Na

ISE Sodium Electrode

Order information

REF	CONTENT	SYSTEM
04838084001	ISE Sodium Electrode	**cobas c** 111

Materials required (but not provided):

04838092001	ISE Reference Electrode	
04842367001	ISE Dummy Electrode	
04838149001	ISE Calibrator indirect/urine (2 × 230 mL)	
04838157001	ISE Reference Solution (2 × 115 mL)	
04838106001	ISE Calibrator Kit (6 × 8 mL)	
04838181001	ISE Deproteinizer (2 × 11 mL)	
04838165001	ISE Etcher (2 × 11 mL)	
04663632190	Activator (9 x 12 mL)	
05947626160	PreciControl ClinChem Multi 1 (4 × 5 mL) Code 20391	
05947774160	PreciControl ClinChem Multi 2 (4 × 5 mL) Code 20392	

English

For use in the USA only

System information

ISE-I; Profile: ISE indirect ACN 980

ISE-U; Profile: ISE Urine ACN 979

ISE Na indirect ACN 989

ISE Na Urine ACN 986

Intended use

The sodium electrode for the **cobas c** 111 system is intended for quantitative determination of sodium in diluted serum, plasma and urine.

Summary

Electrolytes are involved in most major metabolic functions in the body.

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.

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

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, which carries a single charge, R, T, n, and F are combined into a single value representing the slope (S). For determination on a **cobas c 111** ISE module where the sample is diluted 1:6, 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) $E = E^{I}_0 + S \times \ln (C_t)$

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 electrode is based on a neutral carrier.

Precautions and warnings

For in vitro diagnostic use for healthcare 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.

On-board stability

Stability after installation: 34 weeks

The electrode should be replaced after this time period is expired.

Slope range

Serum/plasma/urine	45-63 mV/dec

Specimen collection and preparation

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

Only the specimens listed below were tested and found acceptable.

Serum, free from hemolysis

Plasma: Lithium heparin plasma, free from hemolysis

Urine: Collect 24-hour urine without addition of preservatives and/or stabilizers. Store refrigerated during collection.

For sodium determinations serum is the specimen of choice.[1]

If heparinized plasma is used, ensure that the collection tubes are filled with the correct volume of blood. Underfilling of heparin tubes can result in a high concentration of heparin in the sample which has been shown to result in a small but significant underestimation of sodium when measured by ion-selective electrode methods.[2]

High Li-heparin concentrations can cause interference and down drift on sodium measurements.

It is not recommended to use primary tubes with a Li-heparin concentration higher than in standard commercially available tubes for adults. The standard Li-heparin tubes tested have a Li-heparin concentration of 17 IU/mL (14.3 USP/mL) and show no interference on sodium measurements. A down drift can be expected if the Li-heparin concentration is twice this amount or higher.

The sample types listed were tested with a collection of sample collection tubes containing Li-heparin 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 Li-heparin concentrations which could affect the test results in some cases.

It is important to follow tube supplier's recommendations concerning the filling volume and tube handling after blood collection, ensuring that there is no further impact on sodium measurements.

Samples should be separated from the clot or cells promptly after collection. Grossly lipemic specimens should be cleared by ultracentrifugation.

Note: 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 and clotting times 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 probe and interfering with ISE system.

It is possible to clog the sample probe or the ISE tubing with gel or clots if these precautions are not taken.

Separate from cells if analysis is not performed within 4 hours.[3]

The stabilities of sodium in the specimen kept in tightly closed tubes are given in the table below:

Sample stability (Serum and plasma):[4]	14 days at 15-25 °C
	14 days at 2-8 °C
	stable at (-15)-(-25) °C
Sample stability (Urine):[4]	14 days at 15-25 °C

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.

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

Materials provided

See "Order information" section

Materials required (but not provided)

See "Order information" section

General laboratory equipment

Application for serum, plasma and urine

Test definition

Measuring mode	ISE indirect
Test range	20-250 mmol/L
Unit	mmol/L

The sample, control, and standard solutions are diluted with system water 1:6 (1+5). The dilution and mixing are performed automatically in the mixing tower.

Pipetting parameters

Sample	15 µL
Diluent (H_2O)	75 µL

Calibration

Calibrators	ISE Solution 1, 2
	ISE Calibrator indirect/urine
Calibration replicate	Single
Calibration frequency	24 hours (main calibration)
	after ISE cleaning and maintenance
	after changing the reagent bottles
	after replacing electrodes

Traceability: This method has been standardized against primary calibrators prepared gravimetrically from purified salts.

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

Reference range	PreciControl ClinChem Multi 1
Pathological range	PreciControl ClinChem Multi 2
Control interval	5 hours recommended
Control sequence	User defined
Control after calibration	Recommended

Urine

Quality control	Quantitative urine controls are recommended for routine quality control
Control interval	5 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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.

Calculation

The **cobas c** 111 analyzer automatically calculates the analyte concentration of each sample.

Limitations – interference

Serum/plasma

Criterion: Recovery within ± 10 % of initial value.

Hemolysis: Avoid hemolyzed specimens.
No significant interference up to a hemoglobin concentration of 1000 mg/dL.

Icterus: No significant interference up to a bilirubin concentration of 60 mg/dL.

Lipemia: No significant interference up to a triglycerides concentration of 2000 mg/dL.

Dysproteinemia: No significant interference up to 3000 mg/dL.

Altered protein-/lipid levels may falsely shift sodium results into the opposite direction; i.e. elevated protein level = pseudohyponatremia, decreased protein level = pseudohypernatremia.[1,2]

Note: Gross lipemia causes pseudohyponatremia. Grossly lipemic specimens should be cleared by ultracentrifugation.[5]

Drugs: The following drugs were tested according to the recommendations of the symposium "Drug effects in Clinical Chemistry Methods"[6,7] and caused no significant interference when added to aliquots of pooled normal human serum/plasma up to the indicated concentration.

Acetaminophen	200 mg/L
Acetylcysteine	150 mg/L

Acetylsalicylic acid	1000 mg/L
Ampicillin	1000 mg/L
Ascorbic acid	300 mg/L
Calcium dobesilate	200 mg/L
Cefoxitin	2500 mg/L
Cyclosporine	5 mg/L
Doxycycline	50 mg/L
Heparin	5000 U
Intralipid	10000 mg/L
Ibuprofen	500 mg/L
Levodopa	20 mg/L
Methyldopa	20 mg/L
Metronidazole	200 mg/L
Phenylbutazone	400 mg/L
Rifampicin	60 mg/L
Tetracycline	50 mg/L
Theophylline	100 mg/L

Urine

Criterion: Recovery within ± 20 % of initial value.

Drugs: The following drugs were tested according to the recommendations of the symposium “Drug effects in Clinical Chemistry Methods"[6,7] and caused no significant interference when added to aliquots of pooled normal human urine up to the indicated concentration.

Acetaminophen	3000 mg/L
N-Acetylcysteine	10 mg/L
Salicyluric acid	6000 mg/L
Ascorbic acid	4000 mg/L
Calcium dobesilate	1000 mg/L
Cefoxitin	12000 mg/L
Gentamicin sulfate	400 mg/L
Ibuprofen	4000 mg/L
Levodopa	1000 mg/L
Methyldopa	2000 mg/L
Ofloxacine	900 mg/L
Phenazopyridine	300 mg/L
Doxycycline	300 mg/L

pH: Falsely elevated Sodium values will be obtained with samples having pH <5.5

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

Expected values[8]

ISE indirect and flame emission photometry

Serum (adults)	136-145 mmol/L
Plasma (adults)	136-145 mmol/L
Urine (24 h, adults)	40-220 mmol/day

The urinary excretion of sodium varies significantly with dietary intake. The values given 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.

Specific performance data

Representative performance data on the **cobas c** 111 analyzer are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples in an internal protocol with repeatability (n = 20/21) and intermediate precision (1 aliquot per run, 1 run per day, 10 days). The following results were obtained:

	Serum		Plasma		Urine	
	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2
Mean repeatability (mmol/L)	130	156	127	151	55	234
CV repeatability (%)	0.32	0.31	0.31	0.30	0.91	0.52
Mean intermediate precision (mmol/L)	130	155	128	151	49	218
CV intermediate precision (%)	0.42	0.48	0.80	0.75	1.92	0.94

Method comparison

Sodium values for human serum and urine samples obtained on the **cobas c** 111 system (y) were compared with those obtained on the COBAS INTEGRA 400 analyzer (x). Samples were measured in duplicate. Sample size (n) represents all replicates.

Serum

	COBAS INTEGRA 400 analyzer
Sample size (n) = 51	
Passing/Bablok[9]	y = 0.986x - 0.364 mmol/L
Corr. coeff. (r)	0.983

The sample concentrations were between 130 and 146 mmol/L.

Bias at 135 mmol/L = -2.254 (-1.7 %)
Bias at 150 mmol/L = -2.464 (-1.6 %)

Urine

	COBAS INTEGRA 400 analyzer
Sample size (n) = 51	
Passing/Bablok[9]	y = 1.036x - 2.812 mmol/L
Corr. coeff. (r)	0.998

The sample concentrations were between 25 and 240 mmol/L.

Bias at 20 mmol/L = -2.092 (-10.5 %)
Bias at 220 mmol/L = 5.108 (2.3 %)

References

1 Virk MS, Dean NP, Wong ECC. Severe Underestimation of Serum Na following IVIG Treatment. Laboratory Medicine 2018;49:4:372-376.

2 Stove V, Slabbinck A, Vanoverschelde L, et al. How to Solve the Underestimated Problem of Overestimated Sodium Results in the Hypoproteinemic Patient. Crit Care Med 2016;44 (2):e83-e88.

3 Guder WG, Narayanan S, Wisser H, et al. Samples: From the Patient to the Laboratory; Wiley-Liss, 3rd. Ed., p 53.

4 Young DS. Effects of Preanalytical Variables on Clinical Laboratory Tests, 3rd ed. Washington DC: AACC Press 2007;819-822.

5 Tietz NW. Fundamentals of Clinical Chemistry, 5th ed. Burtis CA, Ashwood ER, eds. WB Saunders Co 2001:726-728.

6 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

7 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

8 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia: WB Saunders, 1995;562-565 (sodium).

9 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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 navifyportal.roche.com for definition of symbols used):

CONTENT	Content of kit
SYSTEM	System(s) on which electrode can be used
GTIN	Global Trade Item Number
INSTALL BEFORE	To indicate the last date by when an electrode has to be installed on the instrument.
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

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.

Additions, deletions or changes are indicated by a change bar in the margin.

For USA: Rx only

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