endogenous substances using the ISE indirect Na for Gen.2, ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2 on the candidate device were determined using two levels of pooled human serum, plasma and urine. Sodium levels of approximately 112 and 148 mmol/L for serum and plasma and at 65 and 183 mmol/L for urine; potassium levels of approximately 3.4 and 6.4 mmol/L for serum and plasma and at 23 and 85 mmol/L for urine, and chloride levels of approximately 80 and 110 mmol/L for serum and plasma and at 66 and 191 mmol/L for urine were tested. Substances with ≤ 10% were considered to have no interference with the assay.

ISE Indirect Na for Gen.2

Potential Interferent		**Highest Concentration Tested Without Significant Interference**
Serum and Plasma	Conjugated Bilirubin	70 mg/dL
	Unconjugated Bilirubin	77 mg/dL
	Hemolysis	1771 mg/dL
	Lipemia	2279 mg/dL
Urine	Hemolysis	1227 mg/dL

ISE Indirect K for Gen.2

Potential Interferent		**Highest Concentration Tested Without Significant Interference**
Serum and Plasma	Conjugated Bilirubin	70 mg/dL
	Unconjugated Bilirubin	77 mg/dL
	Hemolysis	23 mg/dL
	Lipemia	2279 mg/dL
Urine	Hemolysis	23 mg/dL

ISE Indirect Cl for Gen.2

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	Conjugated Bilirubin	70 mg/dL

Potential Interferent		Highest Concentration Tested Without Significant Interference
Serum and Plasma	Unconjugated Bilirubin	77 mg/dL
	Hemolysis	1771 mg/dL
	Lipemia	2279 mg/dL
Urine	Hemolysis	1227 mg/dL

Exogenous Interference

Exogenous drug Interference studies were conducted to evaluate drugs for potential interference with ISE indirect Na for Gen.2, ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2 on the candidate device using human serum, plasma, and urine samples. Sodium levels of approximately 125 and 155 mmol/L for serum and plasma and at 30 and 195 mmol/L for urine; potassium levels of approximately 2.5 and 6.5 mmol/L for serum and plasma and at 19.5 and 78 mmol/L for urine, and chloride levels of approximately 86 and 117 mmol/L for serum and plasma and at 27 and 202 mmol/L for urine were tested. Substances with ≤ 10% bias were considered to have no interference with the assay.

Potential Interferent		Highest concentration tested that showed no interference (mg/L)
Serum and Plasma	N-Acetylcysteine	1660
	Ampicillin-Na	1000
	Ascorbic acid	300
	Cyclosporine	5
	Cefoxitin	2500
	Heparin	5000
	Intralipid	10000
	Levodopa	20
	Methyldopa + 1.5	20
	Metronidazole	200
	Phenylbutazone	400
	Doxycyclin	50
	Acetylsalicylic acid	1000
	Rifampicin	60
	Acetaminophen	200
	Ibuprofen	500
	Theophylline	100
Urine	Acetaminophen	3000
	N-Acetylcysteine	10
	Salicyluric acid	6000
	Ascorbic acid	4000
	Cefoxitin	12000
	Gentamycine sulfate	400
	Ibuprofen	4000

Potential Interferent		Highest concentration tested that showed no interference (mg/L)
	Levodopa	1000
	Methyldopa	2000
	Ofloxacine	900
	Phenazopyridine	300
	Tetracycline	300

4. Detection Limit and Assay Reportable Range:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) were determined in accordance with the CLSI EP17-A2 requirements.

The LoB of the ISE indirect Na for Gen.2, ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2 on the cobas ISE neo analytical unit of cobas pro integrated solutions system were determined as the 95th percentile of measurements of blank samples. For determination of the LoB, one analyte-free sample was measured with three reagent lots in six runs, distributed over three days, 10 replicates per run, on one candidate device. In total, 60 determinations of analyte free samples were obtained. Data analysis was based on determination of the 95th percentile of the 60 measured values. In this design (n=60) the 95th percentile was the average of the 57th and 58th value.

The LoD of the ISE indirect Na for Gen.2, ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2 on the cobas candidate device were determined as the lowest amount of analyte in a sample that can be detected with a 95% probability. Data analysis was based on determination of the 60 measured values of the five low analyte samples. For determination of the LoD, five samples with low analyte content were measured using three reagent lots with two-fold determination per run on one candidate device. Six runs distributed over ≥ three days on one instrument were performed. The LoD is defined as the concentration, at which there is a 95% probability that a sample contains analyte. LoD = LoB + 1.653 x SD_{total}.

The LoQ of the ISE indirect Na for Gen.2, ISE indirect K for Gen.2 and ISE indirect Cl for Gen.2 on the candidate device were determined as the lowest concentration of analyte which can be quantified with a total error of no more than 30%. For determination of the LoQ, five samples with low analyte concentration were measured using three reagent lots on one cobas ISE neo analytical unit. These samples were tested in two runs per day over three days, two replicates per run for each LoQ sample (n=12 per sample).

Detection limit results are summarized in the tables below.

Sodium	
Limit of Blank	5.70 mmol/L
Limit of Detection	6.17 mmol/L
Limit of Quantitation	14.5 mmol/L

Potassium	
Limit of Blank	0.195 mmol/L
Limit of Detection	0.224 mmol/L
Limit of Quantitation	0.891 mmol/L

Chloride	
Limit of Blank	2.70 mmol/L
Limit of Detection	3.42 mmol/L
Limit of Quantitation	10.3 mmol/L

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

   Traceability: All three assays are standardized against primary calibrators prepared gravimetrically from purified salts.

6. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Method Comparison experiments were performed for all sample types. Less than 12% of these samples were spiked or diluted to cover the measuring range. The results of the candidate device were compared to the results of the predicate device. Additionally, the results of the candidate device were compared against flame photometry (Sodium and Potassium) or coulometry (Chloride).The results were evaluated using Passing-Bablok. A summary of results is presented in the table below.

ISE indirect Na for Gen.2

Candidate vs.	Sample Type	N	Sample Concentration Range (mmol/L)	Passing-Bablok Regression
Flame photometer	Plasma	118	79.5-177	y = 0.967x + 5.07; r= 0.987
Predicate	Plasma	119	80.5-176	y = 1.000x + 0.500; r= 0.999
Flame photometer	Serum	117	85.4-182	y = 0.950x + 5.83; r= 0.989
Predicate	Serum	119	80.7-178	y = 1.002x + 0.393; r= 0.999
Flame photometer	Urine	100	25.4-238	y = 1.009x + 0.529; r= 0.999
Predicate	Urine	118	20.9-239	y = 1.010x - 0.555; r= 1.000

ISE indirect K for Gen.2

Candidate vs.	Sample Type	N	Sample Concentration Range (mmol/L)	Passing-Bablok Regression
Flame photometer	Plasma	106	1.59-10.1	y = 1.027x - 0.0254; r= 0.998
Predicate	Plasma	116	1.64-9.69	y = 1.000x - 0.0400; r= 0.999
Flame photometer	Serum	101	1.59-9.69	y = 1.009x + 0.0155; r= 0.998
Predicate	Serum	118	1.62-9.93	y = 1.000x - 0.0400; r= 1.000
Flame photometer	Urine	106	3.20-95.6	y = 1.042x - 0.0282; r= 0.999
Predicate	Urine	113	3.41-93.4	y = 1.056x - 0.777; r= 1.000

ISE indirect Cl for Gen.2

Candidate vs.	Sample Type	N	Sample Concentration Range (mmol/L)	Passing-Bablok Regression
Coulometer	Plasma	117	66.0-138	y = 0.992x + 1.16; r= 0.988
Predicate	Plasma	119	62.4-137	y = 1.010x + 0.152; r= 0.999
Coulometer	Serum	108	63.0-132	y = 0.950x + 5.82; r= 0.986
Predicate	Serum	115	63.1-139	y = 1.021x - 1.41; r= 0.998
Coulometer	Urine	117	21.0-240	y = 1.033x – 3.12; r= 0.999
Predicate	Urine	118	22.6-248	y = 1.004x - 1.20; r= 1.000

A method comparison study was also provided comparing Li-heparin plasma on flame photometry to the candidate device for potassium. The results supported the accuracy of potassium in lithium heparin samples.

2. Matrix Comparison:

To support the use of the ISE indirect Na for Gen.2 Test, ISE indirect K for Gen.2 Test, and ISE indirect Cl for Gen.2. Test on the candidate device with different sample matrices, a matrix comparison study was conducted by comparing values obtained from samples drawn into serum and plasma collection tubes. Two replicates were processed for each sample, the first replicate results were evaluated. The results were evaluated using Passing-Bablok regression analysis. A summary of results is presented in the table below.

ISE indirect Na for Gen.2	N	Slope	Intercept	Coefficient r
Serum vs. Serum w/Gel Separation Tube	106	1.009	-1.41	0.995
Serum vs. Li-Heparin Plasma	104	1.00	-0.300	0.998

ISE indirect K for Gen.2	N	Slope	Intercept	Coefficient r
Serum vs. Serum w/Gel Separation Tube	101	0.996	0.016	0.997

ISE indirect Cl for Gen.2	N	Slope	Intercept	Coefficient r
Serum vs. Serum w/Gel Separation Tube	102	1.000	-0.050	0.991
Serum vs. Li-Heparin Plasma	100	0.997	-0.014	0.995

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Clinical Cut-Off

   Not applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

D Expected Values/Reference Range:

The sponsor provides the following information for expected values in the labeling:

Expected Values		Reference Range		
Sample Type		Sodium	Potassium	Chloride
Serum	Adults	136-145 mmol/L	3.5-5.1 mmol/L	98-107 mmol/L
Plasma	Adults	136-145 mmol/L	3.4-4.5 mmol/L	98-107 mmol/L
Urine	24 hours	40-220 mmol/24 h	25-125 mmol/24 h	110-250 mmol/24 h

Reference: Tietz NW. Fundamentals of Clinical Chemistry, 5th ed. Burtis CA, Ashwood ER, eds. WB Saunders Co 2001:970,1004,1009.

E Other Supportive Instrument Performance Characteristics Data:

1. Carryover Study: Carryover studies was reviewed and found to be acceptable.

2. Electrical safety and electromagnetic compatibility (EMC) testing were performed, and the results were found to be acceptable.

3. Software and cybersecurity documentation was reviewed and found to be acceptable.

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.