ISE indirect Na, K, Cl for Gen.2

cobas®

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Order information

REF	CONTENT		Analyzer(s) on which reagents can be used
11360981 216	ISE Reference Electrolyte (5 x 300 mL)		Roche/Hitachi **cobas c** 311, **cobas c** 501
04522320 190	ISE Internal Standard Gen.2* (5 x 600 mL) *Includes five inserts (chimneys)		
04522630 190	ISE Diluent Gen.2 (5 x 300 mL)		
11298500 160	ISE Cleaning Solution (5 x 100 mL)		
10825468 001	Sodium electrode (1 electrode)		
10825441 001	Potassium electrode (1 electrode)		
03246353 001	Chloride electrode (1 electrode)		
03149501 001	Reference electrode (1 electrode)		
04663632 190	Activator (9 x 12 mL)		
11183974 216	ISE Standard Low (10 x 3 mL)	Code 502	
11183982 216	ISE Standard High (10 x 3 mL)	Code 503 / 763	
12149435 160	Precinorm U Plus (10 x 3 mL)	Code 300	
12149443 160	Precipath U Plus (10 x 3 mL)	Code 301	

English

For use in the USA only

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.

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: 1-800-428-2336

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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

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:

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

To achieve the stated on-board stability, an Internal Standard insert (chimney) must be used.

- Place a new insert (chimney) in the Internal Standard bottle.
- Slowly push the chimney downwards into the bottle. Do not cover the hole of the chimney as it is being pushed down.
- Ensure the chimney is inserted as far as possible.
- Place the bottle, with chimney, into its slot on the analyzer.
- Use a new chimney for each Internal Standard bottle.

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.

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	2-point calibration
S2	2-point calibration
S3	Compensation
Reference Electrolyte	The bottle is connected directly to the ISE Reference electrode. This solution provides a strong stable ion reference potential in the reference electrode necessary for each ISE measurement.
Diluent	For sample dilution
Internal Standard	Baseline calibration which is performed once every ISE cycle.
Cleaning Solution	Intended to clean the ion-selective electrodes, 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: Use serum free of hemolysis and gross lipemia, collected by standard venipuncture technique.

Plasma: Use only lithium heparin.

Comparison of the sample type Serum (x-axis) vs. Li-heparin plasma (y-axis)

Passing/Bablok[7]

Na^+	y = 1.003x - 0.659	r = 1.000
K^+	y = 0.996x + 0.023	r = 0.995
Cl^-	y = 1.009x - 0.754	r = 0.999

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Urine:[8] Collect 24-hour urine without additives. Store refrigerated during collection.

Stability in serum, plasma and urine samples kept in tightly closed tubes are given in the table below.[9]

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

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 and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

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.[10] In internal measurements we observed deviations up to 25 %. 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.[8]

Gross lipemia causes pseudohyponatremia.[11] Grossly lipemic specimens should be cleared by ultracentrifugation. Turbid urine samples should be cleared by centrifugation.

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. Today's global tube suppliers do not employ silicone based gels at all, but it may be that silicone gels are in use by small local suppliers. 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. 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

NOTE: To achieve the stated calibration frequency the Internal Standard insert (chimney) must be used.

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

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.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

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)

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Position 2: ISE Cleaning Solution

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

cobas c 311 maintenance:

The specially designated positions on the sample disk are used.

Position W1: ISE Cleaning Solution.

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

The ISE Wash procedure has to to be manually selected out of maintenance items.

Note: Always use fresh solutions for cleaning.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Hemolysis - serum and urine

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

Hemoglobin levels higher than 90 mg/dL (54 µmol/L) increase the apparent potassium concentrations significantly (approximate 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.

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.[11]

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 Roche/Hitachi **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.

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* or <*Test* data alarm. When this occurs, the analyzer will perform an auto rerun once at the normal samples volume. If the results of auto rerun are still falling outside the measuring range, the operator can request a rerun using the reduced sample volume dilution function on the analyzer. If the results of the reduced sample volume generate the data alarm (<>*Test* or <*Test*), then the results must be checked against the reduced sample volume rerun reportable ranges (see below) due to matrix effects.

The reportable ranges for urine samples with reduced sample volume:

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

The reportable ranges for the urine application with normal sample volume that can be obtained from the analyzer are as follows:

Na^+	20-250 mmol/L
K^+	3-100 mmol/L
Cl^-	20-250 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* or <*Test* data

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alarm attached. Dilution of the urine samples via the reduced sample volume function is a 1:1.5 dilution. Results from the urine samples diluted using the reduced sample volume function are automatically multiplied by a factor of 1.5.

Analysis of sodium on a Roche/Hitachi **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 Roche/Hitachi **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 Roche/Hitachi **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.

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

Precision

Repeatability and intermediate precision were determined using human serum 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 Roche/Hitachi **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 Roche/Hitachi **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	5.15	0.03	0.6	5.15	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 Roche/Hitachi **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, serum and urine samples obtained on Roche/Hitachi **cobas c** 501 analyzers (y) using Standard High as S3 Calibrator, were compared to those determined with the corresponding reference method (x) and with a Roche/Hitachi **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[7]	Coeff. (r)
x: flame photom. y: **cobas c** 501 (S3 = Standard High)	Plasma/52 Serum/51	86.7 97.6	172 178	y = 1.000x + 0.200 y = 0.992x + 1.633	0.999 0.998
Bias at 135 mmol/L = Plasma: 0.200 (0.1 %); Serum: 0.553 (0.4 %) Bias at 150 mmol/L = Plasma: 0.200 (0.1 %); Serum: 0.433 (0.3 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Plasma/52 Serum/51	87.6 97.3	170 176	y = 1.016x - 1.456 y = 1.009x - 0.515	1.000 0.999
Bias at 135 mmol/L = Plasma: 0.704 (0.5 %); Serum: 0.700 (0.5 %) Bias at 150 mmol/L = Plasma: 0.944 (0.6 %); Serum: 0.835 (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 = 3.343 (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

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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[7]	Coeff. (r)
x: flame photom. y: **cobas c** 501 (S3 = Standard High)	Plasma/52	2.10	9.19	y = 1.010x - 0.022	1.000
	Serum/54	1.59	9.56	y = 1.005x - 0.020	1.000
Bias at 3.0 mmol/L = Plasma: 0.008 (0.3 %); Serum: -0.005 (-0.2 %) Bias at 5.8 mmol/L = Plasma: 0.036 (0.6 %); Serum: 0.009 (0.2 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Plasma/52	2.02	9.13	y = 1.008x + 0.018	1.000
	Serum/54	1.52	9.45	y = 1.004x + 0.032	1.000
Bias at 3.0 mmol/L = Plasma: 0.042 (1.4 %); Serum: 0.044 (1.5 %) Bias at 5.8 mmol/L = Plasma: 0.064 (1.1 %); Serum: 0.055 (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[7]	Coeff. (r)
x: coulometry y: **cobas c** 501 (S3 = Standard High)	Plasma/52	69.0	133	y = 1.023x - 0.769	0.998
	Serum/53	62.0	136	y = 1.043x - 2.843	0.999
Bias at 90 mmol/L = Plasma: 1.301 (1.4 %); Serum: 1.027 (1.1 %) Bias at 112 mmol/L = Plasma: 1.807 (1.6 %); Serum: 1.973 (1.8 %)					
x: **cobas c** 501 (S3 = ISE Compensator) y: **cobas c** 501 (S3 = Standard High)	Plasma/52	69.4	134	y = 1.006x - 0.118	0.999
	Serum/53	61.4	138	y = 0.997x + 0.872	1.000
Bias at 90 mmol/L = Plasma: 0.422 (0.5 %); Serum: 0.602 (0.7 %) Bias at 112 mmol/L = Plasma: 0.554 (0.5 %); Serum: 0.536 (0.5 %)					
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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Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see https://usdiagnostics.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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