ISE indirect Na-K-Cl for Gen.2

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Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
11360981216	ISE Reference Electrolyte (5 x 300 mL)		**cobas c** 311, **cobas c** 501
04522320190	ISE Internal Standard Gen.2 (5 x 600 mL)		
04522630190	ISE Diluent Gen.2 (5 x 300 mL)		
11298500316	ISE Cleaning Solution (5 x 100 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 502	
11183982216	ISE Standard High (10 x 3 mL)	Code 503 / 763	
05979854190	Internal Standard Insert - ISE (Set of 20)		
12149435122	Precinorm U Plus (10 x 3 mL)	Code 300	
12149435160	Precinorm U Plus (10 x 3 mL, for USA)	Code 300	
12149443122	Precipath U Plus (10 x 3 mL)	Code 301	
12149443160	Precipath U Plus (10 x 3 mL, for USA)	Code 301	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	

English

Intended use and Test principle

Intended use

The ISE module of the Roche/Hitachi **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, potassium and chloride 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 and serves to regulate the balance of extracellular fluid distribution. 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 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:

(1) $E = E_0 + RT / nF \cdot \ln (f \cdot C_t) / (f \cdot C_i)$

Where:

E	=	electrode EMF
E_0	=	standard EMF
R	=	constant
T	=	temperature
n	=	charge of the ion
F	=	Faraday's constant
ln	=	natural logarithm (base e)
f	=	activity coefficient
C_t	=	ion concentration in test solution
C_i	=	ion concentration in internal filling solution

For sodium, potassium and chloride, which all carry a single charge, R, T, n, and F are combined into a single value representing the slope (S). For determination on a **cobas c** 311/501 analyzer where the sample is diluted 1:31, the ionic strength and therefore the activity coefficients are essentially constant.

The concentration of the test ion in the internal filling solution is also constant. These constants may be combined into the E_0 term. The value of E_0 is also specific for the type of reference electrode used. Equation (1) can hence be rewritten to reflect these conditions:

(2) $E = E'_0 + S \cdot \ln (C_t)$

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.

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Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

REF 04522320190/04522630190:

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

Contains mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1).

EUH 208 May produce an allergic reaction.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

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.

ISE calibrators, auxiliary reagents and electrodes

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^-

Storage and stability

Store S1, S2 and S3 at 15-25 °C.

See label for expiration date.

On-board stability

Calibrators S1, S2 and S3: **to be used for one calibration only.**

Auxiliary reagents

ISE Reference Electrolyte

1 mol/L potassium chloride

ISE Diluent (ready for use)

HEPES buffer: 10 mmol/L

Triethanolamine: 7 mmol/L

Preservative

ISE Internal Standard (ready for use)

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:

12 % with sodium hypochloride solution < 2 % active Cl

Storage and Stability

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

Store ISE Cleaning Solution at 2-8 °C.

See label for expiration date.

On-board stability

ISE Reference Electrolyte	4 weeks
ISE Diluent	2 weeks
ISE Internal Standard	2 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.

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.

NOTE: Customers using **cobas c** 311/501 analyzers: in case of proven or potential ISE Internal Standard evaporation use Internal Standard Insert – ISE (Cat. No. 05979854 190) to reduce the potential for evaporation.

Electrodes

Sodium, Potassium, Chloride, Reference

Storage and Stability

Store electrodes at 7-40 °C.

See label for expiration date.

On-board stability

Sodium	2 months or 9000 tests
Potassium	2 months or 9000 tests
Chloride	2 months or 9000 tests
Reference	at least 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.

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

Specimen collection and preparation[6]

Specimen

Only the specimens listed below were tested and found acceptable.

Serum separation tube: 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.

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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. Turbid urine samples should be cleared by centrifugation.

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

CAUTION:

Serum separator tubes containing acrylic, ester, styrene, urethane or olefin based gels may be used for sample collection as long as they are used in accordance with the manufacturer's recommended procedures. It is especially important that storage temperature, adequate mixing, clotting times and centrifugation at sufficient g-forces for sufficient time periods are respected. Ensure also correct filling levels and ensure a minimum of 1 cm sample above gel layer. If these precautions are not taken, it is possible to accidentally 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 interference with micro fibrin clots. It is strongly recommended to avoid silicone-type gels, due to risk of silicon oil contaminations. In addition, tubes that exhibit a layer of clear liquid, which rises to the top of the serum after centrifugation, should not be used for direct sample aspiration, in order to prevent coating the sample probes and interfering with ISE system.

Pipetting parameters:

The sample volume pipetted by **cobas c** 311/501 systems is 9.7 µL (as well as for automatic rerun). Another 6.5 µL is pipetted for the urine manual rerun.

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.

Procedure of ISE measurements

Assay

Refer to the Operator's Manual of the analyzer.

Calibration

Full calibration for Na^+, K^+ and Cl^- requires the following 3 calibrator solutions: ISE Standard Low, ISE Standard High, and ISE Standard High (compensated). The slope of the calibration curve is calculated from Standards 1 and 2. ISE Compensation affects the intercept, not the slope. An internal standard is also measured during calibration and between samples to compensate for any system deviations.

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

Perform a full calibration

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

Quality control

For serum/plasma quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

For urine quality control, use commercially available urine controls.

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.

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

cobas c 501 maintenance:

The specially labeled wash rack (green) is used.

Position 1: Multiclean (not necessary when only the ISE is cleaned)

Position 2: ISE Cleaning Solution

Position 3: Activator (The ISE system requires conditioning after cleaning and prior to calibration.)

Note: Always use fresh solutions for cleaning.

cobas c 311 maintenance:

The specially designated positions on the sample disk are used. The ISE Wash procedure has to be manually selected out of maintenance items.

Position W1: ISE Cleaning Solution.

Position W2: Activator. (The ISE system requires conditioning after cleaning and prior to calibration.)

Note: Always use fresh solutions for cleaning.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Hemolysis - serum

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Sodium and chloride

Hemoglobin does not interfere in the tested concentration range up to 1000 mg/dL (621 µmol/L) hemoglobin (approximate H index 1000).

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.[14]

Icterus - serum

Bilirubin (conjugated/unconjugated) does not interfere in the tested concentration range up to 60 mg/dL (1026 µmol/L) bilirubin (approximate I index 60).

Icterus - urine

Bilirubin (conjugated) does not interfere in the tested concentration range up to 60 mg/dL (1026 µmol/L) bilirubin (approximate I index 60).

Lipemia - serum

Intralipid does not interfere in the tested concentration range up to 2000 mg/dL Intralipid (corresponding to an approximate L index of 2000). There is poor correlation between the L index (corresponds to turbidity) and the 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.[15,16]

Drugs

The following drugs have been tested and caused no significant interference when added to aliquots of pooled normal human serum or pooled urine 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 determination.

Serum panel:

Acetaminophen (paracetamol)	200 mg/L
Acetylcysteine	150 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
Doxycyclin	50 mg/L
Heparin	5000 U
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
Doxycyclin	300 mg/L
Gentamycin sulfate	400 mg/L
Ibuprofen	4000 mg/L
L-Dopa	1000 mg/L
Methyldopa	2000 mg/L
Na-Cefoxitin	12000 mg/L
Ofloxacine	900 mg/L
Phenazopyridine	300 mg/L
Salicyluric acid	6000 mg/L

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

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

Application for urine:

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

NOTE: All results falling outside the measuring ranges for urine will be reported with a <> / < *Test* data alarm due to the fact that the results are evaluated independently of sample volume. Results for the manual rerun of urine samples with both a reduced sample volume, and the data alarm <> / < *Test* , must be checked against the manual rerun urine sample ranges (see below). When running samples with reduced sample volumes the results of such samples must be assessed on an individual basis. The reason for this is that matrix effects cannot be excluded for such samples.

Manual rerun of urine samples with reduced sample volume:

Na+	250-375 mmol/L
K+	100-150 mmol/L
Cl-	250-375 mmol/L

NOTE: All results outside the following ranges Na+ 20-250 mmol/L, K+ 3-100 mmol/L, Cl- 20-250 mmol/L will always have a <> / < *Test* data alarm attached. Urine rerun results with reduced sample volume with this alarm need to be checked against the ranges for rerun urine samples case by case.

Determine urine samples having higher concentrations via the rerun function. Dilution of urine samples via the rerun function is a 1:1.5 dilution. Results from urine samples diluted using the rerun function are automatically multiplied by a factor of 1.5.

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 %.

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 %.

Specific performance data

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

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Data contained within this section are representative of typical performance for **cobas c** 501 ISE systems and are not be viewed as test specifications.

Precision

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

Sodium						
	Repeatability			**Intermediate precision**		
Sample (on a **cobas c** 501)	Mean mmol/L	SD mmol/L	CV %	Mean mmol/L	SD mmol/L	CV %
Plasma low	84.8	0.2	0.3	84.8	1	1.1
Plasma medium	121.4	0.3	0.3	121.4	0.8	0.6
Plasma high	176.7	0.3	0.2	176.7	0.6	0.4
Precinorm U	126	0.2	0.2	126.0	0.7	0.6
Precipath U	148.2	0.3	0.2	148.2	0.5	0.4
Urine low	30.6	0.1	0.2	30.6	0.9	3.0
Urine medium	131.7	0.2	0.2	131.7	0.6	0.5
Urine high	236.7	0.4	0.2	236.7	1.3	0.6
Liquichek 1	81.6	0.2	0.2	81.6	1.3	1.6
Liquichek 2	172.3	0.2	0.1	172.3	2.6	1.5

Potassium						
	Repeatability			**Intermediate precision**		
Sample (on a **cobas c** 501)	Mean mmol/L	SD mmol/L	CV %	Mean mmol/L	SD mmol/L	CV %
Plasma low	1.62	0.01	0.7	1.62	0.03	1.6
Plasma medium	4.97	0.04	0.7	4.97	0.04	0.8
Plasma high	9.46	0.06	0.6	9.46	0.07	0.7
Precinorm U	3.57	0.03	0.8	3.57	0.04	1.0
Precipath U	6.59	0.04	0.6	6.59	0.05	0.7
Urine low	5.12	0.03	0.6	5.12	0.04	0.7
Urine medium	52.08	0.32	0.6	52.08	0.67	1.3
Urine high	90.34	0.67	0.7	90.34	1.38	1.5
Liquichek 1	31.48	0.19	0.6	31.48	0.53	1.7
Liquichek 2	70.56	0.43	0.6	70.56	1.17	1.7

Chloride						
	Repeatability			**Intermediate precision**		
Sample (on a **cobas c** 501)	Mean mmol/L	SD mmol/L	CV %	Mean mmol/L	SD mmol/L	CV %
Plasma low	68.5	0.2	0.3	68.5	0.6	0.8
Plasma medium	129.0	0.4	0.3	129.0	0.6	0.5
Plasma high	139.0	0.3	0.2	139.0	0.6	0.4
Precinorm U	86.2	0.2	0.3	86.2	0.5	0.6
Precipath U	119.2	0.3	0.2	119.2	0.5	0.4
Urine low	25.8	0.1	0.2	25.8	0.6	2.3
Urine medium	131.4	0.3	0.2	131.4	0.7	0.5
Urine high	243.4	0.6	0.2	243.4	1.8	0.7
Liquichek 1	97.5	0.2	0.2	97.5	1.6	1.6
Liquichek 2	198.2	0.4	0.2	198.2	2.3	1.2

Method comparison

ISE values for human plasma and urine samples obtained on **cobas c** 501 analyzers (y) using Standard High (compensated) as S3 Calibrator, were compared to those determined with the corresponding reference method (x) and with a **cobas c** 501 analyzer using ISE Compensator as S3 Calibrator.

The reference methods used are: Flame Photometer IL 943 for Sodium and Potassium, Chloride Analyzer 926S for Chloride.

Sodium

Instruments	**Sample Type/ N**	**Min.x**	**Max.x**	**P/B Regression**[17]	**Coeff. (r)**
x: flame photom. y: **cobas c** 501 (S3 = Standard High)	Plasma/103	86.7	178	y = 1.000x + 0.300	0.999
Bias at 135 mmol/L = 0.03 (0.2 %) Bias at 150 mmol/L = 0.03 (0.2 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Plasma/103	87.6	176	y = 1.014x - 1.176	1.000
Bias at 135 mmol/L = 0.714 (0.5 %) Bias at 150 mmol/L = 0.924 (0.6 %)					
x: flame photom. y: **cobas c** 501 (S3 = Standard High)	Urine/100	23.5	250	y = 0.964x + 4.032	1.000
Bias at 20 mmol/L = 3.312 (16.6 %) Bias at 220 mmol/L = -3.888 (-1.8 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Urine/100	25.1	245	y = 0.995x + 0.687	1.000
Bias at 20 mmol/L = 0.587 (2.9 %) Bias at 220 mmol/L = -0.413 (-0.2 %)					

Potassium

Instruments	**Sample Type/ N**	**Min.x**	**Max.x**	**P/B Regression**[17]	**Coeff. (r)**
x: flame photom. y: **cobas c** 501 (S3 = Standard High)	Plasma/106	1.59	9.56	y = 1.007x - 0.019	1.000
Bias at 3.0 mmol/L = 0.002 (0.1 %) Bias at 5.8 mmol/L = 0.022 (0.4 %)					

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x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Plasma/106	1.52	9.45	y = 1.006x + 0.024	1.000
Bias at 3.0 mmol/L = 0.042 (1.4 %) Bias at 5.8 mmol/L = 0.059 (1.0 %)					
x: flame photom. y: **cobas c** 501 (S3 = Standard High)	Urine/105	4.00	97.2	y = 1.018x - 0.397	1.000
Bias at 20 mmol/L = 0.757 (3.8 %) Bias at 80 mmol/L = 1.837 (2.3 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Urine/105	4.05	97.4	y = 0.997x + 0.062	0.999
Bias at 20 mmol/L = 0.002 (0.0 %) Bias at 80 mmol/L = -0.178 (-0.2 %)					

Chloride

Instruments	Sample Type/ N	Min.x	Max.x	P/B Regression[17]	Coeff. (r)
x: coulometry y: **cobas c** 501 (S3 = Standard High)	Plasma/105	62.0	136	y = 1.033x - 1.800	0.998
Bias at 90 mmol/L = 1.170 (1.3 %) Bias at 112 mmol/L = 1.896 (1.7 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Plasma/105	61.4	138	y = 1.000x + 0.500	0.999
Bias at 90 mmol/L = 0.500 (0.6 %) Bias at 112 mmol/L = 0.500 (0.4 %)					
x: coulometry y: **cobas c** 501 (S3 = Standard High)	Urine/105	22.0	248	y = 1.020x - 1.700	0.999
Bias at 60 mmol/L = -0.500 (-0.8 %) Bias at 170 mmol/L = 1.700 (1.0 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Urine/105	21.2	250	y = 0.989x + 0.669	1.000
Bias at 60 mmol/L = 0.009 (0.0 %) Bias at 170 mmol/L = -1.201 (-0.7 %)					

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.

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 after reconstitution or mixing
GTIN	Global Trade Item Number

ISE indirect Na-K-Cl for Gen.2

ISE indirect Na-K-Cl for Gen.2

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Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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