ISE indirect Na-K-Cl for Gen.2

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Order information

REF	CONTENT		Analyzer(s) on which reagents can be used
10820652216	ISE Reference Electrolyte (1 x 500 mL)		**cobas c** 303 ISE
08392013190	ISE Reference Electrolyte (2 x 2000 mL)		**cobas pro** ISE
04880455190	ISE Internal Standard Gen.2 (2 x 2000 mL)		
04880480190	ISE Diluent Gen.2 (2 x 2000 mL)		
11298500316	ISE Cleaning Solution (5 x 100 mL)		
20763071122	ISE Deproteinizer (6 x 21 mL)		
10825468001	Sodium electrode (1 electrode)*		
10825441001	Potassium electrode (1 electrode)*		
03246353001	Chloride electrode (1 electrode)*		
03149501001	Reference electrode (1 electrode)*		
04663632190	Activator (9 x 12 mL)		
11183974216	ISE Standard Low (10 x 3 mL)	Code 20502	
11183982216	ISE Standard High (10 x 3 mL)	Codes 20503, 20763	
12149435122	Precinorm U Plus (10 x 3 mL)	Code 20300	
12149443122	Precipath U Plus (10 x 3 mL)	Code 20301	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 20391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 20392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392	

*Roche Diagnostics GmbH is not the legal manufacturer of this device under REGULATION (EU) 2017/746 (IVDR).

English

System information

ISE CL: ACN 29090 (Serum/plasma)
ISE CL-U: ACN 29091 (Urine)
ISE CL-P: ACN 29092 (Plasma)
ISE CL-S: ACN 29093 (Serum)
ISE K: ACN 29080 (Serum/plasma)
ISE K-U: ACN 29081 (Urine)
ISE K-P: ACN 29082 (Plasma)
ISE K-S: ACN 29083 (Serum)
ISE NA: ACN 29070 (Serum/plasma)
ISE NA-U: ACN 29071 (Urine)
ISE NA-P: ACN 29072 (Plasma)
ISE NA-S: ACN 29073 (Serum)

Intended use

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.

Summary

Physiological significance:[1]

Electrolytes are involved in most major metabolic functions in the body. Sodium and potassium are amongst the most important physiological ions and the most often assayed electrolytes. They are supplied primarily through the diet, absorbed in the gastrointestinal tract, and excreted via the kidneys.

Sodium is the major extracellular cation and functions to maintain fluid distribution and osmotic pressure. Some causes of decreased levels of sodium include prolonged vomiting or diarrhea, diminished reabsorption in the kidney and excessive fluid retention. Common causes of increased sodium include excessive fluid loss, high salt intake and increased kidney reabsorption.

Potassium is the major intracellular cation and is critical to neural and muscle cell activity. Some causes of decreased potassium levels include reduced intake of dietary potassium or excessive loss of potassium from the body due to diarrhea, prolonged vomiting or increased renal excretion. Increased potassium levels may be caused by dehydration or shock, severe burns, diabetic ketoacidosis, and retention of potassium by the kidney.

Chloride is the major extracellular anion. Similarly to the other ions, common causes of decreased chloride include reduced dietary intake, prolonged vomiting and reduced renal reabsorption as well as some forms of acidosis and alkalosis. Increased chloride values are found in dehydration, kidney failure, some forms of acidosis, high dietary or parenteral chloride intake, and salicylate poisoning.

Test principle

An Ion-Selective Electrode (ISE) makes use of the unique properties of ion-selective membrane to develop an electrical potential (electromotive force, EMF) for the measurements of ions in solution. 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 according to the Nernst equation for a specific ion in solution:

(1) $E = E_0 + 2.303\ RT / z_i F \cdot \lg a_i$

Where:

E	=	electrode EMF
E_0	=	standard EMF
R	=	universal gas constant
T	=	temperature
z_i	=	charge of the ion
F	=	Faraday's constant
lg	=	decimal logarithm (base 10)
a_i	=	activity of the ion

For sodium, potassium and chloride, which all carry a single charge, R, T, z_i, and F are combined into a single value representing the slope (S).

Equation (1) can hence be rewritten to:

(2) $C_t = C_{IS} \times 10^{\frac{E_t - E_{IS}}{\pm S}}$

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Where:

C_t = concentration of the ion in the sample

C_{IS} = concentration of the ISE Internal Standard

E_t = EMF of the sample

E_{IS} = EMF of the ISE Internal Standard

S = Slope

The complete measurement system for a particular ion includes the ISE, a reference electrode and electronic circuits to measure and process the EMF to give the test ion concentration.

The sodium[2,3] and potassium[4] electrodes are based on neutral carriers and the chloride[5] electrode is based on an ion exchanger.

Reagents - working solutions

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

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

Preservative

ISE Cleaning Solution

Sodium hydroxide solution: 3 mol/L with sodium hypochlorite solution < 2 % active Cl

ISE Deproteinizer

Sodium hydroxide solution: approximately 1.2 % active Cl

Electrodes

Sodium, Potassium, Chloride, Reference

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

REF 04880455190/04880480190:

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

EUH 208 Contains mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1). May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

Handle patient samples and human-based controls as potentially infectious specimens.

As with any diagnostic test procedure, results should be interpreted taking all other test results and the clinical status of the patient into consideration.

In addition, pay attention to all precautions and warnings listed in the Operator's Manual of the analyzer.

Reagent handling

Ready for use

Storage and stability

Store S1, S2 and S3 at 15-25 °C.

Store Reference Electrolyte, Internal Standard, Diluent at 15-25 °C.

Store ISE Cleaning Solution at 2-8 °C.

Store ISE Deproteinizer at 2-8 °C.

Store electrodes at 7-40 °C.

See labels for expiration dates.

On-board stability

Calibrators S1, S2 and S3: **to be used only once.**

ISE Reference Electrolyte	up to expiration date
ISE Diluent	6 weeks
ISE Internal Standard	6 weeks

If always closed immediately after usage and stored at 2-8 °C the ISE Cleaning Solution can be used up to the expiration date.

ISE Deproteinizer for the **cobas c** 303 / **cobas pro** maintenance action ISE flow path cleaning is to be prepared freshly.

For daily maintenance use only fresh cleaning solution.

NOTE: If one of the reagent bottles is nearly empty do not just refill the bottle with new reagent. Discard the old reagent bottle, including any remaining reagent.

NOTE: Dissolved gases can cause performance problems if present in high amounts in the Diluent, Internal Standard or Reference Electrolyte. In this case mix the contents of the bottle gently before use.

Electrodes

Sodium	2 months or 9000 tests
Potassium	2 months or 9000 tests
Chloride	2 months or 9000 tests
Reference	6 months

The electrodes should be replaced after this time period has expired.

For replacement refer to instructions in the Operator's Manual.

Slope ranges

Sodium	50 to 68	mV/dec
Potassium	50 to 68	mV/dec
Chloride	-40 to -68	mV/dec

The slope ranges for newly installed electrodes should be in the upper half of the recommended electrode slope range (excluding chloride).

ISE solution summary

Solution	Usage
S1	Full calibration
S2	Full calibration
S3	Full calibration (Compensation)
Reference Electrolyte	Provides a reference potential.
Diluent	For dilution.
Internal Standard	Monitoring of Electrode potential.
Cleaning Solution	Cleans the ion-selective electrodes, dilution vessel and tubing.
Deproteinizer	Cleans the ISE reagent flow path.

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CAUTION: The above-mentioned ISE calibrators, auxiliary reagents and electrodes are required to calibrate and calculate results for the ISE analytical unit. Use of any other products may result in inaccurate measurements of routine samples and/or damage to the electrodes or any other component of the ISE analytical units.

Specimen collection and preparation[6]

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum: Use serum free of hemolysis and gross lipemia, collected by standard venipuncture technique.
Plasma: Use only lithium heparin.
Urine:[7] Collect 24-hour urine without additives. Store refrigerated during collection.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature.[8]

Stability in serum, plasma and urine samples kept in tightly closed tubes are given in the table below.[8]

	15-25 °C	2-8 °C	-20 °C
Sodium	14 days	14 days	stable
Potassium	14 days	14 days	stable
Chloride	7 days	7 days	stable

Preparation

Do not allow serum to remain on the cells after centrifugation. As described in the literature, potassium values in serum are increased compared to plasma. Serum potassium is released from platelets during clotting. The higher the platelet count, the greater the error.[9] While serum is susceptible to preanalytic handling (hemolysis) and leakage from erythrocytes, plasma is preferable to serum as sample material for potassium determination.

The chloride content of serum or plasma is stable for several days when the sample is separated from erythrocytes and stored in a tightly closed container.[7]

Gross lipemia causes pseudohyponatremia.[10] Grossly lipemic specimens should be cleared by ultracentrifugation.

Potassium: For certain types of hematological neoplasias, (severe) pseudohyperkalemia using lithium heparin samples has been reported.[11,12,13]

CAUTION:

Serum separator tubes have to be used in accordance with the manufacturer's recommended procedures. If these procedures are not considered, it is possible to coat the sample probe with gel (interfering with proper sample level detection), or even to aspirate gel into the ISE system (resulting in a clogged system). Inadequate mixing of plasma tubes can cause introduction of fibrin microclots into and subsequent clogging of the ISE.

Pipetting parameters:

cobas c 303 ISE unit / cobas pro ISE analytical unit

Serum/plasma:

Sample volumes	*Sample dilution*	
	Sample	*ISE Diluent*
Normal	15 µL	450 µL

Urine:

Sample volumes	*Sample dilution*	
	Sample	*ISE Diluent*
Normal	15 µL	450 µL
Decreased	10 µL	450 µL
Increased	n.a.	n.a.

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

NOTE: Each laboratory should establish guidelines for determining acceptability of specimens and the corrective action to be taken if a specimen is considered unacceptable. Compile a laboratory-specific guideline.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

See "Order information" section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Calibration

Full calibration for Na^+, K^+ and Cl^- requires the following 3 calibrator solutions: ISE Standard Low (S1), ISE Standard High (S2), and ISE Standard High (S3). The slope of the calibration curve is calculated from Standards 1 and 2. ISE Internal Standard is measured to provide E_0 for all measurements. Refer to the Operator's Manual of the analyzer for detailed calibration instructions.
Traceability: This method has been standardized against primary calibrators prepared gravimetrically from purified salts.

Calibration frequency

Full calibration

- every 24 hours
- after ISE cleaning and maintenance
- after changing any reagent bottle
- after replacing any electrode
- as required following quality control procedures

Quality control

For quality control, use control materials as listed in the "Order information" section. In addition, other suitable control material can be used.

Serum/plasma:	PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2, Precinorm U Plus, Precipath U Plus
Urine:	Quantitative urine controls are recommended for routine quality control.

Quality controls should be performed daily and after every additional calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Refer to appropriate value sheets/package inserts for additional information.

Expected values[1]

Serum	Sodium	136-145 mmol/L
(Adults)	Potassium	3.5-5.1 mmol/L
	Chloride	98-107 mmol/L
Plasma	Sodium	136-145 mmol/L
(Adults)	Potassium	3.4-4.5 mmol/L

	Chloride	98-107 mmol/L

Plasma potassium levels are reported to be lower than serum levels.

Urine (24 h)	Sodium	40-220 mmol/24 h
(Adults)	Potassium	25-125 mmol/24 h
	Chloride	110-250 mmol/24 h

The urinary excretion of sodium, potassium and chloride varies significantly with dietary intake. The values given here are typical of people on an average diet.

NOTE: It is recommended that each laboratory establishes and maintains its own reference ranges. The values given here are only to be used as a guideline.

Maintenance

The system maintenance procedures and frequencies stated in the Operator's Manual must be performed each day at the end of the daily sample run or after an elevated sample throughput.

cobas c 303 ISE /**cobas pro** ISE analytical unit maintenance:

The specially labeled wash rack (green) is used.

Position 1: ISE Cleaning Solution (used for weekly wash rack)

Position 2: ISE Cleaning Solution (used for daily wash rack)

Position 3: Activator

The system recognizes the wash rack and switches automatically to cleaning mode.

NOTE: Always use fresh solutions for cleaning.

The ISE system requires conditioning after cleaning and prior to calibration.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Hemolysis - serum

Sodium and chloride

Hemolysis:[14] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Hemolysis - urine

Sodium and chloride

Hemolysis: No significant interference up to a hemoglobin concentration of 621 µmol/L or 1000 mg/dL.

Hemolysis - serum and urine

Potassium

Do not use hemolyzed samples.

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.

An H-index of ≤ 20 equals an increase of the potassium concentration of ≤ 0.1 mmol/L.[15]

Icterus - serum

Icterus:[14] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Icterus - urine

Icterus: No significant interference up to a conjugated bilirubin concentration of 1026 µmol/L or 60 mg/dL.

Lipemia - serum

Lipemia (Intralipid):[14] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Pseudohyponatremia may be seen with lipemic specimens as a result of fluid displacement.[10]

Sodium: Altered protein-/lipid levels may falsely shift sodium results into the opposite direction; i.e. elevated protein level = pseudohyponatremia, decreased protein level = pseudohypernatremia.[16,17]

Drugs

The following drugs have been tested and caused no significant interference when added to aliquots of pooled normal human serum up to the indicated concentration. Falsely high chloride values have been reported from patients receiving perchlorate medication. This is due to an interference of perchlorate ions with chloride ISE determinations.

Serum panel:

Acetaminophen (paracetamol)	200 mg/L
Acetylcysteine	1660 mg/L
Acetylsalicylic acid	1000 mg/L
Ampicillin-Na	1000 mg/L
Ascorbic acid	300 mg/L
Cefoxitin	2500 mg/L
Cyclosporin	5 mg/L
Doxycycline	50 mg/L
Heparin	5000 IU/L
Ibuprofen	500 mg/L
Intralipid	10000 mg/L
L-Dopa	20 mg/L
Methyldopa	20 mg/L
Metronidazol	200 mg/L
Phenylbutazone	400 mg/L
Rifampicin	60 mg/L
Theophylline	100 mg/L

Urine panel:

Acetaminophen (paracetamol)	3000 mg/L
Acetylcysteine	10 mg/L
Ascorbic acid	4000 mg/L
Gentamycin sulfate	400 mg/L
Ibuprofen	4000 mg/L
Levodopa	1000 mg/L
Methyldopa	2000 mg/L
Cefoxitin	12000 mg/L
Ofloxacine	900 mg/L
Phenazopyridine	300 mg/L
Salicyluric acid	6000 mg/L
Tetracycline	300 mg/L

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges

Measuring range

Measuring mode ISE indirect:

Application for serum and plasma:

Na^+	80-180 mmol/L
K^+	1.5-10.0 mmol/L
Cl^-	60-140 mmol/L

Analysis of sodium on a **cobas c** system with serum and plasma specimens should yield a linear relationship from 80-180 mmol/L with a deviation from the linear line of less than 5 %.

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Analysis of potassium on a **cobas c** system with serum and plasma specimens should yield a linear relationship from 1.5-10.0 mmol/L with a deviation from the linear line of less than 5 %.
Analysis of chloride on a **cobas c** system with serum and plasma specimens should yield a linear relationship from 60-140 mmol/L with a deviation from the linear line of less than 5 %.

Application for urine:

Na^+	20-250 mmol/L
K^+	3-100 mmol/L
Cl^-	20-250 mmol/L

Determine samples having higher concentrations via the rerun function. Dilution of samples via rerun function is a 1:46 dilution. Results from samples diluted using the rerun function are automatically multiplied by the dilution factor.

Rerun for urine samples with decreased sample volume:

Na^+	251-375 mmol/L
K^+	101-150 mmol/L
Cl^-	251-375 mmol/L

Analysis of sodium on a **cobas c** system with urine specimens should yield a linear relationship from 20-250 mmol/L with a deviation from the linear line of less than 10 %.

Analysis of potassium on a **cobas c** system with urine specimens should yield a linear relationship from 3-100 mmol/L with a deviation from the linear line of less than 10 %.

Analysis of chloride on a **cobas c** system with urine specimens should yield a linear relationship from 20-250 mmol/L with a deviation from the linear line of less than 10 %.

For Urine Rerun Application:

Analysis of sodium on a **cobas c** system with urine specimens should yield a linear relationship from 251-375 mmol/L with a deviation from the linear line of less than 10 %.

Analysis of potassium on a **cobas c** system with urine specimens should yield a linear relationship from 101-150 mmol/L with a deviation from the linear line of less than 10 %.

Analysis of chloride on a **cobas c** system with urine specimens should yield a linear relationship from 251-375 mmol/L with a deviation from the linear line of less than 10 %.

Lower limits of measurement for urine samples

Limit of Blank, Limit of Detection and Limit of Quantitation

Sodium

Limit of Blank	= 3.5 mmol/L
Limit of Detection	= 4.5 mmol/L
Limit of Quantitation	= 12.2 mmol/L

Potassium

Limit of Blank	= 0.16 mmol/L
Limit of Detection	= 0.21 mmol/L
Limit of Quantitation	= 0.89 mmol/L

Chloride

Limit of Blank	= 3.7 mmol/L
Limit of Detection	= 3.9 mmol/L
Limit of Quantitation	= 11.6 mmol/L

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 30 %. It has been determined using low concentration sodium/potassium/chloride samples.

Values below Limit of Quantitation are not reliable due to possible higher uncertainty.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

cobas pro ISE analytical unit:

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas pro** ISE analytical unit.

Sodium

	Repeatability			Intermediate precision		
Sample (on a **cobas pro** ISE analytical unit)	Mean mmol/L	SD mmol/L	CV %	Mean mmol/L	SD mmol/L	CV %
PCCC1[a)]	111	0.36	0.3	111	0.97	0.9
PCCC2[b)]	134	0.40	0.3	134	0.90	0.7
Human plasma 1	84.7	0.28	0.3	84.7	1.25	1.5
Human plasma 2	129	0.45	0.3	129	0.88	0.7
Human plasma 3	135	0.52	0.4	135	0.93	0.7
Human plasma 4	149	0.52	0.3	149	0.82	0.6
Human plasma 5	174	0.62	0.4	174	0.95	0.5
Human serum 1	83.0	0.29	0.3	83.0	1.38	1.7
Human serum 2	131	0.52	0.4	131	0.93	0.7
Human serum 3	135	0.47	0.3	135	1.02	0.8
Human serum 4	150	0.52	0.3	150	0.80	0.5
Human serum 5	173	0.63	0.4	173	0.95	0.5
Liquichek 1	78.1	0.34	0.4	78.1	1.06	1.4
Liquichek 2	175	0.71	0.4	175	1.05	0.6
Human urine 1	24.8	0.25	1.0	24.8	1.19	4.8
Human urine 2	136	0.47	0.3	136	0.94	0.7
Human urine 3	111	0.38	0.3	111	0.94	0.8
Human urine 4	204	0.96	0.5	204	1.23	0.6
Human urine 5	241	0.95	0.4	241	1.63	0.7

Potassium

	Repeatability			Intermediate precision		
Sample (on a **cobas pro** ISE analytical unit)	Mean mmol/L	SD mmol/L	CV %	Mean mmol/L	SD mmol/L	CV %
PCCC1[a)]	3.66	0.02	0.4	3.66	0.04	1.1
PCCC2[b)]	6.77	0.02	0.3	6.77	0.05	0.8
Human plasma 1	1.65	0.01	0.7	1.65	0.05	2.9
Human plasma 2	5.82	0.02	0.4	5.82	0.04	0.6
Human plasma 3	2.97	0.01	0.5	2.97	0.05	1.6
Human plasma 4	7.50	0.03	0.4	7.50	0.06	0.8
Human plasma 5	9.52	0.04	0.4	9.52	0.11	1.1

Human serum 1	1.59	0.01	0.7	1.59	0.04	2.3
Human serum 2	5.96	0.02	0.4	5.96	0.03	0.5
Human serum 3	2.96	0.01	0.4	2.96	0.04	1.2
Human serum 4	7.79	0.03	0.4	7.79	0.05	0.7
Human serum 5	9.86	0.05	0.5	9.86	0.08	0.8
Liquichek 1	31.1	0.24	0.8	31.1	0.55	1.8
Liquichek 2	69.9	0.45	0.6	69.9	1.56	2.2
Human urine 1	3.31	0.03	0.8	3.31	0.05	1.5
Human urine 2	50.8	0.30	0.6	50.8	1.01	2.0
Human urine 3	32.4	0.26	0.8	32.4	0.58	1.8
Human urine 4	82.4	0.85	1.0	82.4	2.07	2.5
Human urine 5	95.7	1.20	1.3	95.7	2.56	2.7

Chloride

	Repeatability			Intermediate precision		
Sample (on a **cobas pro** ISE analytical unit)	Mean mmol/L	SD mmol/L	CV %	Mean mmol/L	SD mmol/L	CV %
PCCC1[a)]	82.5	0.31	0.4	82.5	1.22	1.5
PCCC2[b)]	112	0.46	0.4	112	1.15	1.0
Human plasma 1	71.2	0.31	0.4	71.2	1.20	1.7
Human plasma 2	112	0.51	0.5	112	1.06	0.9
Human plasma 3	91.6	0.44	0.5	91.6	1.38	1.5
Human plasma 4	123	0.50	0.4	123	0.85	0.7
Human plasma 5	137	0.53	0.4	137	1.03	0.7
Human serum 1	73.4	0.23	0.3	73.4	1.08	1.5
Human serum 2	111	0.53	0.5	111	0.98	0.9
Human serum 3	91.4	0.35	0.4	91.4	1.17	1.3
Human serum 4	124	0.54	0.4	124	0.89	0.7
Human serum 5	133	0.62	0.5	133	0.82	0.6
Liquichek 1	95.2	0.41	0.4	95.2	1.18	1.2
Liquichek 2	184	0.69	0.4	184	1.79	1.0
Human urine 1	28.5	0.14	0.5	28.5	1.08	3.8
Human urine 2	139	0.58	0.4	139	1.44	1.0
Human urine 3	115	0.55	0.5	115	1.37	1.2
Human urine 4	207	0.93	0.5	207	1.92	0.9
Human urine 5	236	0.99	0.4	236	2.59	1.1

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

The data obtained on **cobas pro** analyzer(s) are representative for **cobas c** 303 analyzer(s).

Method comparison

ISE values for human plasma samples obtained on a **cobas pro** ISE analytical unit (y) were compared with those determined using the corresponding reference method (x) (sodium only) and with a **cobas c** 501 analyzer (x).

ISE values for human urine samples obtained on a **cobas pro** ISE analytical unit (y) were compared with those determined using the corresponding reference method (x) (sodium only) and with a **cobas c** 501 analyzer (x).

The reference method used was: Flame Photometer FP 8400 for sodium.

Sodium					
Instruments	**Sample Type/ N**	**Min x**	**Max x**	**P/B Regression[18]**	**Coeff. (r)**
x: flame photom. y: **cobas pro** ISE	Plasma / 118	80.4	175	y = 1.031x - 4.12	0.997
Bias at 135 mmol/L = 0.037 (0.0 %) Bias at 155 mmol/L = 0.652 (0.4 %)					
x: **cobas c** 501 y: **cobas pro** ISE	Plasma / 120	84.2	177	y = 1.003x - 1.72	1.000
Bias at 135 mmol/L = -1.33 (-1.0 %) Bias at 155 mmol/L = -1.27 (-0.8 %)					
x: flame photom. y: **cobas pro** ISE	Serum / 120	81.3	174	y = 1.016x - 1.11	0.996
Bias at 135 mmol/L = 1.09 (0.8 %) Bias at 155 mmol/L = 1.41 (0.9 %)					
x: **cobas c** 501 y: **cobas pro** ISE	Serum / 120	84.4	175	y = 1.027x - 4.38	1.000
Bias at 135 mmol/L = -0.766 (-0.6 %) Bias at 155 mmol/L = -0.230 (-0.1 %)					
x: flame photom. y: **cobas pro** ISE	Urine / 120	22.5	249	y = 0.993x - 2.46	1.000
x: **cobas c** 501 y: **cobas pro** ISE	Urine / 120	25.5	241	y = 1.019x - 2.90	1.000

Potassium					
Instruments	**Sample Type/ N**	**Min x**	**Max x**	**P/B Regression[18]**	**Coeff. (r)**
x: **cobas c** 501 y: **cobas pro** ISE	Plasma / 120	1.71	9.57	y = 0.998x - 0.00004	1.000
Bias at 3.5 mmol/L = -0.041 (-1.2 %) Bias at 5.5 mmol/L = -0.064 (-1.2 %)					
x: **cobas c** 501 y: **cobas pro** ISE	Serum / 120	1.62	10.0	y = 1.004x - 0.082	1.000
Bias at 3.5 mmol/L = -0.068 (-1.9 %) Bias at 5.5 mmol/L = -0.060 (-1.1 %)					
x: **cobas c** 501 y: **cobas pro** ISE	Urine / 119	3.28	96.4	y = 1.035x - 0.507	1.000

Chloride					
Instruments	**Sample Type/ N**	**Min x**	**Max x**	**P/B Regression[18]**	**Coeff. (r)**

ISE indirect Na-K-Cl for Gen.2

x: **cobas c** 501 y: **cobas pro** ISE	Plasma / 118	60.5	140	y = 0.997x - 0.127	1.000
Bias at 95 mmol/L = -0.384 (-0.4 %) Bias at 110 mmol/L = -0.423 (-0.4 %)					
x: **cobas c** 501 y: **cobas pro** ISE	Serum / 118	61.7	135	y = 1.000x - 0.600	1.000
Bias at 95 mmol/L = -0.600 (-0.6 %) Bias at 110 mmol/L = -0.600 (-0.5 %)					
x: **cobas c** 501 y: **cobas pro** ISE	Urine / 119	25.0	245	y = 1.023x - 2.09	1.000

Bias at the medical decision level (MDL) was calculated as follows:
Bias [mmol/L] = intercept + (slope x MDL) - MDL
Bias [%] = (Bias [mmol/L] x 100) / MDL

ISE values for human plasma and serum samples obtained on a **cobas c** 303 ISE unit (y) were compared with those determined using the corresponding reference method (x) (sodium only), with a **cobas pro** ISE analytical unit (x) and with a **cobas c** 501 analyzer (x).

ISE values for human urine samples obtained on a **cobas c** 303 ISE unit (y) were compared with those determined using the corresponding reference method (x) (sodium only), with a **cobas pro** ISE analytical unit (x) and with a **cobas c** 501 analyzer (x).

The reference method used was: Flame Photometer FP 8400 for sodium.

Sodium					
Instruments	**Sample Type/ N**	**Min x**	**Max x**	**P/B Regression**[18]	**Coeff. (r)**
x: flame photom. y: **cobas c** 303 ISE	Plasma / 118	81.6	176	y = 0.985x + 1.38	0.994
Bias at 135 mmol/L = -0.581 (-0.4 %) Bias at 155 mmol/L = -0.871 (-0.6 %)					
x: **cobas pro** ISE y: **cobas c** 303 ISE	Plasma / 119	84.5	174	y = 0.980x + 2.38	0.999
Bias at 135 mmol/L = -0.256 (-0.2 %) Bias at 155 mmol/L = -0.647 (-0.4 %)					
x: **cobas c** 501 y: **cobas c** 303 ISE	Plasma / 119	85.8	175	y = 1.000x - 1.20	0.999
Bias at 135 mmol/L = -1.20 (-0.9 %) Bias at 155 mmol/L = -1.20 (-0.8 %)					
x: flame photom. y: **cobas c** 303 ISE	Serum / 120	81.5	182	y = 1.007x - 1.19	0.996
Bias at 135 mmol/L = -0.307 (-0.2 %) Bias at 155 mmol/L = -0.176 (-0.1 %)					
x: **cobas pro** ISE y: **cobas c** 303 ISE	Serum / 120	81.6	178	y = 0.984x + 1.23	1.000
Bias at 135 mmol/L = -0.988 (-0.7 %) Bias at 155 mmol/L = -1.32 (-0.8 %)					
x: **cobas c** 501 y: **cobas c** 303 ISE	Serum / 120	82.9	178	y = 1.000x - 1.50	1.000
Bias at 135 mmol/L = -1.50 (-1.1 %) Bias at 155 mmol/L = -1.50 (-1.0 %)					
x: flame photom. y: **cobas c** 303 ISE	Urine / 105	24.9	256	y = 0.973x + 1.97	0.999
x: **cobas pro** ISE y: **cobas c** 303 ISE	Urine / 119	19.9	246	y = 0.997x + 0.355	1.000
x: **cobas c** 501 y: **cobas c** 303 ISE	Urine / 113	22.2	237	y = 0.990x + 3.11	1.000

Potassium					
Instruments	**Sample Type/ N**	**Min x**	**Max x**	**P/B Regression**[18]	**Coeff. (r)**
x: **cobas pro** ISE y: **cobas c** 303 ISE	Plasma / 120	1.52	9.95	y = 0.990x + 0.029	1.000
Bias at 3.5 mmol/L = -0.006 (-0.2 %) Bias at 5.5 mmol/L = -0.025 (-0.5 %)					
x: **cobas c** 501 y: **cobas c** 303 ISE	Plasma / 120	1.55	10.0	y = 0.997x - 0.029	1.000
Bias at 3.5 mmol/L = -0.041 (-1.2 %) Bias at 5.5 mmol/L = -0.047 (-0.9 %)					
x: **cobas pro** ISE y: **cobas c** 303 ISE	Serum / 116	1.62	9.81	y = 0.990x - 0.004	1.000
Bias at 3.5 mmol/L = -0.038 (-1.1 %) Bias at 5.5 mmol/L = -0.058 (-1.1 %)					
x: **cobas c** 501 y: **cobas c** 303 ISE	Serum / 116	1.56	9.78	y = 0.984x + 0.059	1.000
Bias at 3.5 mmol/L = 0.002 (0.1 %) Bias at 5.5 mmol/L = -0.031 (-0.6 %)					
x: **cobas pro** ISE y: **cobas c** 303 ISE	Urine /120	3.55	98.9	y = 0.983x + 0.290	1.000
x: **cobas c** 501 y: **cobas c** 303 ISE	Urine / 119	3.49	93.0	y = 0.950x + 0.628	1.000

Chloride

ISE indirect Na-K-Cl for Gen.2

ISE indirect Na-K-Cl for Gen.2

Instruments	Sample Type/ N	Min x	Max x	P/B Regression[18]	Coeff. (r)
x: **cobas pro** ISE y: **cobas c** 303 ISE	Plasma / 120	65.5	137	y = 0.996x + 0.276	0.999
Bias at 95 mmol/L = -0.110 (-0.1 %) Bias at 110 mmol/L = -0.171 (-0.2 %)					
x: **cobas c** 501 y: **cobas c** 303 ISE	Plasma / 120	66.4	138	y = 1.000x - 1.20	0.999
Bias at 95 mmol/L = -1.20 (-1.3 %) Bias at 110 mmol/L = -1.20 (-1.1 %)					
x: **cobas pro** ISE y: **cobas c** 303 ISE	Serum / 118	62.2	138	y = 1.000x - 0.200	1.000
Bias at 95 mmol/L = -0.200 (-0.2 %) Bias at 110 mmol/L = -0.200 (-0.2 %)					
x: **cobas c** 501 y: **cobas c** 303 ISE	Serum / 118	62.6	138	y = 1.003x - 1.01	1.000
Bias at 95 mmol/L = -0.761 (-0.8 %) Bias at 110 mmol/L = -0.722 (-0.7 %)					
x: **cobas pro** ISE y: **cobas c** 303 ISE	Urine / 119	21.3	243	y = 1.011x - 1.03	1.000
x: **cobas c** 501 y: **cobas c** 303 ISE	Urine / 118	21.3	249	y = 0.984x + 2.29	1.000

Bias at the medical decision level (MDL) was calculated as follows: Bias [mmol/L] = intercept + (slope x MDL) - MDL Bias [%] = (Bias [mmol/L] x 100) / MDL

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606