08057958500V8.0

# LDHI2

cobas®

**Lactate Dehydrogenase acc. to IFCC ver.2**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08057958190* | 08057958500 | Lactate Dehydrogenase acc. to IFCC ver.2 (850 tests) | System-ID 2081 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08057958214* | 08057958500 | Lactate Dehydrogenase acc. to IFCC ver.2 (850 tests) | System-ID 2081 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

## English

### System information

**LDHI2:** ACN 20810

**LDHI2P:** ACN 20811 (with automatic sample pre-dilution)

### Intended use

In vitro test for the quantitative determination of lactate dehydrogenase in human serum and plasma on **cobas c** systems.

### Summary

Lactate dehydrogenase (LDH) measurements, performed with this assay in human serum and plasma are used as an aid for diagnosis and monitoring of various clinical conditions associated with tissue damage (e.g. myocardial infarction, liver disorders such as severe toxic liver injury, malignant tumors such as leukemias), and for the prognosis of certain solid tumors.

LDH is a nicotinamide dinucleotide ($NAD^+$)-dependent oxidoreductase and catalyzes the reversible transformation of lactate to pyruvate under anaerobic conditions, coupled with the oxidation of NADH to $NAD^+$.[1,2] LDH is widely distributed in tissue, particularly in the heart, liver, muscles and kidneys. Upon cell injury and/or necrosis, LDH is released into the circulation. LDH in serum can be separated into five different isoenzymes based on their electrophoretic mobility. Each isoenzyme is a tetramer composed of two different subunits. These two subunits have been designated heart and muscle, based on their polypeptide chains. There are two homotetramers, LDH-1 (heart) and LDH-5 (muscle), and three hybrid isoenzymes.[1,2] In disease conditions, the LDH activity measured in serum is dependent on the isoenzymes entering the plasma from the tissues, the elimination rate of the isoenzymes and their subunits.[1,2]

Elevated serum levels of LDH have been observed in a variety of disease states.[1] The highest levels are seen in patients with megaloblastic anemia (up to 50 times the upper reference limit), disseminated carcinoma, sepsis and other causes of shock (because of damage to multiple organs).[1,2] Moderate increases occur in muscular disorders, nephrotic syndrome and cirrhosis. Mild increases in LDH activity have been reported in cases of myocardial or pulmonary infarction, leukemia, hemolytic anemia and non-viral hepatitis. Because of its wide tissue distribution and its lack of tissue specificity for diagnostic use, serum LDH measurement is relevant in broad indications like hematology and oncology.[1,3] LDH is routinely used as a marker of hemolysis in sickle cell disease, along with the elevated reticulocyte count, elevated levels of unconjugated bilirubin concentration and aspartate aminotransferase, and decreased level of serum haptoglobin. While none of those parameters are specific markers of hemolysis, LDH has however been considered the most relevant biomarker of hemolysis and has been proposed as a diagnostic and prognostic marker of acute and chronic complications of sickle cell disease.[4] LDH has demonstrated to have prognostic significance in several tumor types, including pancreatic cancer, lung cancer, advanced thymic carcinoma, osteosarcoma, renal cell carcinoma, colorectal cancer, melanoma, prostate cancer, bladder cancer, and urologic cancer.[1,5,6,7,8,9] As a biochemical marker of tumor burden, LDH has been incorporated into several prognostic scores and staging for several types of cancer (e.g. renal cell carcinoma, melanoma and colorectal cancer).[5,6]

The method described here is derived from the formulation recommended by the IFCC[10,11] and was optimized for performance and stability.

### Test principle

UV assay

Lactate dehydrogenase catalyzes the conversion of L-lactate to pyruvate; NAD is reduced to NADH in the process.

$$\text{L-Lactate} + NAD^+ \xrightarrow{\text{LDH}} \text{Pyruvate} + NADH + H^+$$

The initial rate of the NADH formation is directly proportional to the catalytic LDH activity. It is determined by photometrically measuring the increase in absorbance.

### Reagents - working solutions

**R1** N-methylglucamine: 400 mmol/L, pH 9.4 (37 °C); lithium lactate: 62 mmol/L; stabilizers

**R3** NAD: 62 mmol/L; stabilizers; preservatives

R1 is in position B and R3 is in position C.

### Precautions and warnings

For in vitro diagnostic use for laboratory 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.

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

Warning

H317 May cause an allergic skin reaction.

**Prevention:**

P261 Avoid breathing mist or vapours.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

**Response:**

| | |
|---|---|
| P333 + P313 | If skin irritation or rash occurs: Get medical advice/attention. |
| P362 + P364 | Take off contaminated clothing and wash it before reuse. |

**Disposal:**

| | |
|---|---|
| P501 | Dispose of contents/container to an approved waste disposal plant. |

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

**Hazardous components:**

- hydroxylammonium chloride
- 2-methyl-2H-isothiazol-3-one hydrochloride

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |

**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
Plasma: Li-heparin plasma. Plasma must be free from cells.

Caution: Plasma from primary tubes handled according to the manufacturer's instructions can still contain cells, leading to implausibly high results. One option for these cases is an application with automatic sample pre-dilution (ACN 20811). Alternatively it is recommended to transfer the plasma from the primary tube to a secondary sample tube.

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.

Separate the serum or plasma from the clot or cells promptly.

Centrifuge samples containing precipitates before performing the assay.

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

| | |
|---|---|
| Stability:[12] | 7 days at 15-25 °C<br>The sample may be stored for 4 days at 2-8 °C or 6 weeks at -20 °C (±5 °C). In connection with certain diseases (e.g. hepatopathy, diseases of skeletal muscle, malignant tumors), the LDH-4 and LDH-5 isoenzyme portions are increased and unstable in cooled and frozen samples; this may lead to an incorrect LDH value in samples collected from patients suffering from such diseases. |

Freeze only once.

**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.

**Application for serum and plasma**

**Test definition**

| | | | |
|---|---|---|---|
| Reporting time | 10 min | | |
| Wavelength (sub/main) | 700/340 nm | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 79 µL | – | |
| R3 | 16 µL | – | |
| *Sample volumes LDHI2* | *Sample* | *Sample dilution* | |
| | | Sample | Diluent ($H_2O$) |
| Normal | 2.2 µL | – | – |
| Decreased | 2.8 µL | 25.0 µL | 56 µL |
| Increased | 2.2 µL | – | – |
| *Sample volumes LDHI2P* | *Sample* | *Sample dilution* | |
| | | Sample | Diluent (NaCl) |
| Normal | 11.0 µL | 16.0 µL | 64 µL |
| Decreased | 4.4 µL | 16.0 µL | 64 µL |
| Increased | 11.0 µL | 16.0 µL | 64 µL |

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

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$<br>S2: C.f.a.s. |
| Calibration mode | Linear |
| Calibration frequency | Automatic full calibration<br>- after reagent lot change<br>Full calibration<br>- as required following quality control procedures |

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

Traceability: This method has been standardized against the original IFCC[11] formulation using calibrated pipettes together with a manual photometer providing absolute values and the substrate-specific absorptivity, ε.

**Quality control**

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

The control intervals and limits should be adapted to each laboratory’s individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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**

**cobas c** systems automatically calculate the analyte activity of each sample in the unit U/L (µkat/L).

Conversion factor: U/L × 0.0167 = µkat/L

**Limitations - interference**

Criterion: Recovery within ± 20 U/L of initial values of samples ≤ 200 U/L and within ± 10 % for samples > 200 U/L

Icterus:[13] 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).

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Hemolysis:[13] No significant interference up to an H index of 15 (approximate hemoglobin concentration: 9.6 µmol/L or 15 mg/dL).

Contamination with erythrocytes will elevate results, because the analyte level in erythrocytes is higher than in normal sera. The level of interference may be variable depending on the content of analyte in the lysed erythrocytes.

Lipemia (Intralipid):[13] No significant interference up to an L index of 900. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[14,15]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[16]

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**

10-1000 U/L (0.17-16.7 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

| | |
|---|---|
| Limit of Blank | = 10 U/L (0.17 µkat/L) |
| Limit of Detection | = 10 U/L (0.17 µkat/L) |
| Limit of Quantitation | = 10 U/L (0.17 µkat/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 95$^{th}$ percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the activity 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 activity samples.

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

The Limit of Quantitation is the lowest analyte activity that can be reproducibly measured with a total error of 20 %. It has been determined using low activity lactate dehydrogenase samples.

**Expected values**

**U/L**

Acc. to IFCC measured at 37 °C:[17]

| | |
|---|---|
| Females | 135-214 U/L |
| Males | 135-225 U/L |
| Children (2-15 y) | 120-300 U/L |
| Newborns (4-20 d) | 225-600 U/L |

Consensus values:[18]

| | |
|---|---|
| Males & Females | up to 250 U/L |

**µkat/L**

Acc. to IFCC measured at 37 °C:[17]

| | |
|---|---|
| Females | 2.25-3.55 µkat/L |
| Males | 2.25-3.75 µkat/L |
| Children (2-15 y) | 2.00-5.00 µkat/L |
| Newborns (4-20 d) | 3.75-10.0 µkat/L |

Consensus values:[18]

| | |
|---|---|
| Males & Females | up to 4.2 µkat/L |

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

*LDHI2*

| *Repeatability* | *Mean* *U/L* | *SD* *U/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[a)] | 172 | 1.06 | 0.6 |
| PCCC2[b)] | 294 | 1.35 | 0.5 |
| Human serum 1 | 22.4 | 0.646 | 2.9 |
| Human serum 2 | 164 | 1.29 | 0.8 |
| Human serum 3 | 265 | 1.56 | 0.6 |
| Human serum 4 | 520 | 2.09 | 0.4 |
| Human serum 5 | 943 | 3.31 | 0.4 |
| *Intermediate precision* | *Mean* *U/L* | *SD* *U/L* | *CV* *%* |
| PCCC1[a)] | 166 | 1.43 | 0.9 |
| PCCC2[b)] | 287 | 2.20 | 0.8 |
| Human serum 1 | 22.4 | 0.779 | 3.5 |
| Human serum 2 | 164 | 2.38 | 1.4 |
| Human serum 3 | 265 | 2.32 | 0.9 |
| Human serum 4 | 520 | 4.30 | 0.8 |
| Human serum 5 | 943 | 5.65 | 0.6 |

*LDHI2P*

| *Repeatability* | *Mean* *U/L* | *SD* *U/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[a)] | 165 | 1.01 | 0.6 |
| PCCC2[b)] | 292 | 1.26 | 0.4 |
| Human serum 1 | 21.5 | 0.555 | 2.6 |
| Human serum 2 | 164 | 1.47 | 0.9 |
| Human serum 3 | 262 | 1.78 | 0.7 |
| Human serum 4 | 519 | 1.80 | 0.3 |
| Human serum 5 | 941 | 2.92 | 0.3 |

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| *Intermediate precision* | *Mean* *U/L* | *SD* *U/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[a)] | 168 | 1.25 | 0.7 |
| PCCC2[b)] | 292 | 2.08 | 0.7 |
| Human serum 1 | 21.5 | 0.783 | 3.6 |
| Human serum 2 | 164 | 2.48 | 1.5 |
| Human serum 3 | 262 | 2.39 | 0.9 |
| Human serum 4 | 520 | 4.43 | 0.9 |
| Human serum 5 | 940 | 5.58 | 0.6 |

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Lactate dehydrogenase values for human serum and plasma samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

*LDHI2*

Sample size (n) = 66

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 0.999x - 2.72 U/L | y = 1.001x - 3.32 U/L |
| τ = 0.992 | r = 1.000 |

The sample activities were between 19.8 and 973 U/L.

*LDHI2P*

Sample size (n) = 66

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 0.997x - 2.26 U/L | y = 1.003x - 3.70 U/L |
| τ = 0.982 | r = 1.000 |

The sample activities were between 19.8 and 973 U/L.

Lactate dehydrogenase values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

*LDHI2*

Sample size (n) = 60

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 1.007x - 0.451 U/L | y = 1.016x - 3.51 U/L |
| τ = 0.982 | r = 1.000 |

The sample activities were between 60.1 and 960 U/L.

*LDHI2P*

Sample size (n) = 60

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 0.998x - 0.521 U/L | y = 0.999x - 1.75 U/L |
| τ = 0.983 | r = 1.000 |

The sample activities were between 62.1 and 973 U/L.

Lactate dehydrogenase values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

*LDHI2*

Sample size (n) = 65

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 1.002x + 0.668 U/L | y = 1.008x - 0.274 U/L |
| τ = 0.963 | r = 1.000 |

The sample concentrations were between 14.1 and 955 U/L.

*LDHI2P*

Sample size (n) = 65

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 1.002x + 1.55 U/L | y = 1.001x + 1.91 U/L |
| τ = 0.974 | r = 1.000 |

The sample concentrations were between 13.1 and 952 U/L.

**References**


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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:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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# LDLC3

cobas®

**LDL-Cholesterol Gen.3**

Order information

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08057966190* | 08057966500 | LDL-Cholesterol Gen.3 (600 tests) | System-ID 2082 002 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08057966214* | 08057966500 | LDL-Cholesterol Gen.3 (600 tests) | System-ID 2082 002 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 12172623122 | Calibrator f.a.s. Lipids (3 × 1 mL) | Code 20424 | |
| 05117003190 | PreciControl ClinChem Multi 1 (20 × 5 mL) | Code 20391 | |
| 05947626190 | PreciControl ClinChem Multi 1 (4 × 5 mL) | Code 20391 | |
| 05117216190 | PreciControl ClinChem Multi 2 (20 × 5 mL) | Code 20392 | |
| 05947774190 | PreciControl ClinChem Multi 2 (4 × 5 mL) | Code 20392 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

**English**

**System information**

**LDLC3:** ACN 20820

**Intended use**

In vitro test for the quantitative determination of LDL-cholesterol in human serum and plasma on **cobas c** systems.

**Summary**

Measurements of LDL-cholesterol, performed with this assay in human serum or plasma, are used for screening, aid in diagnosis and monitoring of dyslipidaemias as well as for assessment of cardiovascular risk such as in ASCVD and CHD.

The Low Density Lipoproteins (LDLs) are derived from VLDLs (Very Low Density Lipoproteins) that are enriched in triglycerides by the action of various lipolytic enzymes and are synthesized in the liver. The elimination of LDL from plasma takes place mainly by liver parenchymal cells via specific LDL receptors. Elevated LDL concentrations in blood and an increase in their residence time (coupled with an increase in the biological modification rate) result in the destruction of the endothelial function and a higher LDL-cholesterol uptake in the monocyte/macrophage system as well as into smooth muscle cells in vessel walls. The majority of cholesterol stored in atherosclerotic plaques originates from LDL.

LDL particles play a key role in causing and influencing the progression of atherosclerotic cardiovascular diseases (ASCVDs), including coronary heart disease (CHD), ischemic stroke, peripheral artery disease, and aortic aneurysm.[1] Atherosclerosis is a condition when the arteries are hardened and narrowed by plaque formation, which is a deposition of fats, cholesterol and other substances in and on the artery walls. Over time, the plaques can remain asymptomatic or become obstructive (stable angina). Eventually, plaque rupture can occur, where the contact of blood with the exposed plaque content can lead to thrombus formation and subsequent myocardial infarction or stroke.[1] The LDL-cholesterol value is a measure of the cholesterol mass carried by LDL particles and is used as a clinical predictor for ASCVD.[2] As a result, measurements of LDL-cholesterol are used for screening, aid in diagnosis and monitoring of dyslipidaemias, as well as for assessment of cardiovascular risk such as in ASCVD and CHD.[3,4] Therapies focusing on lipid reduction primarily target the reduction of LDL-cholesterol which is then expressed in an improvement of the endothelial function, prevention of atherosclerosis and reducing its progression as well as preventing plaque rupture and myocardial infarction.[3,4] Non-fasting sample results are slightly lower than fasting results.[5]

Various methods are available for the determination of LDL-cholesterol such as ultracentrifugation as the reference method, lipoprotein electrophoresis, high performance liquid chromatography (HPLC) and precipitation methods.[6,7] In the precipitation methods apolipoprotein B-containing LDL-cholesterol is, for example, precipitated using either polyvinyl sulfate, dextran sulfate or polycyclic anions. The LDL-cholesterol content is usually calculated from the difference between total cholesterol and cholesterol in the remainder (VLDL and HDL-cholesterol) in the supernate after precipitation with polyvinyl sulfate and dextran sulfate.[8] Lipid Research Clinics recommend a combination of ultracentrifugation and precipitation methods using polyanions in the presence of divalent cations. The precipitation methods are, however, time-consuming, cannot be automated and are susceptible to interference by hyperlipidemic serum, particularly at high concentrations of free fatty acids. A more recent method is based on the determination of LDL-cholesterol after the sample is subjected to immunoadsorption and centrifugation.[9]

The calculation of the LDL-cholesterol concentration according to Friedewald's formula is based on 2 cholesterol determinations (total cholesterol and HDL-cholesterol) and 1 triglyceride determination.[10]

Friedewald's formula for calculation of LDL-cholesterol presumes that a direct relationship exists between VLDL-cholesterol and triglycerides in fasting blood samples (VLDL-cholesterol = Trigl./5 mg/dL, VLDL-cholesterol = Trigl./2.2 mmol/L). The bias in calculating LDL-cholesterol using this assumption is only acceptable in samples with a triglyceride concentration < 2.0 mmol/L (177 mg/dL).[11,12] Even in the presence of small amounts of chylomicrons or abnormal lipoproteins, the formula gives rise to artificially low LDL-cholesterol values. Non-fasting samples cannot be used for the calculation of LDL-cholesterol because they contain a high concentration of chylomicrons and in many cases the limit of acceptable triglyceride concentration is exceeded. For these reasons, a simple and reliable method for routine measurement of LDL-cholesterol without any preparatory steps was developed. This automated method for the direct determination of LDL-cholesterol takes advantage of the selective micellary solubilization of LDL-cholesterol by a nonionic detergent and the interaction of a sugar compound and lipoproteins (VLDL and chylomicrons). When a detergent is included in the enzymatic method for cholesterol determination (cholesterol esterase - cholesterol oxidase coupling reaction), the relative reactivities of cholesterol in the lipoprotein fractions increase in this order: HDL < chylomicrons < VLDL < LDL.

The combination of a sugar compound with detergent enables the selective determination of LDL-cholesterol in serum and plasma samples.

Comparable non-fasting results were observed with the beta quantification method.[13] This direct assay meets the 1995 NCEP goals of < 4 % total coefficient of variation (CV), bias ≤ 4 % versus reference method, and ≤ 12 % total analytical error.[14,15,16]

**Test principle**

Homogeneous enzymatic colorimetric assay

Cholesterol esters and free cholesterol in LDL are measured on the basis of a cholesterol enzymatic method using cholesterol esterase and cholesterol oxidase in the presence of surfactants which selectively solubilize only LDL. The enzyme reactions to the lipoproteins other than LDL are inhibited by surfactants and a sugar compound. Cholesterol in HDL, VLDL and chylomicron is not determined.

$$\text{LDL-cholesterol esters} + H_2O \xrightarrow[\text{cholesterol esterase}]{\text{detergent}} \text{cholesterol} + \text{free fatty acids (selective micellary solubilization)}$$

# LDLC3

**LDL-Cholesterol Gen.3**

cobas®

Cholesterol esters are broken down quantitatively into free cholesterol and fatty acids by cholesterol esterase.

$$\text{LDL-cholesterol} + O_2 \xrightarrow{\text{cholesterol oxidase}} \Delta^4\text{-cholestenone} + H_2O_2$$

In the presence of oxygen, cholesterol is oxidized by cholesterol oxidase to $\Delta^4$-cholestenone and hydrogen peroxide.

$$2\ H_2O_2 + \text{4-aminoantipyrine} + \text{EMSE}^{a)} + H_2O + H^+ \xrightarrow{\text{peroxidase}} \text{red purple pigment} + 5\ H_2O$$

a) N-ethyl-N-(3-methylphenyl)-N-succinylethylenediamine

In the presence of peroxidase, the hydrogen peroxide generated reacts with 4-aminoantipyrine and EMSE to form a red purple dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.

**Reagents - working solutions**

**R1** Bis-tris[b)] buffer: 20.1 mmol/L, pH 7.0; 4-aminoantipyrine: 0.98 mmol/L; ascorbate oxidase (AOD, Acremonium spec.): ≥ 66.7 µkat/L; peroxidase (recombinant from Basidiomycetes): ≥ 166.7 µkat/L; BSA: 4.0 g/L; preservative

**R3** MOPS[c)] buffer: 20.1 mmol/L, pH 7.0; EMSE: 2.16 mmol/L; cholesterol esterase (Pseudomonas spec.): ≥ 33.3 µkat/L; cholesterol oxidase (recombinant from E. coli): ≥ 31.7 µkat/L; peroxidase (recombinant from Basidiomycetes): ≥ 333.3 µkat/L; BSA: 4.0 g/L; detergents; preservative

b) bis(2-hydroxyethyl)-amino-tris-(hydroxymethyl)-methane

c) 3-morpholinopropane-1-sulfonic acid

R1 is in position B and R3 is in position C.

**Precautions and warnings**

For in vitro diagnostic use for laboratory 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.

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

Warning

| | |
|---|---|
| H317 | May cause an allergic skin reaction. |
| H319 | Causes serious eye irritation. |
| H411 | Toxic to aquatic life with long lasting effects. |

**Prevention:**

| | |
|---|---|
| P261 | Avoid breathing mist or vapours. |
| P273 | Avoid release to the environment. |
| P280 | Wear protective gloves/ eye protection/ face protection. |

**Response:**

| | |
|---|---|
| P333 + P313 | If skin irritation or rash occurs: Get medical advice/attention. |
| P337 + P313 | If eye irritation persists: Get medical advice/attention. |
| P391 | Collect spillage. |

**Hazardous components:**

- reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1)

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |

**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
Plasma: Li-heparin, $K_2$- and $K_3$-EDTA plasma.

Fasting and non-fasting samples can be used.[9]

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.

| | |
|---|---|
| Stability:[17,18] | 7 days at 2-8 °C |
| | 12 months at -20 °C (± 5 °C) |
| | 12 months at -70 °C (± 5 °C) |

Freeze only once.

It is reported that EDTA stabilizes lipoproteins.[16]

**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.

**Application for serum and plasma**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 700/600 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 82 µL | – |
| R3 | 27 µL | – |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | *Sample* | *Diluent (NaCl)* |

| | | | |
|---|---|---|---|
| Normal | 1.1 µL | – | – |
| Decreased | 5.5 µL | 10 µL | 90 µL |
| Increased | 1.1 µL | – | – |

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

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. Lipids |
| Calibration mode | Linear |
| Calibration frequency | Automatic full calibration<br>- after reagent lot change |
| | Full calibration<br>- as required following quality control procedures |

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

Traceability: This method has been standardized against the beta quantification method as defined in the recommendations in the LDL Cholesterol Method Certification Protocol for Manufacturers.[19]

**Quality control**

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

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, g/L).

| | |
|---|---|
| Conversion factors: | mmol/L × 38.66 = mg/dL |
| | mmol/L × 0.3866 = g/L |

**Limitations – interference**

Criterion: Recovery within ± 0.40 mmol/L of initial values of samples ≤ 4.0 mmol/L and within ±10 % for samples > 4.0 mmol/L.

Icterus:[20] 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).

Hemolysis:[20] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[20] No significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

No significant interference from HDL-C (≤ 3.03 mmol/L or ≤ 117 mg/dL), VLDL-C (≤ 3.63 mmol/L or ≤ 140 mg/dL), or chylomicrons (≤ 22.6 mmol/L or ≤ 2000 mg/dL triglycerides).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[21,22]

Nicotinic acid (Niacin), statins (Simvastatin) and fibrates (Clofibrate) tested at therapeutic concentration ranges did not interfere.

Acetaminophen intoxications are frequently treated with N-acetylcysteine. N-acetylcysteine at the therapeutic concentration when used as an antidote and the acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low LDL-C results. Venipuncture should be performed prior to the administration of metamizole. Venipuncture immediately after or during the administration of metamizole may lead to falsely low results.

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 28.4 mmol/L (500 mg/dL).

Abnormal liver function affects lipid metabolism; consequently HDL and LDL results are of limited diagnostic value. In some patients with abnormal liver function, the LDL-cholesterol result is significantly negatively biased versus beta quantification results.

EDTA plasma may cause decreased values compared to serum.[23]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[24]

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**

0.10-14.2 mmol/L (3.87-549 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

| | |
|---|---|
| Limit of Blank | = 0.10 mmol/L (3.87 mg/dL) |
| Limit of Detection | = 0.10 mmol/L (3.87 mg/dL) |
| Limit of Quantitation | = 0.10 mmol/L (3.87 mg/dL) |

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 95$^{th}$ 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 for LDL-C is 0.10 mmol/L determined in accordance with the guidelines in CLSI document EP17-A2, based on a minimum of 48 determinations, and a total error goal of 10 % calculated using RMS error model.

**Expected values[25]**

Levels in terms of risk for coronary heart disease.

**mmol/L***

Adult levels:

| | |
|---|---|
| Optimal | < 2.59 mmol/L |
| Near optimal/above optimal | 2.59-3.34 mmol/L |
| Borderline high | 3.37-4.12 mmol/L |
| High | 4.14-4.89 mmol/L |
| Very high | ≥ 4.92 mmol/L |

* calculated by unit conversion factor

**mg/dL**

Adult levels:

| | |
|---|---|
| Optimal | < 100 mg/dL |
| Near optimal/above optimal | 100-129 mg/dL |

| | |
|---|---|
| Borderline high | 130-159 mg/dL |
| High | 160-189 mg/dL |
| Very high | ≥ 190 mg/dL |

Risk classification of patients and treatment therapies are described in international guidelines.[26]

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

| *Repeatability* | *Mean* *mmol/L* | *SD* *mmol/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[d)] | 1.43 | 0.00779 | 0.5 |
| PCCC2[e)] | 2.60 | 0.0129 | 0.5 |
| Human serum 1 | 0.163 | 0.00288 | 1.8 |
| Human serum 2 | 1.27 | 0.00627 | 0.5 |
| Human serum 3 | 2.57 | 0.0131 | 0.5 |
| Human serum 4 | 7.54 | 0.0358 | 0.5 |
| Human serum 5 | 13.8 | 0.0627 | 0.5 |

| *Intermediate precision* | *Mean* *mmol/L* | *SD* *mmol/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[d)] | 1.43 | 0.0147 | 1.0 |
| PCCC2[e)] | 2.60 | 0.0298 | 1.1 |
| Human serum 1 | 0.163 | 0.00337 | 2.1 |
| Human serum 2 | 1.27 | 0.00940 | 0.7 |
| Human serum 3 | 2.57 | 0.0160 | 0.6 |
| Human serum 4 | 7.54 | 0.0509 | 0.7 |
| Human serum 5 | 13.8 | 0.0931 | 0.7 |

d) PreciControl ClinChem Multi 1

e) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

LDL-cholesterol values for human serum samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 86

| Passing/Bablok[27] | Linear regression |
|---|---|
| y = 1.021x + 0.0546 mmol/L | y = 1.015x + 0.0745 mmol/L |
| τ = 0.984 | r = 1.000 |

The sample concentrations were between 0.120 and 14.0 mmol/L.

LDL-cholesterol values for human serum samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 86

| Passing/Bablok[27] | Linear regression |
|---|---|
| y = 1.005x + 0.0713 mmol/L | y = 1.008x + 0.0574 mmol/L |
| τ = 0.981 | r = 1.000 |

The sample concentrations were between 0.130 and 13.8 mmol/L.

LDL-cholesterol values for human serum samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 75

| Passing/Bablok[27] | Linear regression |
|---|---|
| y = 0.973x - 0.0361 mmol/L | y = 0.981x - 0.0623 mmol/L |
| τ = 0.986 | r = 1.000 |

The sample concentrations were between 0.208 and 13.9 mmol/L.

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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:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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# LIPC

cobas®

**Lipase colorimetric assay**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08057982190 | 08057982500 | Lipase colorimetric assay (200 tests) | System-ID 2085 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

## English

### System information

**LIP:** ACN 20850

### Intended use

Enzymatic in vitro test for the quantitative determination of lipase in human serum and plasma on **cobas c** systems.

### Summary

Lipase measurements, performed with this assay in human serum and plasma, are used as an aid in the diagnosis and monitoring of various pancreatic conditions, particularly acute pancreatitis.

Lipases are triglyceride hydrolases which catalyze the cleavage of triglycerides into fatty acids and glycerol.[1,2] Most of the lipase activity found in serum derives from pancreatic acinar cells, but some is secreted by gastric and intestinal mucosa.[1,2] Human pancreatic lipase is a glycoprotein with a molecular weight of 45-48 kDa.[1,2,3] It is secreted into the duodenum through the duct system of the pancreas, and the concentration in blood is normally very low: the concentration gradient between pancreatic tissue and serum lipase is approximately 20,000-fold. Upon pancreatic injury, the pancreas starts to release the lipase into blood at higher amounts. This can occur in conditions such as acute pancreatitis, chronic pancreatitis, pancreatic cancer, or pancreatic duct obstruction. Therefore, the measurement of pancreatic lipase in blood can be used as an aid to diagnose acute pancreatitis and other pancreatic diseases.[2,3]

In addition to α-amylase, pancreatic lipases have for many years been undeniably the most important clinical chemistry parameters for the differential diagnosis of diseases of the pancreas.[4,5,6,7] The lipase activity determination has gained increasing international recognition because of its high specificity and rapid response. After acute pancreatitis the lipase activity increases within 4-8 hours, reaches a peak after 24 hours and decreases after 8 to 14 days.[2,4,5,6]

Lipase activity in serum can also be influenced by factors other than pancreatic disorders, such as kidney disease, intestinal ischemia, or certain medications.[1,2] Therefore, clinical interpretation of lipase levels should be done in conjunction with a comprehensive assessment of the patient's medical history, symptoms, and other diagnostic tests.

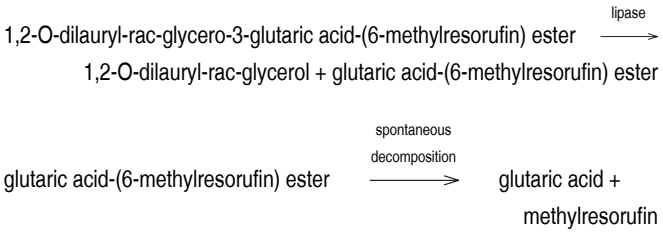
The hydrolyzation action of lipase can only take place when the substrate is present in an emulsified form and the rate of action depends on the free surface area of the substrate. Bile and co-lipase are thus essential for the activity of pancreatic lipase as bile helps emulsify fats, increasing their surface area for lipase action, and co-lipase enhances the binding and activity of lipase at the lipid-water interface.[1]

Numerous methods have been described for the determination of lipase which determine the decrease in substrate turbidimetrically or nephelometrically or determine degradation products.[1,3,8,9] The method of this assay is based on the cleavage of a specific chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester emulsified with bile acids. The pancreatic enzyme activity is determined specifically by the combination of bile acid and colipase used in this assay. Virtually no lipase activity is detected in the absence of colipase. Colipase only activates pancreatic lipase, but not other lipolytic enzymes found in serum. The high amount of cholates ensures that the esterases present in the serum do not react with the chromogenic substrate due to the highly negative surface charge.

### Test principle[10,11,12,13]

Enzymatic colorimetric assay with 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester as substrate.

The chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric-acid-(6-methylresorufin) ester is cleaved by the catalytic action of alkaline lipase solution to form 1,2-O-dilauryl-rac-glycerol and an unstable intermediate, glutaric acid-(6-methylresorufin) ester. This decomposes spontaneously in alkaline solution to form glutaric acid and methylresorufin. Addition of detergent and colipase increases the specificity of the assay for pancreatic lipase.




The color intensity of the red dye formed is directly proportional to the lipase activity and can be determined photometrically.

### Reagents - working solutions

**R1** BICIN[a)] buffer: 50 mmol/L, pH 8.0; colipase (porcine pancreas): ≥ 0.9 mg/L; Na-deoxycholate: 1.6 mmol/L; calcium chloride: 10 mmol/L; detergent; preservative

**R3** Tartrate buffer: 10 mmol/L, pH 4.16; 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester: 0.27 mmol/L; taurodeoxycholate: 8.8 mmol/L; detergent; preservative

a) BICIN = N,N-bis(2-hydroxyethyl)glycine

R1 is in position B and R3 is in position C.

### 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.

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

Warning

# LIPC

cobas®

**Lipase colorimetric assay**

| | |
|---|---|
| H317 | May cause an allergic skin reaction. |
| H319 | Causes serious eye irritation. |

**Prevention:**

| | |
|---|---|
| P261 | Avoid breathing mist or vapours. |
| P280 | Wear protective gloves/ eye protection/ face protection. |

**Response:**

| | |
|---|---|
| P333 + P313 | If skin irritation or rash occurs: Get medical advice/attention. |
| P337 + P313 | If eye irritation persists: Get medical advice/attention. |
| P362 + P364 | Take off contaminated clothing and wash it before reuse. |

**Disposal:**

| | |
|---|---|
| P501 | Dispose of contents/container to an approved waste disposal plant. |

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 4 weeks |

**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
Plasma: Li-heparin plasma

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.

| | |
|---|---|
| Stability in serum:[14] | 7 days at 20-25 °C |
| | 7 days at 4-8 °C |
| | 1 year at -20 °C (±5 °C) |

Freeze only once.

| | |
|---|---|
| Stability in plasma: | 1 week at 15-25 °C |
| | 1 week at 2-8 °C |
| | 2 months at -20 °C (±5 °C) |

Freeze only once.

**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.

**Application for serum and plasma**

**Test definition**

| | | | |
|---|---|---|---|
| Reporting time | 10 min | | |
| Wavelength (sub/main) | 700/570 nm | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 60 µL | 15 µL | |
| R3 | 36 µL | – | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 1.5 µL | – | – |
| Decreased | 1.5 µL | 10 | 90 |
| Increased | 1.5 µL | – | – |

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

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. |
| Calibration mode | Linear |
| Calibration frequency | Full calibration<br>- after reagent lot change<br>- as required following quality control procedures |

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

Traceability: This method has been standardized manually against Roche reagent using the substrate-specific absorptivity, ε.

**Quality control**

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

The control intervals and limits should be adapted to each laboratory’s individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 4 weeks. 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**

**cobas c** systems automatically calculate the analyte activity of each sample in the unit U/L (µkat/L).

Conversion factor: U/L × 0.0167 = µkat/L

**Limitations - interference**

Criterion: Recovery within ± 6 U/L of initial values of samples ≤ 60 U/L and within ± 10 % for samples > 60 U/L.

Icterus:[15] 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).

Hemolysis:[15] No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L or 100 mg/dL).

Lipemia (Intralipid):[15] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

# LIPC

**Lipase colorimetric assay**

Drugs: No interference was found at therapeutic concentrations using common drug panels.[16,17]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[18]

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**

3-300 U/L (0.05-5.01 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

| | |
|---|---|
| Limit of Blank | = 3 U/L (0.05 µkat/L) |
| Limit of Detection | = 3 U/L (0.05 µkat/L) |
| Limit of Quantitation | = 5 U/L (0.08 µkat/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 95$^{th}$ percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the activity 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 activity samples.

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

The Limit of Quantitation is the lowest analyte activity that can be reproducibly measured with a total error of 20 %. It has been determined using low activity lipase samples.

**Expected values[19]**

Adults: 13-60 U/L (0.22-1.00 µkat/L*)

*calculated by unit conversion factor

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

| *Repeatability* | *Mean* *U/L* | *SD* *U/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[b)] | 45.5 | 0.295 | 0.6 |
| PCCC2[c)] | 102 | 0.425 | 0.4 |
| Human serum 1 | 6.59 | 0.230 | 3.5 |
| Human serum 2 | 40.2 | 0.245 | 0.6 |
| Human serum 3 | 94.4 | 0.445 | 0.5 |
| Human serum 4 | 152 | 0.617 | 0.4 |
| Human serum 5 | 250 | 0.866 | 0.3 |

| *Intermediate precision* | *Mean* *U/L* | *SD* *U/L* | *CV* *%* |
|---|---|---|---|
| PCCC1[b)] | 45.5 | 0.498 | 1.1 |
| PCCC2[c)] | 99.3 | 1.08 | 1.1 |
| Human serum 1 | 6.59 | 0.267 | 4.1 |
| Human serum 2 | 40.2 | 0.368 | 0.9 |
| Human serum 3 | 94.4 | 1.01 | 1.1 |
| Human serum 4 | 142 | 1.57 | 1.1 |
| Human serum 5 | 250 | 2.79 | 1.1 |

b) PreciControl ClinChem Multi 1

c) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Lipase values for human serum and plasma samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 72

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.013x + 0.718 U/L | y = 1.033x + 0.415 U/L |
| τ = 0.962 | r = 0.998 |

The sample activities were between 3.29 and 261 U/L.

Lipase values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 71

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.039x + 0.475 U/L | y = 1.027x + 0.689 U/L |
| τ = 0.975 | r = 0.999 |

The sample activities were between 4.30 and 282 U/L.

Lipase values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 75

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 0.980x + 0.265 U/L | y = 0.976x + 0.625 U/L |
| τ = 0.955 | r = 1.000 |

The sample concentrations were between 5.06 and 288 U/L.

**References**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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:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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

# MG2

cobas®

**Magnesium Gen.2**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08058016190* | 08058016500 | Magnesium Gen.2 (690 tests) | System-ID 2089 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08058016214* | 08058016500 | Magnesium Gen.2 (690 tests) | System-ID 2089 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

## English

### System information

**MG2:** ACN 20890 (Serum/plasma)

**MG2U:** ACN 20891 (Urine)

### Intended use

In vitro test for the quantitative determination of magnesium in human serum, plasma and urine on **cobas c** systems.

### Summary

Magnesium measurements, performed with this assay, in human serum, plasma and urine are used as an aid in diagnosis and monitoring disorders of magnesium metabolism associated with hypomagnesemia (magnesium deficiency) and hypermagnesemia (magnesium excess).

Magnesium is mainly found in the intracellular space (40 %) and in bones and teeth (60 %). Approximately 0.3 % of the body's total magnesium is found in serum.[1] As important intracellular cation, $Mg^{2+}$ is a cofactor in more than 300 enzyme-catalyzed reactions involved in phosphorylation, protein synthesis, and DNA metabolism processes. All ATP-dependent enzymatic reactions require $Mg^{2+}$ as a cofactor. In addition, magnesium is a dynamic ion for transcellular transport, altering membrane potentials and ion transport. It is involved in neuromuscular conduction and excitability of skeletal and cardiac muscle.[2]

Approximately 99 % of magnesium ions are stored in bone, skeletal muscle and other soft tissues and less than 1 % is present in the extracellular fluid. The $Mg^{2+}$ serum level is kept constant within very narrow limits (0.7-1.10 mmol/L). Approximately 20 % of this is protein bound (especially to albumin), 65 % is ionized and the rest is complexed with various anions such as phosphate and citrate.[3] Serum levels are mainly regulated via the kidneys, especially via the ascending loop of Henle.[4,5] Emerging evidence suggests that the serum magnesium/calcium quotient is an important indicator of magnesium status and/or turnover.[1]

Hypomagnesemia is common, with a prevalence of up to 15 % in the general population and up to 65 % in patients in the intensive care units.[5] Hypomagnesemia is usually due to loss or impaired absorption of magnesium from the gastrointestinal tract or increased excretion by the kidneys.[2,5] Symptomatic magnesium depletion is often correlated with multiple other biochemical abnormalities, such as hypokalaemia, hypocalcaemia and metabolic acidosis. Manifestations of severe hypomagnesaemia include neuromuscular symptoms (muscular weakness, apathy, tremors, paraesthesia, tetany, vertical nystagmus and positive Chvostek and Trousseau signs) and cardiovascular manifestations (e.g. atrial and ventricular arrhythmias).[4] Intravenous magnesium is usually prescribed in cases of symptomatic hypomagnesaemia, while oral replacement is indicated for asymptomatic patients.[4]

Hypermagnesemia is generally occurring in the setting of renal insufficiency (acute and chronic renal failure) and excessive magnesium intake resulting in neuromuscular and cardiovascular manifestations as well as non-specific manifestations like nausea, vomiting and cutaneous flushing.[4]

In addition to atomic absorption spectrometry (AAS), complexometric methods can also be used to determine magnesium.[2,6]

The method described here is based on the reaction of magnesium with xylidyl blue in alkaline solution containing EGTA to mask the calcium in the sample.[7]

Urine magnesium is also often measured as part of a magnesium loading test.[8]

### Test principle[7]

Colorimetric endpoint method

- Sample and addition of R1
- Addition of R2 and start of reaction:

  In alkaline solution, magnesium forms a purple complex with xylidyl blue, diazonium salt. The magnesium concentration is measured photometrically via the decrease in the xylidyl blue absorbance.

### Reagents - working solutions

**R1** TRIS[a)]/6-aminocaproic acid buffer: 500 mmol/L, pH 11.25; EGTA: 129 µmol/L; preservative

**R3** Xylidyl blue: 0.28 mmol/L; detergent; preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

R1 is in position B and R3 is in position C.

### 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.

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

Warning

H315 Causes skin irritation.

H319 Causes serious eye irritation.

**Prevention:**

P264 Wash skin thoroughly after handling.

P280 Wear protective gloves/ eye protection/ face protection.

**Response:**

P302 + P352 IF ON SKIN: Wash with plenty of water.

P332 + P313 If skin irritation occurs: Get medical advice/attention.

P337 + P313 If eye irritation persists: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 15-25 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |

**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
Plasma: Li-heparin plasma

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.

Chelating anticoagulants such as EDTA, fluoride and oxalate must be avoided.

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.

| | |
|---|---|
| Stability in *serum/plasma*:[9] | 7 days at 15-25 °C |
| | 7 days at 2-8 °C |
| | 1 year at -20 °C (± 5 °C) |

Freeze only once.

*Urine:*

Urine samples should be acidified to pH 1 with concentrated HCl to prevent precipitation of magnesium ammonium phosphate. Collect urine samples in metal-free container.[10] Urine samples are automatically prediluted with 0.9 % NaCl by the instrument. If stabilizers are added to the sample, the sample index feature must not be used.

| | |
|---|---|
| Stability in *urine*:[9] | 3 days at 15-25 °C |
| | 3 days at 2-8 °C |
| | 1 year at -20 °C (± 5 °C) |

Freeze only once.

**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.

**Application for serum and plasma**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 505/600 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 78 µL | – |
| R3 | 78 µL | – |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 2.4 µL | – | – |
| Decreased | 1.2 µL | – | – |
| Increased | 2.4 µL | – | – |

**Application for urine**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 505/600 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 78 µL | - |
| R3 | 78 µL | - |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | Sample | *Diluent (NaCl)* |
| Normal | 2.4 µL | 20 µL | 90 µL |
| Decreased | 2.4 µL | 10 µL | 100 µL |
| Increased | 2.4 µL | 20 µL | 90 µL |

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

**Calibration**

*Application for serum/plasma (ACN 20890)*

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. |
| Calibration mode | Linear |
| Calibration frequency | Automatic full calibration<br>- after reagent lot change |
| | Full calibration<br>- every 4 weeks on-board<br>- as required following quality control procedures |

*Application for urine (ACN 20891)*
Transfer of calibration from serum/plasma application (ACN 20890)

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

Traceability: This method has been standardized against atomic absorption spectrometry.

**Quality control**

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

# MG2

**Magnesium Gen.2**

cobas®

| | |
|---|---|
| Serum/plasma: | PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2 |
| Urine: | Quantitative urine controls are recommended for routine quality control. |

The control intervals and limits should be adapted to each laboratory's individual requirements.

It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, mg/L, mval/L).

| | |
|---|---|
| Conversion factors: | mmol/L x 2.43 = mg/dL |
| | mmol/L x 24.3 = mg/L |
| | mmol/L x 2.0 = mval/L |
| | mval/L = mEq/L |

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial value at a magnesium concentration of 0.7 mmol/L (1.7 mg/dL, 1.4 mval/L).

*Serum/plasma*

Icterus:[11] No significant interference up to an I index of 60 for conjugated bilirubin and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 60 mg/dL or 1026 µmol/L).

Hemolysis:[11] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 496 µmol/L (800 mg/dL)).

Hemolysis elevates results depending on the content of the analyte in the lysed erythrocytes.

Lipemia (Intralipid):[11] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[12,13]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[14]

*Urine*

Drugs: No interference was found at therapeutic concentrations using common drug panels.[13]

Criterion: Recovery within ± 10 % of initial value at a magnesium concentration of 1.7 mmol/L (4.1 mg/dL, 3.4 mval/L).

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

Urea: No significant interference from urea up to a concentration of 1500 mmol/L (9009 mg/dL).

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**

*Serum/plasma*

0.10-2.0 mmol/L (0.243-4.86 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

*Urine*

0.56-11.0 mmol/L (1.36-26.7 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

*Serum/plasma*

| | |
|---|---|
| Limit of Blank | = 0.05 mmol/L (0.122 mg/dL) |
| Limit of Detection | = 0.10 mmol/L (0.243 mg/dL) |
| Limit of Quantitation | = 0.10 mmol/L (0.243 mg/dL) |

*Urine*

| | |
|---|---|
| Limit of Blank | = 0.28 mmol/L (0.68 mg/dL) |
| Limit of Detection | = 0.56 mmol/L (1.36 mg/dL) |
| Limit of Quantitation | = 0.56 mmol/L (1.36 mg/dL) |

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 95$^{th}$ 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 20 %. It has been determined using low concentration magnesium samples.

**Expected values[15]**

**mmol/L**

*Serum/plasma:*

| | |
|---|---|
| Newborn: | 0.62-0.91 mmol/L |
| 5 months-6 years: | 0.70-0.95 mmol/L |
| 6-12 years: | 0.70-0.86 mmol/L |
| 12-20 years: | 0.70-0.91 mmol/L |
| Adults: | 0.66-1.07 mmol/L |
| 60-90 years: | 0.66-0.99 mmol/L |
| > 90 years: | 0.70-0.95 mmol/L |
| *Urine (24 h):* | 3.0-5.0 mmol/d |

**mg/dL**

*Serum/plasma:*

| | |
|---|---|
| Newborn: | 1.5-2.2 mg/dL |
| 5 months-6 years: | 1.7-2.3 mg/dL |
| 6-12 years: | 1.7-2.1 mg/dL |
| 12-20 years: | 1.7-2.2 mg/dL |
| Adults: | 1.6-2.6 mg/dL |
| 60-90 years: | 1.6-2.4 mg/dL |
| > 90 years: | 1.7-2.3 mg/dL |
| *Urine (24 h):* | 72.9-121.5 mg/d |

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

*Serum/plasma*

| *Repeatability* | *Mean mmol/L* | *SD mmol/L* | *CV %* |
|---|---|---|---|
| PCCC1[b)] | 0.812 | 0.00352 | 0.4 |
| PCCC2[c)] | 1.30 | 0.00546 | 0.4 |
| Human serum 1 | 0.258 | 0.00386 | 1.5 |
| Human serum 2 | 0.624 | 0.00384 | 0.6 |
| Human serum 3 | 0.986 | 0.00346 | 0.4 |
| Human serum 4 | 1.36 | 0.00567 | 0.4 |
| Human serum 5 | 1.74 | 0.00577 | 0.3 |

| *Intermediate precision* | *Mean mmol/L* | *SD mmol/L* | *CV %* |
|---|---|---|---|
| PCCC1[b)] | 0.812 | 0.00940 | 1.2 |
| PCCC2[c)] | 1.30 | 0.0127 | 1.0 |
| Human serum 1 | 0.258 | 0.00648 | 2.5 |
| Human serum 2 | 0.624 | 0.00699 | 1.1 |
| Human serum 3 | 0.986 | 0.00651 | 0.7 |
| Human serum 4 | 1.37 | 0.00812 | 0.6 |
| Human serum 5 | 1.74 | 0.00896 | 0.5 |

b) PreciControl ClinChem Multi 1
c) PreciControl ClinChem Multi 2

*Urine*

| *Repeatability* | *Mean mmol/L* | *SD mmol/L* | *CV %* |
|---|---|---|---|
| Control 1[d)] | 1.73 | 0.0231 | 1.3 |
| Control 2[d)] | 3.67 | 0.0252 | 0.7 |
| Human urine 1 | 1.50 | 0.0243 | 1.6 |
| Human urine 2 | 2.90 | 0.0238 | 0.8 |
| Human urine 3 | 4.08 | 0.0262 | 0.6 |
| Human urine 4 | 5.30 | 0.0334 | 0.6 |
| Human urine 5 | 9.02 | 0.0425 | 0.5 |

| *Intermediate precision* | *Mean mmol/L* | *SD mmol/L* | *CV %* |
|---|---|---|---|
| Control 1[d)] | 1.72 | 0.0302 | 1.8 |
| Control 2[d)] | 3.67 | 0.0313 | 0.9 |
| Human urine 1 | 1.50 | 0.0288 | 1.9 |
| Human urine 2 | 2.89 | 0.0336 | 1.2 |
| Human urine 3 | 4.08 | 0.0298 | 0.7 |
| Human urine 4 | 5.27 | 0.0424 | 0.8 |
| Human urine 5 | 9.02 | 0.0609 | 0.7 |

d) commercially available control material

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Magnesium values for human serum, plasma and urine samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

*Serum/plasma*

Sample size (n) = 97

| Passing/Bablok[16] | Linear regression |
|---|---|
| y = 1.013x - 0.00748 mmol/L | y = 1.011x - 0.00537 mmol/L |
| τ = 0.984 | r = 1.000 |

The sample concentrations were between 0.100 and 1.96 mmol/L.

*Urine*

Sample size (n) = 62

| Passing/Bablok[16] | Linear regression |
|---|---|
| y = 0.963x - 0.0757 mmol/L | y = 0.973x - 0.114 mmol/L |
| τ = 0.974 | r = 0.999 |

The sample concentrations were between 0.670 and 11.0 mmol/L.

Magnesium values for human serum, plasma and urine samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

*Serum/plasma*

Sample size (n) = 72

| Passing/Bablok[16] | Linear regression |
|---|---|
| y = 1.011x + 0.000944 mmol/L | y = 1.012x + 0.000238 mmol/L |
| τ = 0.979 | r = 1.000 |

The sample concentrations were between 0.140 and 1.94 mmol/L.

*Urine*

Sample size (n) = 67

| Passing/Bablok[16] | Linear regression |
|---|---|
| y = 1.007x + 0.00729 mmol/L | y = 1.008x + 0.00459 mmol/L |
| τ = 0.984 | r = 1.000 |

The sample concentrations were between 0.610 and 10.7 mmol/L.

Magnesium values for human serum, plasma and urine samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

*Serum/plasma*

Sample size (n) = 68

| Passing/Bablok[16] | Linear regression |
|---|---|
| y = 0.995x - 0.00153 mmol/L | y = 0.994x + 0.000658 mmol/L |
| τ = 0.995 | r = 1.000 |

The sample concentrations were between 0.115 and 1.90 mmol/L.

*Urine*

Sample size (n) = 62

| Passing/Bablok[16] | Linear regression |
|---|---|
| y = 0.994x + 0.0290 mmol/L | y = 0.992x + 0.0298 mmol/L |
| τ = 0.9996 | r = 1.000 |

The sample concentrations were between 0.674 and 10.8 mmol/L.

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

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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Roche

# Na Electrode

cobas®

**Sodium**

**Order information**

| REF | CONTENT | Analyzer(s) on which the electrode can be used |
|---|---|---|
| 10825468001 | Na Electrode 1 (electrode) | **cobas c** 311 analyzer<br>**cobas** 6000 analyzer series: **cobas c** 501 module<br>**cobas** 8000 modular analyzer series: **cobas** 8000 ISE 900 / 1800 module<br>**cobas pure** integrated solutions: **cobas c** 303 analytical unit<br>**cobas pro** integrated solutions: **cobas pro** ISE analytical unit, **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit |

Materials required (but not provided):

| | | |
|---|---|---|
| 03149501001 | REF Electrode (1 electrode) | |
| 11360981216 | ISE Reference Electrolyte (5 x 300 mL) ①② | |
| 10820652216 | ISE Reference Electrolyte (1 x 500 mL) ③④ | |
| 08392013190 | ISE Reference Electrolyte (2 x 2000 mL) ⑤⑥ | |
| 04522320190 | ISE Internal Standard Gen.2 (5 x 600 mL) ①② | |
| 04880455190 | ISE Internal Standard Gen.2 (2 x 2000 mL) ③④⑤ | |
| 09137742190 | ISE Internal Standard Gen.2 conc. (1 x 510 mL) ⑥ | |
| 05979854190 | Internal Standard Insert - ISE (Set of 20) ①② | |
| 04522630190 | ISE Diluent Gen.2 (5 x 300 mL) ①② | |
| 04880480190 | ISE Diluent Gen.2 (2 x 2000 mL) ③④⑤ | |
| 11298500316 | ISE Cleaning Solution (5 x 100 mL) | |
| 20763071122 | ISE Deproteinizer (6 x 21 mL) ④⑤⑥ | |
| 03110435180 | Deproteinizer (1 x 125 mL) ⑥ | |
| 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 |

ISE reagents on:

① **cobas c** 311 analyzer

② **cobas** 6000 analyzer series: **cobas c** 501 module

③ **cobas** 8000 modular analyzer series: **cobas** 8000 ISE 900 / 1800 module

④ **cobas pure** integrated solutions: **cobas c** 303 analytical unit

⑤ **cobas pro** integrated solutions: **cobas pro** ISE analytical unit

⑥ **cobas pro** integrated solutions: **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit

**English**

**System information**

| | ACN (Serum/ plasma) | ACN (Urine) | ACN (Plasma) | ACN (Serum) |
|---|---|---|---|---|
| | **ISE NA** | **ISE NA-U** | **ISE NA-P** | **ISE NA-S** |
| **cobas c** 311 analyzer, **cobas c** 501 module, **cobas** 8000 ISE 900 / 1800 module | 989 | 989 | --- | --- |

| | ACN (Serum/ plasma) | ACN (Urine) | ACN (Plasma) | ACN (Serum) |
|---|---|---|---|---|
| | **ISE NA** | **ISE NA-U** | **ISE NA-P** | **ISE NA-S** |
| **cobas c** 303 analytical unit, **cobas pro** ISE analytical unit | 29070 | 29071 | 29072 | 29073 |

# Na Electrode

cobas®

**Sodium**

| | ACN (Serum/ plasma) | ACN (Urine) | ACN (Plasma) | ACN (Serum) |
|---|---|---|---|---|
| | **NA** | **NA-U** | **NA-P** | **NA-S** |
| **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit | 29230 | 29231 | 29232 | 29233 |

**Intended use**

The Na Electrode is a device intended for the in-vitro quantitative determination of sodium in human origin serum, plasma and urine.

**Summary**[1]

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**

Ion-selective electrode, using automatically diluted serum/plasma or urine specimens. The sodium electrode is based on a neutral carrier.[2,3]

**Calculation**

The equation given below is used for the calculation of sample and/or QC results:

$$C_S = C_{IS} \times 10^{\frac{E_S - E_{IS}}{\pm S}}$$

Where:

| | |
|---|---|
| $C_S$ | concentration of the ion in the sample |
| $C_{IS}$ | concentration of the ion in the ISE Internal Standard |
| $E_S$ | EMF of the sample |
| $E_{IS}$ | EMF of the ISE Internal Standard |
| S | Slope of the electrode |

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.

**Precautions and warnings**

For in vitro diagnostic use for trained laboratory technicians.

**Warning**

- Samples containing material of human origin are potentially infectious. Wear personal protective equipment when replacing or installing electrodes at analyzers. If any biohazardous material is spilled, wipe it up immediately and apply a disinfectant.
- If sample or waste contacts with your skin, wash the affected area immediately with soap and water, then apply a disinfectant. Consult a physician.
- When disposing of used electrodes, treat them as biohazardous.

**Caution**

- Do not use electrodes after the shelf life or on-board stability period has expired. Otherwise, it may lead to unstable sodium, potassium, and chloride results due to the unstable potential reading of electrodes.
- In case of lower or higher concentration of sodium results (hypo- or hypernatremia) caused by altered lipid and/or protein content of patients' samples, rerun and/or sample checking may be necessary. Altered lipid and/or protein levels in human blood may falsely shift sodium results into the opposite direction.
- Perform electrode flow path cleaning as stated in the Instructions for Use for applicable analyzers, at the end of a daily sample run. Improper electrode flow path cleaning may cause unstable reading of electrodes and it results in calibration failures.

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.

**NOTE:** Boric acid (CAS Registry No. 10043-35-3) is contained in the gel solution inside the electrode at 0.2 % of the total weight as a preservative.

**Storage and stability**

Store at 7-40 °C.

See labels for expiration dates.

**On-board stability**

After installation the electrode is stable for the following time period:
2 months or 9000 tests, whichever comes first.

The electrodes should be replaced after this time period has expired. For replacement refer to instructions in the operator's manual of the applicable analyzers.

**NOTE:** When replacing the electrode in **cobas pro** or **cobas pure**, the user should scan the barcode affixed on the rear side of the package instead of the barcode placed on the product's label.

**Slope range** 50 to 68 mV/dec

**NOTE:** The slope ranges for newly installed electrodes should be in the upper half of the recommended electrode slope range.

**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.

It is important to follow tube manufacturers recommended procedures at and after blood collection.

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

**Serum**

For sodium determinations, serum is the specimen of choice.

**CAUTION:** Serum separator tubes have to be used in accordance with the tube 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).

**Plasma:** Lithium heparin plasma

**CAUTION:** Inadequate mixing of plasma tubes can cause introduction of fibrin microclots into and subsequent clogging of the ISE.

**NOTE:** 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, in order to prevent coating the sample probes and interfering with ISE system. It is possible to clog the sample probes or the ISE tubing with gel or clots if these precautions are not taken.

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

**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.

**Sample stability (serum, plasma):** [5]

14 days at 15-25 °C

14 days at 2-8 °C

stable at (-15)-(-25) °C

up to 10 freeze-thaw cycles possible.[6]

**Sample stability (urine):** [5,7]

14 days at 15-25 °C

stable at (-15)-(-25) °C

up to 6 freeze-thaw cycles possible.[8]

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

# Na Electrode

**Sodium**

Sample stability claims were established by experimental data by the manufacturer or based on reference literature[5] 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 for its laboratory.

**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**

**Serum/plasma**

| | *Sample dilution* | |
|---|---|---|
| *Sample volume* | *Sample* | *Diluent* |
| *cobas c 311 analyzer, cobas c 501 module* | | |
| Normal | 9.7 µL | 291 µL / ISE Diluent |
| *cobas 8000 ISE 900 / 1800 module, cobas c 303 analytical unit, cobas pro ISE analytical unit* | | |
| Normal | 15 µL | 450 µL / ISE Diluent |
| *cobas ISE neo 900 analytical unit, cobas ISE neo 1800 analytical unit* | | |
| Normal | 15 µL | 450 µL / System Water |

Measuring range on *cobas c 311 analyzer, cobas c 501 module, cobas 8000 ISE 900 / 1800 module, cobas c 303 analytical unit, cobas pro ISE analytical unit, cobas ISE neo 900 analytical unit, cobas ISE neo 1800 analytical unit:* 80-180 mmol/L

Analysis of sodium on ISE analytical units listed 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 %.

The sample volumes given above under “Normal” are for samples, calibrators, and quality controls.

**Urine**

| | *Sample dilution* | |
|---|---|---|
| *Sample volume* | *Sample* | *Diluent* |
| *cobas c 311 analyzer, cobas c 501 module* | | |
| Normal | 9.7 µL | 291 µL / ISE Diluent |
| Decreased | 6.5 µL | 291 µL / ISE Diluent |
| *cobas 8000 ISE 900 / 1800 module* | | |
| Normal | 10 µL | 450 µL / ISE Diluent |
| Increased | 15 µL | 450 µL / ISE Diluent |
| *cobas c 303 analytical unit, cobas pro ISE analytical unit* | | |
| Normal | 15 µL | 450 µL / ISE Diluent |
| Decreased | 10 µL | 450 µL / ISE Diluent |
| *cobas ISE neo 900 analytical unit, cobas ISE neo 1800 analytical unit* | | |
| Normal | 15 µL | 450 µL / System Water |
| Decreased | 10 µL | 450 µL / System Water |

Measuring range on *cobas c 311 analyzer, cobas c 501 module, cobas c 303 analytical unit, cobas pro ISE analytical unit, cobas ISE neo 900 analytical unit, cobas ISE neo 1800 analytical unit:* 20-250 mmol/L

Analysis of sodium on ISE analytical units listed with urine specimens should yield a linear relationship from 20-250 mmol/L with a deviation from the linear line of less than 10 %.

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.

Measuring range on *cobas c 311 analyzer, cobas c 501 module, cobas c 303 analytical unit, cobas pro ISE analytical unit, cobas ISE neo 900 analytical unit, cobas ISE neo 1800 analytical unit* for urine samples with decreased sample volume (Rerun): 251-375 mmol/L.

Analysis of sodium on ISE analytical units listed with urine specimens should yield a linear relationship from 251-375 mmol/L with a deviation from the linear line of less than 10 %.

The sample volumes given above under “Normal” are for samples, calibrators, and quality controls.

Measuring range on *cobas 8000 ISE 900 / 1800 module:* 60-350 mmol/L

Analysis of sodium on **cobas** 8000 ISE 900 / 1800 module with urine specimens should yield a linear relationship from 60-350 mmol/L with a deviation from the linear line of less than 10 %.

Determine samples having lower concentrations via the rerun function. Dilution of samples via rerun function is a 1:31 dilution. Results from samples diluted using the rerun function are automatically multiplied by the dilution factor.

Measuring range on *cobas 8000 ISE 900 / 1800 module* for urine samples with increased sample volume (Rerun): 20-59.9 mmol/L

Analysis of sodium on **cobas** 8000 ISE 900 / 1800 module with urine specimens should yield a linear relationship from 20-59.9 mmol/L with a deviation from the linear line of less than 10 %.

The sample volumes given above under “Normal” are for samples and quality controls.

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

**Lower limits of measurement**

**Limit of Blank, Limit of Detection and Limit of Quantitation**

| | |
|---|---|
| Limit of Blank | = 10 mmol/L |
| Limit of Detection | = 10 mmol/L |
| Limit of Quantitation | = 20 mmol/L |

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

The Limit of Blank is the 95$^{th}$ 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 samples.

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

**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.

**Calibration**

Calibration requires the following calibrators: 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 / ISE Internal Standard conc. is measured to provide $E_{IS}$ for all measurements. Refer to the operator’s manual of the analyzer for detailed calibration instructions.

Traceability: ISE Standard Low and ISE Standard High are prepared gravimetrically from highly purified inorganic salts.

# Na Electrode

cobas®

**Sodium**

Purity of these salts has been certified by argentometric titration, acidimetric titration or perchloric acid titration.

**Calibration frequency**

Calibration

- every 24 hours
- after ISE washing and maintenance
- after changing the reagent bottle ①
- after changing ISE Reference Electrolyte and/or Internal Standard conc. (depending on AutoCal settings) ②
- after replacing any electrode
- as required following quality control procedures

ISE reagents on:

① **cobas c** 311 analyzer, **cobas c** 501 module, **cobas** 8000 ISE 900 / 1800 module, **cobas c** 303 analytical unit, **cobas pro** ISE analytical unit

② **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit

Refer to the operator's manual for a detailed description of the Calibration/AutoCal function.

**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.

Traceability: Each Roche Diagnostics control listed above has been standardized against ISE Standard Low and ISE Standard High.

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial value.

**Hemolysis - serum/plasma**

Hemolysis:[9] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

**Hemolysis - urine**

Hemolysis:[9] No significant interference up to a hemoglobin concentration of 621 µmol/L or 1000 mg/dL.

**Icterus - serum/plasma**

Icterus:[9] 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).

**Lipemia - serum/plasma**

Lipemia (Intralipid, SMOFlipid):[9] 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]

**Altered protein-/lipid levels** may falsely shift sodium results into the opposite direction; i.e. elevated protein level = pseudohyponatremia, decreased protein level = pseudohypernatremia.[11,12]

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

**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.

**Serum/plasma**

| | |
|---|---|
| Acetaminophen (Paracetamol) | 200 mg/L |
| Acetylsalicylic acid | 1000 mg/L |
| Ampicillin-Na | 1000 mg/L |
| Ascorbic acid | 300 mg/L |
| Cefoxitin | 2500 mg/L |
| Cyclosporine | 5 mg/L |
| Doxycyclin | 50 mg/L |
| Heparin | 5000 IU/L |
| Ibuprofen | 500 mg/L |
| Intralipid | 10000 mg/L |
| Levodopa | 20 mg/L |
| Methyldopa | 20 mg/L |
| Metronidazole | 200 mg/L |
| N-Acetylcysteine | 1660 mg/L |
| Phenylbutazone | 400 mg/L |
| Rifampicin | 60 mg/L |
| Theophylline | 100 mg/L |

**Urine**

| | |
|---|---|
| Acetaminophen (Paracetamol) | 3000 mg/L |
| Ascorbic acid | 4000 mg/L |
| Cefoxitin | 12000 mg/L |
| Gentamycine sulfate | 400 mg/L |
| Ibuprofen | 4000 mg/L |
| Levodopa | 1000 mg/L |
| Methyldopa | 2000 mg/L |
| N-Acetylcysteine | 10 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.

**Expected values**[13]

| | | |
|---|---|---|
| Serum, Plasma | Infant | 139-146 mmol/L |
| | Child | 138-145 mmol/L |
| | Adult | 136-145 mmol/L |
| | >90 y | 132-146 mmol/L |
| Urine 24 h | 6-10 y, M | 41-115 mmol/24 h |
| | 6-10 y, F | 20-69 mmol/24 h |
| | 10-14 y, M | 63-177 mmol/24 h |

# Na Electrode

**Sodium**

| | |
|---|---|
| 10-14 y, F | 48-168 mmol/24 h |
| Adult, M | 40-220 mmol/24 h |
| Adult, F | 27-287 mmol/24 h |

The urinary excretion of sodium 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.

**Precision**

see precision data of the following analyzers in "Appendix 1: Precision":

**cobas c** 311 analyzer

**cobas** 6000 analyzer series: **cobas c** 501 module

**cobas** 8000 modular analyzer series: **cobas** 8000 ISE 900 / 1800 module

**cobas pure** integrated solutions: **cobas c** 303 analytical unit

**cobas pro** integrated solutions: **cobas pro** ISE analytical unit, **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit

**Method comparison**

see method comparison data of the following analyzers in "Appendix 2: Method comparison":

**cobas c** 311 analyzer

**cobas** 6000 analyzer series: **cobas c** 501 module

**cobas** 8000 modular analyzer series: **cobas** 8000 ISE 900 / 1800 module

**cobas pure** integrated solutions: **cobas c** 303 analytical unit

**cobas pro** integrated solutions: **cobas pro** ISE analytical unit, **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit

**Maintenance**

*ISE washing procedure for cobas c 311 analyzer, cobas c 501 module, cobas 8000 ISE 900 / 1800 module, cobas c 303 and cobas pro ISE analytical unit.*

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

| | |
|---|---|
| *cobas c 311:* | The specially designated positions on the sample disk are used. |
| Position W1: | ISE Cleaning Solution |
| Position W2: | Activator |

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

| | |
|---|---|
| *cobas c 501:* | 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 system recognizes the wash rack and switches automatically to cleaning mode.

| | |
|---|---|
| *cobas 8000 ISE:* | The specially labeled wash rack (green) is used. |
| Position 1: | Cell Cleaning Solution (not necessary when only the ISE is cleaned) |
| Position 2: | ISE Cleaning Solution |
| Position 3: | Activator |

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

| | |
|---|---|
| *cobas c 303, cobas pro ISE:* | 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.

The ISE systems require conditioning after cleaning and prior to calibration.

**NOTE:** Always use fresh solutions for cleaning.

*ISE washing procedure for cobas ISE neo analytical unit*

| | |
|---|---|
| *cobas ISE neo:* | The ISE system wash tube holder is used. |
| Position CS: | ISE Cleaning Solution |
| Position A: | Activator |

The maintenance task "ISE system wash" is scheduled and initiated automatically. For detailed description, refer to the operator's manual.

On-board stability of auxiliary reagents: ISE Cleaning Solution 4 days, Activator 4 days.

**NOTE:** Always exchange the tubes on the ISE tube holder, using new tubes for fresh reagents. **You must not refill them**, as this will lead to deterioration of the ISE measuring unit(s). Refer to the operator's manual for further information.

**Appendix 1: Precision**

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

**cobas c 311 analyzer**

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

**cobas 6000 analyzer series: cobas c 501 module**

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:

| | 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 |

**cobas 8000 modular analyzer series: cobas 8000 ISE 900 / 1800 module**

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:

# Na Electrode

**Sodium**

| | Repeatability | | | Intermediate precision | | |
|---|---|---|---|---|---|---|
| Sample (on a **cobas** 8000) | Mean mmol/L | SD mmol/L | CV % | Mean mmol/L | SD mmol/L | CV % |
| Plasma low | 88.7 | 0.3 | 0.4 | 88.7 | 0.9 | 1.1 |
| Plasma medium | 120.6 | 0.4 | 0.3 | 120.6 | 0.9 | 0.7 |
| Plasma high | 175.8 | 0.6 | 0.3 | 175.8 | 1.0 | 0.6 |
| Precinorm U | 112.0 | 0.4 | 0.4 | 112.0 | 0.9 | 0.8 |
| Precipath U | 144.0 | 0.4 | 0.3 | 144.0 | 0.8 | 0.5 |
| Urine low[1)] | 24.7 | 0.2 | 0.9 | 24.7 | 0.9 | 3.7 |
| Urine medium[2)] | 174.5 | 0.5 | 0.3 | 174.5 | 1.1 | 0.7 |
| Urine high[2)] | 347.2 | 0.9 | 0.3 | 347.2 | 2.8 | 0.8 |
| Liquichek 1[2)] | 83.4 | 0.3 | 0.3 | 83.4 | 1.3 | 1.6 |
| Liquichek 2[2)] | 175.6 | 1.3 | 0.8 | 175.6 | 1.7 | 1.0 |

1) Data obtained with urine rerun function.

2) Data obtained with default urine mode.

**cobas pure integrated solutions: cobas c 303 analytical unit**

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

**cobas pro integrated solutions: 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.

| | 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 |

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

**cobas pro integrated solutions:** *cobas ISE neo 900 analytical unit, cobas ISE neo 1800 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 ISE neo** analytical unit.

| | Repeatability | | | Intermediate precision | | |
|---|---|---|---|---|---|---|
| Sample (on a **cobas** ISE neo analytical unit) | Mean mmol/L | SD mmol/L | CV % | Mean mmol/L | SD mmol/L | CV % |
| PCCC1[a)] | 116 | 0.71 | 0.6 | 116 | 1.40 | 1.2 |
| PCCC2[b)] | 139 | 0.83 | 0.6 | 140 | 1.41 | 1.0 |
| Human serum 1 | 87.0 | 0.40 | 0.5 | 86.5 | 1.49 | 1.7 |
| Human serum 2 | 132 | 0.82 | 0.6 | 132 | 1.07 | 0.8 |
| Human serum 3 | 136 | 0.79 | 0.6 | 137 | 0.98 | 0.7 |
| Human serum 4 | 159 | 0.80 | 0.5 | 159 | 1.24 | 0.8 |
| Human serum 5 | 176 | 0.81 | 0.5 | 175 | 1.30 | 0.7 |
| Human plasma 1 | 88.1 | 0.39 | 0.4 | 87.8 | 1.52 | 1.7 |
| Human plasma 2 | 131 | 0.82 | 0.6 | 131 | 1.36 | 1.0 |
| Human plasma 3 | 136 | 0.73 | 0.5 | 136 | 1.21 | 0.9 |
| Human plasma 4 | 156 | 0.74 | 0.5 | 157 | 1.38 | 0.9 |
| Human plasma 5 | 173 | 0.82 | 0.5 | 173 | 1.57 | 0.9 |
| Liquichek 1 | 81.1 | 0.38 | 0.5 | 81.1 | 1.17 | 1.4 |
| Liquichek 2 | 171 | 0.95 | 0.6 | 171 | 1.72 | 1.0 |
| Human urine 1 | 27.0 | 0.30 | 1.1 | 26.1 | 1.20 | 4.6 |
| Human urine 2 | 135 | 0.49 | 0.4 | 135 | 1.33 | 1.0 |
| Human urine 3 | 111 | 0.43 | 0.4 | 111 | 1.02 | 0.9 |
| Human urine 4 | 198 | 0.85 | 0.4 | 198 | 2.04 | 1.0 |
| Human urine 5 | 237 | 1.02 | 0.4 | 237 | 2.84 | 1.2 |

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

### Appendix 2: Method comparison

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

**cobas c 311 analyzer**

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

**cobas 6000 analyzer series: cobas c 501 module**

ISE values for human plasma and urine samples obtained on **cobas c** 501 analyzers (y) using ISE 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 method used was: Flame Photometer IL 943 for sodium.

| Instruments | Sample Type/ N | Min.x | Max.x | P/B Regression[14] | Coeff. (r) |
|---|---|---|---|---|---|
| x: flame photom.<br>y: **cobas c** 501 (S3 = ISE Standard High) | Plasma / 103 | 86.7 | 178 | y = 1.000x + 0.300 | 0.999 |
| Bias at 135 mmol/L = 0.03 (0.2 %)<br>Bias at 150 mmol/L = 0.03 (0.2 %) | | | | | |

# Na Electrode

**Sodium**

| | | | | | |
|---|---|---|---|---|---|
| x: **cobas c** 501 (S3 = ISE Compensator)<br>y: **cobas c** 501 (S3 = ISE Standard High) | Plasma / 103 | 87.6 | 176 | y = 1.014x - 1.176 | 1.000 |
| Bias at 135 mmol/L = 0.714 (0.5 %)<br>Bias at 150 mmol/L = 0.924 (0.6 %) | | | | | |
| x: flame photom.<br>y: **cobas c** 501 (S3 = ISE Standard High) | Urine / 100 | 23.5 | 250 | y = 0.964x + 4.032 | 1.000 |
| Bias at 20 mmol/L = 3.312 (16.6 %)<br>Bias at 220 mmol/L = -3.888 (-1.8 %) | | | | | |
| x: **cobas c** 501 (S3 = ISE Compensator)<br>y: **cobas c** 501 (S3 = ISE Standard High) | Urine / 100 | 25.1 | 245 | y = 0.995x + 0.687 | 1.000 |
| Bias at 20 mmol/L = 0.587 (2.9 %)<br>Bias at 220 mmol/L = -0.413 (-0.2 %) | | | | | |

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

**cobas 8000 modular analyzer series:cobas 8000 ISE 900 / 1800 module**

ISE values for human plasma and urine samples obtained on a **cobas** 8000 analyzer (y) using ISE Standard High as S3 Calibrator, were compared with those determined using the corresponding reference method (x) and with **cobas c** 501 (x) using ISE Standard High as S3 Calibrator.

| Instruments | Sample Type/ N | Min.x | Max.x | P/B Regression[14] | Coeff. (r) |
|---|---|---|---|---|---|
| x: flame photom.<br>y: **cobas** 8000 (S3 = ISE Standard High) | Plasma / 100 | 85.6 | 180.6 | y = 1.015x - 3.553 | 0.9943 |
| Bias at 135 mmol/L = -1.528 (-1.1 %)<br>Bias at 150 mmol/L = -1.303 (-0.9 %) | | | | | |
| x: **cobas c** 501 (S3 = ISE Standard High)<br>y: **cobas** 8000 (S3 = ISE Standard High) | Plasma / 100 | 81.5 | 181.9 | y = 0.969x + 3.381 | 0.9984 |
| Bias at 135 mmol/L = -0.804 (-0.6 %)<br>Bias at 150 mmol/L = -1.269 (-0.8 %) | | | | | |
| x: flame photom.<br>y: **cobas** 8000 (S3 = ISE Standard High) | Urine[2] / 105 | 69.2 | 337.4 | y = 0.996x + 1.248 | 0.9995 |
| Bias at 60 mmol/L = 1.008 (1.7 %)<br>Bias at 220 mmol/L = 0.368 (0.2 %) | | | | | |
| x: **cobas c** 501 (S3 = ISE Standard High)<br>y: **cobas** 8000 (S3 = ISE Standard High) | Urine[2] / 105 | 68.3 | 349.5 | y = 0.969x + 8.259 | 0.9998 |
| Bias at 60 mmol/L = 6.339 (10.7 %)<br>Bias at 220 mmol/L = 1.439 (0.7 %) | | | | | |
| x: flame photom.<br>y: **cobas** 8000 (S3 = ISE Standard High) | Urine[1] / 92 | 22.2 | 58.7 | y = 0.943x + 3.149 | 0.9991 |
| Bias at 30 mmol/L = 1.439 (4.8 %) | | | | | |
| x: **cobas c** 501 (S3 = ISE Standard High)<br>y: **cobas** 8000 (S3 = ISE Standard High) | Urine[1] / 92 | 24.2 | 59.8 | y = 0.962x + 1.110 | 0.9995 |
| Bias at 30 mmol/L = - 0.03 (-0.1 %) | | | | | |

1) Data obtained with urine rerun function.

2) Data obtained with default urine mode.

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

**cobas pure integrated solutions: cobas c 303 analytical unit**

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.

| Instruments | Sample Type/ N | Min.x | Max.x | P/B Regression[14] | Coeff. (r) |
|---|---|---|---|---|---|
| x: flame photom.<br>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 %)<br>Bias at 155 mmol/L = -0.871 (-0.6 %) | | | | | |
| x: **cobas pro** ISE<br>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 %)<br>Bias at 155 mmol/L = -0.647 (-0.4 %) | | | | | |
| x: **cobas c** 501<br>y: **cobas c** 303 ISE | Plasma / 119 | 85.8 | 175 | y = 1.000x - 1.20 | 0.999 |

# Na Electrode

**Sodium**

| | | | | | |
|---|---|---|---|---|---|
| Bias at 135 mmol/L = -1.20 (-0.9 %)<br>Bias at 155 mmol/L = -1.20 (-0.8 %) | | | | | |
| x: flame photom.<br>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 %)<br>Bias at 155 mmol/L = -0.176 (-0.1 %) | | | | | |
| x: **cobas pro** ISE<br>y: **cobas c** 303 ISE | Serum / 120 | 81.6 | 178 | y = 0.984x + 1.23 | 1.000 |
| Bias at 135 mmol/L = -0.998 (-0.7 %)<br>Bias at 155 mmol/L = -1.32 (-0.8 %) | | | | | |
| x: **cobas c** 501<br>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 %)<br>Bias at 155 mmol/L = -1.50 (-1.0 %) | | | | | |
| x: flame photom.<br>y: **cobas c** 303 ISE | Urine / 105 | 24.9 | 256 | y = 0.973x + 1.97 | 0.999 |
| x: **cobas pro** ISE<br>y: **cobas c** 303 ISE | Urine / 119 | 19.9 | 246 | y = 0.997x + 0.355 | 1.000 |
| x: **cobas c** 501<br>y: **cobas c** 303 ISE | Urine / 113 | 22.2 | 237 | y = 0.990x + 3.11 | 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

**cobas pro integrated solutions: cobas pro ISE analytical unit**

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.

| Instruments | Sample Type/ N | Min.x | Max.x | P/B Regression[14] | Coeff. (r) |
|---|---|---|---|---|---|
| x: flame photom.<br>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 %)<br>Bias at 155 mmol/L = 0.652 (0.4 %) | | | | | |
| x: **cobas c** 501<br>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 %)<br>Bias at 155 mmol/L = -1.27 (-0.8 %) | | | | | |
| x: flame photom.<br>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 %)<br>Bias at 155 mmol/L = 1.41 (0.9 %) | | | | | |
| x: **cobas c** 501<br>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 %)<br>Bias at 155 mmol/L = -0.230 (-0.1 %) | | | | | |
| x: flame photom.<br>y: **cobas pro** ISE | Urine / 120 | 22.5 | 249 | y = 0.993x - 2.46 | 1.000 |
| x: **cobas c** 501<br>y: **cobas pro** ISE | Urine / 120 | 25.5 | 241 | y = 1.019x - 2.90 | 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

**cobas pro integrated solutions: cobas ISE neo 900 analytical unit, cobas ISE neo 1800 analytical unit**

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

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

The reference method used was: Flame Photometer (FP 8400).

| Instruments | Sample Type/ N | Min.x | Max.x | P/B Regression[14] | Coeff. (r) |
|---|---|---|---|---|---|
| x: flame photom.<br>y: **cobas** ISE neo | Serum / 117 | 85.4 | 182 | y = 0.950x + 5.83 | 0.989 |
| Bias at 135 mmol/L = -0.888 (-0.7 %)<br>Bias at 155 mmol/L = -1.88 (-1.2 %) | | | | | |
| x: **cobas c** 501<br>y: **cobas** ISE neo | Serum / 120 | 80.8 | 178 | y = 1.009x - 1.31 | 0.999 |
| Bias at 135 mmol/L = -0.112 (-0.1 %)<br>Bias at 155 mmol/L = 0.0658 (0.0 %) | | | | | |

# Na Electrode

**Sodium**

| | | | | | |
|---|---|---|---|---|---|
| x: **cobas pro** ISE<br>y: **cobas** ISE neo | Serum / 119 | 80.7 | 178 | y = 1.002x + 0.393 | 0.999 |
| Bias at 135 mmol/L = 0.699 (0.5 %)<br>Bias at 155 mmol/L = 0.744 (0.5 %) | | | | | |
| x: flame photom.<br>y: **cobas** ISE neo | Plasma / 118 | 79.5 | 177 | y = 0.967x + 5.07 | 0.987 |
| Bias at 135 mmol/L = 0.591 (0.4 %)<br>Bias at 155 mmol/L = -0.073 (0.0 %) | | | | | |
| x: **cobas c** 501<br>y: **cobas** ISE neo | Plasma / 118 | 85.0 | 176 | y = 0.987x + 1.60 | 0.999 |
| Bias at 135 mmol/L = -0.123 (-0.1 %)<br>Bias at 155 mmol/L = -0.377 (-0.2 %) | | | | | |
| x: **cobas pro** ISE<br>y: **cobas** ISE neo | Plasma / 119 | 80.5 | 176 | y = 1.000x + 0.500 | 0.999 |
| Bias at 135 mmol/L = 0.500 (0.4 %)<br>Bias at 155 mmol/L = 0.500 (0.3 %) | | | | | |
| x: flame photom.<br>y: **cobas** ISE neo | Urine / 100 | 25.4 | 238 | y = 1.009x + 0.529 | 0.999 |
| x: **cobas c** 501<br>y: **cobas** ISE neo | Urine / 116 | 24.1 | 238 | y = 1.003x + 0.262 | 1.000 |
| x: **cobas pro** ISE<br>y: **cobas** ISE neo | Urine / 118 | 20.9 | 239 | y = 1.010x - 0.555 | 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

**References**


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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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

**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):

| | |
|---|---|
| Cont. | Quantity contained in the package |
| **CONTENT** | Quantity contained in the package |
| GTIN | Global Trade Item Number |
| INSTALL BEFORE | Latest date by which the electrode has to be installed on the analyzer |
| RoHS | Directive for the restriction of the use of certain hazardous substances in electrical and electronic equipment |

**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.

10825468001V2.0

# Na Electrode

**Sodium**

CE 0123


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# NACL

**Diluent NaCl 9 %**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08063494190* | 08063494500 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08063494214* | 08063494500 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

* Some kits shown may not be available in all countries.

**English**

**System information**

**NACL:** ACN 29060

**Intended use**

Diluent NaCl 9 % is used as a sample diluent in conjunction with assay reagents on **cobas c** systems.

**Summary**

Dilution of samples is necessary when analyte concentrations exceed the measuring range of the respective **cobas c** test method. In addition, general predilution of samples is specified for some tests. For dilution of human body liquids, physiological sodium chloride solution (0.9 % NaCl in water) is recommended. The present diluent is concentrated and will be diluted on the instrument by a factor of 10.

**Reagents - working solutions**

9 % NaCl

**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.

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |

**Materials provided**

See “Reagents – working solutions” section for reagents.

**Materials required (but not provided)**

See “Order information” section

**cobas c** analyzers and assay reagents.

See appropriate package insert and operator's manual for additional required materials.

**Assay**

Use Diluent NaCl 9 % as specified in the respective instructions for use of the system reagents.

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

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
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+800 5505 6606

# NAOHD - SMS - SCCS

cobas®

**Special Wash Requirements Method Sheet**

| CONTENT | REF | | | Analyzer(s) on which kit(s) can be used |
|---|---|---|---|---|
| NAOHD (123 mL) | 08063451190* | 08063451500 | System-ID 2902 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| NAOHD (123 mL) | 08063451214* | 08063451500 | System-ID 2902 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| SMS (123 mL) | 08063478190* | 08063451500 | System-ID 2903 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| SMS (123 mL) | 08063478214* | 08063451500 | System-ID 2903 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| SCCS (Special Cell Cleaning Solution) (50 mL) | 08463093190* | 08063451500 | System-ID 2905 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| SCCS (Special Cell Cleaning Solution) (50 mL) | 08463093214* | 08063451500 | System-ID 2905 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| Basic Wash (2 × 2000 mL) | 08302545190* | 08063451500 | System-ID 2998 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703, **cobas** ISE neo |
| Basic Wash (2 × 2000 mL) | 08302545214* | 08063451500 | System-ID 2998 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703, **cobas** ISE neo |
| Basic Wash (1 × 980 mL) | 08453209190 | 08063451500 | System-ID 2998 003 | **cobas c** 303, **cobas c** 503, **cobas c** 703, **cobas** ISE neo |
| Acid Wash (2 × 2000 mL) | 08302723190 | 08063451500 | System-ID 2998 002 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

* Some kits shown may not be available in all countries.

**English**

**System information**

**NAOHD:** ACN 29020

**SMS:** ACN 29030

**SCCS:** ACN 29050

**Basic Wash:** ACN 29980

**Acid Wash:** ACN 29981

**Intended use**

*NAOHD and SMS:*
Wash solution for reagent probes and reaction cells on **cobas c** systems.
*SCCS:*
Wash solution for reaction cells on **cobas c** systems.
*Basic Wash:*
Basic Wash is used as alkaline wash solution for reaction cells and for sample probes on the **cobas c** analyzers.
*Acid Wash:*
Acid Wash is used as acid wash solution for reaction cells on **cobas c** analyzers.

**Summary**

Reagent and sample probe or cell washes may be required due to potential interference from other reagents or samples. These special washes maintain reagent and sample integrity.

*Reagent probe carry over*

Extra wash cycles are required with specific reagent combinations, e.g. if a preceding test interferes with an assay through carry over by the reagent probe.

*Sample probe carry over*

Extra wash cycles are required with specific sample type combinations, e.g. if a preceding sample interferes with an assay through carry over by the sample probe. Extra wash cycles for the sample probe are performed using Basic Wash or water.

*Reaction cell carry over*

Extra wash cycles are required with specific reagent combinations, e.g. if a preceding cuvette content interferes with an assay through carry over via the cuvette.

**Reagents - working solutions**

**NAOHD, Basic Wash:** NaOH 1 mol/L (approximately 4 %); detergent

**SMS:** HCl 200 mmol/L

**SCCS:** NaOH 3 mol/L (approximately 12 %); sodium hypochlorite solution (< 2 % active chlorine); additive

**Acid Wash:** Citric acid monohydrate: 310 mmol/L; buffer; detergent

**Precautions and warnings**

For in vitro diagnostic use for laboratory 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.

These kits contain components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

*NAOHD*

Danger

| | |
|---|---|
| H290 | May be corrosive to metals. |
| H314 | Causes severe skin burns and eye damage. |
| **Prevention:** | |
| P280 | Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. |
| **Response:** | |
| P301 + P330 + P331 | IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. |
| P303 + P361 + P353 | IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. |
| P304 + P340 + P310 | IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. |
| P305 + P351 + P338 + P310 | IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. |
| P390 | Absorb spillage to prevent material damage. |

# NAOHD - SMS - SCCS

**Special Wash Requirements Method Sheet**

**Hazardous components:**

- sodium hydroxide

*SMS*

Warning

| | |
|---|---|
| H290 | May be corrosive to metals. |

**Prevention:**

| | |
|---|---|
| P234 | Keep only in original packaging. |

**Response:**

| | |
|---|---|
| P390 | Absorb spillage to prevent material damage. |

*SCCS*

Danger

| | |
|---|---|
| H290 | May be corrosive to metals. |
| H314 | Causes severe skin burns and eye damage. |
| H410 | Very toxic to aquatic life with long lasting effects. |

**Prevention:**

| | |
|---|---|
| P273 | Avoid release to the environment. |
| P280 | Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. |

**Response:**

| | |
|---|---|
| P303 + P361 + P353 | IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. |
| P304 + P340 + P310 | IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. |
| P305 + P351 + P338 + P310 | IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. |
| P391 | Collect spillage. |

**Hazardous components:**

- sodium hydroxide
- sodium hypochlorite

*Basic Wash*

Danger

| | |
|---|---|
| H290 | May be corrosive to metals. |
| H314 | Causes severe skin burns and eye damage. |

**Prevention:**

| | |
|---|---|
| P280 | Wear protective gloves/ protective clothing/ eye protection/ face protection/ hearing protection. |

**Response:**

| | |
|---|---|
| P301 + P330 + P331 | IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. |
| P303 + P361 + P353 | IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water. |
| P304 + P340 + P310 | IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor. |
| P305 + P351 + P338 + P310 | IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. |
| P390 | Absorb spillage to prevent material damage. |

**Hazardous components:**

- sodium hydroxide

*Acid Wash*

Danger

| | |
|---|---|
| H318 | Causes serious eye damage. |

**Prevention:**

| | |
|---|---|
| P280 | Wear eye protection/ face protection. |

**Response:**

| | |
|---|---|
| P305 + P351 + P338 + P310 | IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor. |

**Hazardous components:**

- Secondary alcohols, C11-15, ethoxylated

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

*Note for NAOHD*

Over time, a slight discoloration or small particles may be observed on the bottom of the bottle. The discoloration or particles do not affect reagent performance.

**Storage and stability**

*NAOHD*

| | |
|---|---|
| Shelf life at 15-25 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 12 weeks |

*SMS*

| | |
|---|---|
| Shelf life at 15-25 °C: | See expiration date on **cobas c** pack label. |

# NAOHD - SMS - SCCS

**Special Wash Requirements Method Sheet**

| | |
|---|---|
| On-board in use and refrigerated on the analyzer: | 12 weeks |

*SCCS*

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 7 days |

*Basic Wash*

| | |
|---|---|
| Shelf life at 15-25 °C: | See expiration date on bottle label. |
| On-board in use: | 10 weeks |

*Acid Wash*

| | |
|---|---|
| Shelf life at 15-25 °C: | See expiration date on labels. |
| On-board stability: | 12 weeks |

**Materials provided**

See “Reagents – working solutions” section for reagents.

**Materials required (but not provided)**

See “Order information” section

**cobas c** 303, **cobas c** 503 or **cobas c** 703 analyzer and assay reagents.

See appropriate instructions for use and the operator's manual for additional required materials.

**Assay**

The definition and configuration of extra wash cycles is described in detail in the appropriate chapter of the operator's manual for the respective **cobas c** analyzer.

For further information, please refer to the appropriate operator’s manual for the analyzer concerned, the respective application sheets and method sheets of all necessary components.

For optimal performance of the wash solutions, follow the directions given in this document for the analyzer concerned.

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

**Carry over evasion list**

1. Reagent probe carry over:

The table on the following pages lists all tests that require extra wash cycles under certain circumstances.

2. Reaction cell carry over:

The table on the following pages lists all tests that require extra wash cycles under certain circumstances.

3. Sample probe carry over:

The table on the following pages lists all tests that require extra wash cycles under certain circumstances.

**Please note:** The programming for the carry-over evasion will be downloaded via TSN on **cobas** link.

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:

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



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



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# NAOHD - SMS - SCCS

cobas®

**Special Wash Requirements Method Sheet**

**1. Reagent probe carry-over on cobas c 503 analyzer**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **A1CD2** [20690] | DIL | **AMPS2** [20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167*, 20168] | R1 | NAOHD | 135 | 1 |
| R1 | **A1CX3** [20661, 20664] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **A1CX4** [21601, 21605] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **ACET2** [20040, 20042] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **AMIK2** [20150] | R1 | **ALBT2** [20061] | R1 | NAOHD | 135 | 1 |
| R1 | **FRA** [20580] | R1 | **CHE2** [20370, 20371] | R1 | SMS | 100 | 1 |
| R1 | **FRA** [20580] | R1 | **TPUC3** [21122, 21123] | R1 | SMS | 135 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **GLDH3** [20610] | R3 | NAOHD | 100 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **HBDH2** [20650] | R2 | NAOHD | 100 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **LDHI2** [20810, 20811] | R3 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R1 | **MG2** [20890, 20891] | R1 | SMS | 135 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **MG2** [20890, 20891] | R3 | SMS | 135 | 1 |
| R1 | **HDLC4** [20710] | R1 | **LI** [20840] | R1 | SMS | 135 | 2 |
| R1 | **OPI2** [20950, 20951, 20952, 20953, 20954] | R1 | **ALBT2** [20061] | R1 | NAOHD | 135 | 1 |
| R2/R3 | **TP2** [21110] | R3 | **MTX** [21610] | R3 | SMS | 30 | 1 |
| R1 | **TRIGL** [21130] | R1 | **LIPC** [20850] | R1 | NAOHD | 135 | 1 |

*only available in CE countries

**2. Reaction cell carry-over on cobas c 503 analyzer**

| Detergent | Trigger Counter | Offenders |
|---|---|---|
| SCCS | 10 | **A1CX3** [20661, 20664] **A1CX4** [21601], 21605] |

**3. Sample probe carry-over on cobas c 503 analyzer**

| Victim [Applications] | Sample Type | Washing Method | Material |
|---|---|---|---|
| **ALBT2** [20061] | Urine | Water | RS/QC |
| **ALBT2** [20062] | CSF | Wash solution | RS/QC |
| **IGA-2** [20720, 20721] | Serum/Plasma | Water | RS |
| **IGA-C** [20730] | CSF | Water | RS/QC |
| **IGA-C** [20731] | Serum/Plasma | Water | RS |
| **IGG-2** [20740, 20744] | Serum/Plasma | Wash Solution | RS |
| **IGG-2** [20741] | CSF | Wash solution + Ultrasonic Cleaning | RS/QC |
| **IGG-2** [20743] | Urine | Wash solution + Ultrasonic Cleaning | RS/QC |
| **IGM-2** [20750, 20751] | Serum/Plasma | Water | RS |
| **IGM-C** [20760] | CSF | Wash solution + Ultrasonic Cleaning | RS/QC |
| **IGM-C** [20761] | Serum/Plasma | Water | RS |
| **KAPP2** [20780] | Serum/Plasma | Water | RS |
| **LAMB2** [20800] | Serum/Plasma | Water | RS |
| **MTX** [21610] | Serum/Plasma | Water | RS/QC |
| **TPUC3** [21122] | Urine | Water | RS/QC |
| **TPUC3** [21123] | CSF | Water | RS/QC |
| **TRSF2** [21151] | Urine | Water | RS/QC |

Wash Solution = Basic Wash (NaOH); RS = Routine Sample; QC = Quality Control

**Closed Development Channels**

# NAOHD - SMS - SCCS

**Special Wash Requirements Method Sheet**

Please note that non-Roche reagents may cause carry-over interference. Roche is not responsible for any carry-over interference caused by non-Roche reagents.

CDCnn = CDC01 [28800], CDC02 [28801], CDC03 [28802], CDC04 [28803], CDC05 [28804], CDC06 [28805], CDC07 [28806], CDC08 [28807], CDC09 [28808], CDC10 [28809], CDC11 [28810], CDC12 [28811], CDC13 [28812], CDC14 [28813], CDC15 [28814], additional ACNs 28815-28829. For ACNs 28815-28829 manual addition of Reagent probe carry-over rules according to the following list is needed. These ACNs are not included in the provided RCE-file.

**1. Reagent probe carry-over on cobas c 503 analyzer**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **CDCnn** | R1 | **All Tests** | R1 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R1 | **All Tests** | DIL | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R2 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R2 | **All Tests** | R3 | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R3 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R3 | **All Tests** | R3 | NAOHD | 135 | 2 |

**2. Reaction cell carry-over on cobas c 503 analyzer**

| **Detergent** | **Trigger Counter** | **Offenders** |
|---|---|---|
| NaOHD | 1 | **CDCnn** |

# NAOHD - SMS - SCCS

cobas®

**Special Wash Requirements Method Sheet**

**1. Reagent probe carry-over on cobas c 303 analyzer**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **A1CD2** [20690] | Dil | **AMPS2** [20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167, 20168] | R1 | NaOHD | 135 | 1 |
| R1 | **A1CD2** [20690] | Dil | **AMPS2** [20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167, 20168] | R2 | NaOHD | 135 | 1 |
| R1 | **A1CX3** [20661, 20664] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **A1CX3** [20661, 20664] | R1 | **TPUC3** [21122, 21123] | R3 | NAOHD | 135 | 1 |
| R1 | **A1CX4** [21601, 21605] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **A1CX4** [21601, 21605] | R1 | **TPUC3** [21122, 21123] | R3 | NAOHD | 135 | 1 |
| R1 | **A2MG** [21450] | R1 | **MG2** [20890, 20891] | R3 | SMS | 135 | 1 |
| R1 | **A2MG** [21450] | R3 | **MG2** [20890, 20891] | R3 | SMS | 135 | 1 |
| R1 | **A2MG** [21450] | R3 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **ACET2** [20040] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **ALBT2** [20060, 20061, 20062, 20067] | R2 | **TPUC3** [21122, 21123] | R1 | SMS | 135 | 1 |
| R1 | **ALBT2** [20060, 20061, 20062, 20067] | R2 | **TPUC3** [21122, 21123] | R3 | SMS | 135 | 1 |
| R1 | **ALP2** [20110] | R1 | **MG2** [20890, 20891] | R3 | SMS | 135 | 1 |
| R1 | **AMIK2** [20150] | R1 | **ALBT2** [20061, 20062] | R1 | NAOHD | 135 | 1 |
| R1 | **AMIK2** [20150] | R1 | **ALBT2** [20061, 20062] | R2 | NAOHD | 135 | 1 |
| R1 | **AMPS2** [20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167, 20168] | R1 | **TOBR2** [21100] | R2 | NAOHD | 135 | 1 |
| R1 | **AMPS2** [20160, 20161, 20162, 20163, 20164, 20165, 20166, 20167, 20168] | R1 | **TOBR2** [21100] | R3 | NAOHD | 135 | 1 |
| R1 | **APOAT** [20190] | R3 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R1 | **APOBT** [20200] | R3 | **TPUC3** [21122, 21123] | R1 | SMS | 135 | 1 |
| R1 | **C3C-2** [20320] | R3 | **TPUC3** [21122, 21123] | R1 | SMS | 135 | 1 |
| R1 | **COC2** [20450, 20451, 20452, 20453, 20454, 20455, 20456] | R1 | **TOBR2** [21100] | R2 | NAOHD | 135 | 1 |
| R1 | **COC2** [20450, 20451, 20452, 20453, 20454, 20455, 20456] | R1 | **TOBR2** [21100] | R3 | NAOHD | 135 | 1 |
| R1 | **FRA** [20580] | R1 | **TPUC3** [21122, 21123] | R1 | SMS | 135 | 1 |
| R1 | **FRA** [20580] | R1 | **TPUC3** [21122, 21123] | R3 | NAOHD | 135 | 1 |
| R1 | **GENT2** [20590, 20591] | R1 | **TOBR2** [21100] | R2 | Water | - | 1 |
| R1 | **GENT2** [20590, 20591] | R1 | **TOBR2** [21100] | R3 | Water | - | 1 |
| R1 | **HCYS** [20700] | R2 | **GLDH3** [20610] | R1 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R2 | **GLDH3** [20610] | R3 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R2 | **HBDH2** [20650] | R1 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R2 | **HBDH2** [20650] | R2 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R2 | **LDHI2** [20810, 20811] | R1 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R2 | **LDHI2** [20810, 20811] | R3 | NAOHD | 135 | 1 |
| R1 | **HCYS** [20700] | R1 | **MG2** [20890, 20891] | R3 | SMS | 135 | 1 |
| R1 | **HDLC4** [20710] | R3 | **CREP2** [20460, 20461] | R1 | Water | 135 | 1 |

# NAOHD - SMS - SCCS

cobas®

**Special Wash Requirements Method Sheet**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **HDLC4** [20710] | R1 | **CREP2** [20460, 20461] | R1 | NAOHD | 135 | 1 |
| R1 | **HDLC4** [20710] | R3 | **CREP2** [20460, 20461] | R3 | NAOHD | 135 | 1 |
| R1 | **LDLC3** [20820] | R3 | **LIPC** [20850] | R1 | SMS | 135 | 1 |
| R1 | **MDN2** [20880, 20881, 20882, 20883, 20884] | R1 | **TOBR2** [21100] | R2 | NaOHD | 135 | 1 |
| R1 | **MDN2** [20880, 20881, 20882, 20883, 20884] | R1 | **TOBR2** [21100] | R3 | NaOHD | 135 | 1 |
| R1 | **OPI2** [20950, 20951, 20952, 20953, 20954] | R1 | **ALBT2** [20061, 20062] | R1 | NAOHD | 135 | 1 |
| R1 | **OPI2** [20950, 20951, 20952, 20953, 20954] | R1 | **TOBR2** [21100] | R2 | NAOHD | 135 | 2 |
| R1 | **OPI2** [20950, 20951, 20952, 20953, 20954] | R1 | **TOBR2** [21100] | R3 | NAOHD | 135 | 2 |
| R1 | **PHNO2** [20970] | R1 | **TOBR2** [21100] | R2 | Water | - | 1 |
| R1 | **PHNO2** [20970] | R1 | **TOBR2** [21100] | R3 | Water | - | 1 |
| R1 | **THC2** [21070, 21071, 21072, 21073, 21074, 21075, 21076, 21077, 21078] | R1 | **TOBR2** [21100] | R2 | NAOHD | 135 | 1 |
| R1 | **THC2** [21070, 21071, 21072, 21073, 21074, 21075, 21076, 21077, 21078] | R1 | **TOBR2** [21100] | R3 | NAOHD | 135 | 1 |
| R1 | **THEO2** [21090] | R1 | **TOBR2** [21100] | R2 | NAOHD | 135 | 1 |
| R1 | **THEO2** [21090] | R1 | **TOBR2** [21100] | R3 | NAOHD | 135 | 1 |
| R1 | **TP2** [21110] | R1 | **MTX** [21610] | R1 | SMS | 90 | 1 |
| R1 | **TP2** [21110] | R3 | **MTX** [21610] | R3 | SMS | 30 | 1 |
| R1 | **TP2** [21110] | R3 | **MTX** [21610] | R1 | SMS | 30 | 1 |
| R1 | **TPUC3** [21122, 21123] | R3 | **CHE2** [20370, 20371] | R1 | SMS | 135 | 1 |
| R1 | **TPUC3** [21122, 21123] | R3 | **CHE2** [20370, 20371] | R3 | SMS | 135 | 1 |
| R1 | **TRIGL** [21130] | R1 | **LIPC** [20850] | R1 | NAOHD | 135 | 1 |
| R1 | **VANC3** [21210, 21211] | R1 | **TOBR2** [21100] | R2 | NAOHD | 135 | 1 |

**2. Reaction cell carry-over on cobas c 303 analyzer**

| Detergent | Trigger Counter | Offenders |
|---|---|---|
| SCCS | 10 | **A1CX3** [20661, 20664] **A1CX4** [21601], 21605] |

**3. Sample probe carry-over on cobas c 303 analyzer**

| Victim [Applications] | Sample Type | Washing Method | Material |
|---|---|---|---|
| **IGA-C** [20730] | CSF | Wash solution | RS |
| **IGG-2** [20741] | CSF | Wash Solution | RS/QC |
| **IGG-2** [20743] | Urine | Wash Solution | RS/QC |
| **IGG-2** [20744] | Serum/Plasma | Water | RS |
| **IGM-C** [20760] | CSF | Wash solution | RS/QC |
| **MTX** [21610] | Serum/Plasma | Water | RS/QC |
| **TOBR2** [21100] | Serum/Plasma | Wash solution | RS |

**Closed Development Channels**

Please note that non-Roche reagents may cause carry-over interference. Roche is not responsible for any carry-over interference caused by non-Roche reagents.

# NAOHD - SMS - SCCS

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**Special Wash Requirements Method Sheet**

CDCnn = CDC01 [28800], CDC02 [28801], CDC03 [28802], CDC04 [28803], CDC05 [28804], CDC06 [28805], CDC07 [28806], CDC08 [28807], CDC09 [28808], CDC10 [28809], CDC11 [28810], CDC12 [28811], CDC13 [28812], CDC14 [28813], CDC15 [28814], additional ACNs 28815-28829. For ACNs 28815-28829 manual addition of Reagent probe carry-over rules according to the following list is needed. These ACNs are not included in the provided RCE-file.

**1. Reagent probe carry-over on cobas c 303 analyzer**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **CDCnn** | R1 | **All Tests** | R1 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R2 | **All Tests** | R1 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R3 | **All Tests** | R1 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R1 | **All Tests** | DIL | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R2 | **All Tests** | DIL | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R3 | **All Tests** | DIL | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R1 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R2 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R3 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R1 | **All Tests** | R3 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R2 | **All Tests** | R3 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R3 | **All Tests** | R3 | NAOHD | 135 | 2 |

**2. Reaction cell carry-over on cobas c 303 analyzer**

| Detergent | Trigger Counter | Offenders |
|---|---|---|
| NaOHD | 1 | **CDCnn** |

# NAOHD - SMS - SCCS

cobas®

**Special Wash Requirements Method Sheet**

**1. Reagent probe carry-over on cobas c 703 analyzer**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **ACET2** [20042] | R1 | **TPUC3** [21122, 21123] | R1 | NAOHD | 135 | 1 |
| R2/R3 | **ALBT2** [20060, 20061, 20062, 20067] | R2 | **TPUC3** [21122, 21123] | R3 | NAOHD | 135 | 1 |
| R2/R3 | **APOAT** [20190] | R3 | **TPUC3** [21122, 21123] | R3 | NAOHD | 135 | 1 |
| R1 | **FRA** [20580] | R1 | **TPUC3** [21122, 21123] | R1 | SMS | 135 | 1 |
| R1 | **FRA** [20580] | R1 | **CHE2** [20370, 20371] | R1 | SMS | 100 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **GLDH3** [20610] | R3 | NAOHD | 135 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **HBDH2** [20650] | R2 | NAOHD | 135 | 1 |
| R2/R3 | **HCYS** [20700] | R2 | **LDHI2** [20810, 20811] | R3 | NAOHD | 135 | 1 |
| R1 | **TRIGL** [21130] | R1 | **LIPC** [20850] | R1 | NAOHD | 135 | 1 |

**LI**, **LDHI2**, **HDLC4** assays:
Please note: **LI** [20840] must not be run on the same rotor as **LDHI2** [20810, 20811] and **HDLC4** [20710].

**2. Reaction cell carry-over on cobas c 703 analyzer**

| Detergent | Trigger Counter | Offenders |
|---|---|---|
| - | - | - |

**TOBR2**, **GENT2**, **THEO2**, **VANC3** assays:
Please note: **TOBR2** [21100] must not be run on the same rotor as **THEO2** [21090], **GENT2** [20591] and **VANC3** [21211].

**3. Sample probe carry-over on cobas c 703 analyzer**

| Victim [Applications] | Sample Type | Washing Method | Material |
|---|---|---|---|
| **ALBT2** [20061] | Urine | Water | RS/QC |
| **ALBT2** [20062] | CSF | Wash Solution | RS/QC |
| **IGA-2** [20720, 20721] | Serum/Plasma | Water | RS/QC |
| **IGA-C** [20730] | CSF | Water | RS/QC |
| **IGA-C** [20731] | Serum/Plasma | Water | RS |
| **IGG-2** [20740, 20744] | Serum/Plasma | Wash solution | RS/QC |
| **IGG-2** [20741] | CSF | Wash solution + Ultrasonic Cleaning | RS/QC |
| **IGG-2** [20743] | Urine | Wash Solution | RS/QC |
| **IGM-2** [20750, 20751] | Serum/Plasma | Water | RS |
| **IGM-C** [20760] | CSF | Wash Solution + Ultrasonic Cleaning | RS/QC |
| **IGM-C** [20761] | Serum/Plasma | Water | RS |
| **KAPP2** [20780] | Serum/Plasma | Water | RS |
| **LAMB2** [20800] | Serum/Plasma | Water | RS |
| **MTX** [21610] | Serum/Plasma | Water | RS/QC |
| **TPUC3** [21122] | Urine | Water | RS/QC |
| **TPUC3** [21123] | CSF | Water | RS/QC |
| **TRSF2** [21151] | Urine | Water | RS/QC |

Wash Solution = Basic Wash (NaOH); RS = Routine Sample; QC = Quality Control

**4. Sample probe carry-over on cobas c 503 and cobas c 703 analyzers, cobas ISE and cobas ISE neo analytical units**

| Victim [Applications] | Sample Type | Washing Method | Material |
|---|---|---|---|
| **Anti-SARS-CoV-2 S** [10230, 11230] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys HCG STAT** [10093, 10203] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys HCG+ß** [10072] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys sFlt-1** [10046] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys hGH** [10096] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |

# NAOHD - SMS - SCCS

cobas®

**Special Wash Requirements Method Sheet**

| Victim [Applications] | Sample Type | Washing Method | Material |
|---|---|---|---|
| **Elecsys BRAHMS PCT** [10092, 10173, 10161, 10241] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys IL-6** [10085] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Anti-HBs II** [10138, 10179] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Anti-HCV II** [10104, 11104, 10189, 11189] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Chagas** [10146, 10214] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys HTLV-I/II** [10039, 11039, 10219, 11219] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys CMV IgG** [10070, 11070, 10090, 10218] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys CMV IgG Avidity** [11149, 11150, 11151] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Rubella IgG** [10024] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Rubella IgM** [10021] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Toxo IgG** [10047, 11047] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Toxo IgG Avidity** [11004, 11005, 11006] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Toxo IgM** [10016, 11016] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys PIVKA-II** [10157] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys EBV VCA IgG** [10125, 11125] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Anti-SARS-CoV-2** [10226] | Serum/Plasma | Cancel | RS |
| **Elecsys HBsAG II** [10049] | Serum/Plasma | Cancel | RS |
| **Elecsys HBsAG II quant II** [10055] | Serum/Plasma | Cancel | RS |
| **Elecsys Tg II** [10077, 10215] | Serum/Plasma | Cancel | RS |
| **Elecsys Anti-HBc II** [10142, 10166] | Serum/Plasma | Cancel | RS |
| **Elecsys AFP-L3** [10064] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Anti-HBs** [10031] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys SARS-CoV-2 Antigen** [10231] | OraFlu | Cancel | RS |
| **Elecsys ß-Amyloid (1-42) CSF II** [10097] | CSF | Cancel | RS |
| **Elecsys PCT** [10229] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Anti-HEV IgG** [10222] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Anti-HBs III** [10265] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |
| **Elecsys Troponin T hs Gen 6** [10252, 10253] | Serum/Plasma | Wash solution + Ultrasonic Cleaning | RS |

Wash Solution = Basic Wash (NaOH); RS = Routine Sample; QC = Quality Control

The Elecsys assays listed with "Washing Method" set to "Cancel" are "High Priority" assays. Adding a user defined sample probe wash to these assays will negate the "High Priority" setting. In order to avoid this, these assays are added and set to "Cancel".

**Closed Development Channels**

Please note that non-Roche reagents may cause carry-over interference. Roche is not responsible for any carry-over interference caused by non-Roche reagents.

CDCnn = CDC01 [28800], CDC02 [28801], CDC03 [28802], CDC04 [28803], CDC05 [28804], CDC06 [28805], CDC07 [28806], CDC08 [28807], CDC09 [28808], CDC10 [28809], CDC11 [28810], CDC12 [28811], CDC13 [28812], CDC14 [28813], CDC15 [28814]

**1. Reagent probe carry-over on cobas c 703 analyzer**

| | Offender | | Victim | | Detergent | | |
|---|---|---|---|---|---|---|---|
| **Probe** | **Test [Applications]** | **Reagent type** | **Test [Applications]** | **Reagent type** | **Type** | **Volume [µL]** | **Repe-titions** |
| R1 | **CDCnn** | R1 | **All Tests** | R1 | NAOHD | 135 | 2 |
| R1 | **CDCnn** | R1 | **All Tests** | DIL | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R2 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R2 | **All Tests** | R3 | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R3 | **All Tests** | R2 | NAOHD | 135 | 2 |
| R2/R3 | **CDCnn** | R3 | **All Tests** | R3 | NAOHD | 135 | 2 |

**2. Reaction cell carry-over on cobas c 703 analyzer**

# NAOHD - SMS - SCCS

**Special Wash Requirements Method Sheet**

| Detergent | Trigger Counter | Offenders |
|---|---|---|
| NaOHD | 1 | **CDCnn** |

# PreciControl ClinChem Multi 1

cobas®

| | | |
|---|---|---|
| REF 05947626190 | 05947626500 | → 4 x 5 mL Control |
| REF 05117003190 | 05947626500 | → 20 x 5 mL Control |
| REF 05117208922 | 05947626500 | → 20 x 5 mL Control (QCS) |

**English**

**System information**

For use on **cobas c** and COBAS INTEGRA analyzer systems, refer to the corresponding method sheet of the assay for the identification on the systems.

**Intended use**

PreciControl ClinChem Multi 1 is for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

**Summary**

PreciControl ClinChem Multi 1 is a lyophilized control based on human serum. The adjusted concentrations and activities of the control components are usually in the normal range or at the normal/pathological threshold.

Some methods specified in the relevant value sheet may not be available in all countries.

**Reagents – working solutions**

*Reactive components in the lyophilizate:*

Human serum with chemical additives and material of biological origin as specified.

The origin of the biological additives is as follows:

| *Analyte* | *Origin* |
|---|---|
| ALT (GPT) | human, recombinant |
| AST (GOT) | human, recombinant |
| Aldolase | rabbit muscle |
| Alkaline phosphatase | human placenta (recombinant) |
| Amylase, total | human saliva / porcine pancreas |
| Amylase, pancreatic | porcine pancreas |
| Creatine kinase | human CK-MM / human CK-MB (recombinant) |
| CK-MB | human CK-MB (recombinant) |
| γ-GT | human, recombinant |
| GLDH | bacterial, recombinant |
| LDH | porcine heart |
| Lipase | human pancreas (recombinant) |
| Acid phosphatase | human prostate / potato |
| ASLO | sheep |
| CRP | human |
| Transferrin | human |
| Ferritin | human |

*Non-reactive components in the lyophilizate:*

Stabilizers

The concentrations and activities of the components are lot-specific. The exact target values are given in the electronically available or enclosed value sheets.

The values are also encoded in the enclosed control barcode sheets for COBAS INTEGRA and **cobas c** 111 analyzers.

For the **cobas c** analyzers (except for the **cobas c** 111 analyzer) the values are encoded in electronic files sent via the **cobas** link to the analyzers.

**Target values and ranges**

The target values were determined using the method stated in the electronically available or enclosed value sheets. Determinations for Roche methods were performed under strictly standardized conditions on Roche analyzers using Roche system reagents and the Roche master calibrator. The target value specified is the mean of all values obtained. The corresponding control range is calculated as the target value ± 3 standard deviations (the standard deviation being the value obtained from several target value determinations). Results should be within the defined ranges. Each laboratory should establish corrective measures to be taken if values fall outside the range.

A clinically insignificant difference may be seen between the value(s) listed on the value sheet and the value(s) obtained from the instrument readable data. This is caused by:

- the rounding of value(s) during conversion from the unit in the instrument readable data to the unit that is being used.
- the calculation of the ranges by the analyzer using the percentage values for the ranges encoded in the barcodes.

The traceability of the target value is given in the respective Method Sheets for the system reagents to be used in combination with the recommended calibrator.

**Precautions and warnings**

For in vitro diagnostic use for laboratory 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.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A). However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

**Handling**

Carefully open one bottle, avoiding the loss of lyophilizate, and pipette in exactly 5.0 mL of distilled/deionized water. Carefully close the bottle and dissolve the contents completely by occasional gentle swirling within 30 minutes. Avoid the formation of foam.

The enclosed barcoded labels are intended exclusively for the **cobas c** systems (except for the **cobas c** 513 analyzer) to identify the control. Attach the barcoded labels to the tubes carrying the sample cups containing the control material.

**Storage and stability**

Store at 2-8 °C.

Criterion for the stability data stated by Roche:

Recovery within ± 10 % of initial value.

Stability of the lyophilized control serum:

Up to the stated expiration date at 2-8 °C.

Stability of components after reconstitution*:

| | | |
|---|---|---|
| at | 15-25 °C | 12 hours |
| at | 2-8 °C | 5 days |
| at | -20 °C (± 5 °C) | 28 days (when frozen once) |

*Exceptions: see below

Stability of total bilirubin, acid phosphatase, non-prostatic acid phosphatase, prostatic acid phosphatase and UIBC in reconstituted control serum (stored protected from light):

| | | |
|---|---|---|
| at | 15-25 °C | 8 hours |

# PreciControl ClinChem Multi 1

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| | | |
|---|---|---|
| at | 2-8 °C | 24 hours |
| at | -20 °C (± 5 °C) | 14 days (when frozen once) |

Stability of direct bilirubin in reconstituted control serum (stored protected from light):

| | | |
|---|---|---|
| at | 15-25 °C | 8 hours |
| at | 2-8 °C | 24 hours |
| at | -20 °C (± 5 °C) | 10 days (when frozen once) |

Stability of ALT in reconstituted control serum:

| | | |
|---|---|---|
| at | 15-25 °C | 12 hours |
| at | 2-8 °C | 5 days |
| at | -20 °C (± 5 °C) | 14 days (when frozen once) |

The possible appearance of a slight green coloration has no effect on the recovery of the values.

Store control tightly capped and protected from light when not in use.

**Materials provided**

- See “Reagents – working solutions” section
- Barcoded labels

**Materials required (but not provided)**

- Roche system reagents and clinical chemistry analyzers
- General laboratory equipment

**Assay**

Dispense the required volume into a sample cup and analyze in the same way as patient samples.

The controls should be run daily in parallel with patient samples and after every calibration. Control intervals must be adapted to individual laboratory’s requirements.

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

**References**


1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.


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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

**Symbols**

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



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Roche

# PreciControl ClinChem Multi 2

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| | |
|---|---|
| REF 05947774190 | → 4 x 5 mL Control |
| REF 05117216190 | → 20 x 5 mL Control |
| REF 05117291922 | → 20 x 5 mL Control (QCS) |

**English**

**System information**

For use on **cobas c** and COBAS INTEGRA analyzer systems, refer to the corresponding method sheet of the assay for the identification on the systems.

**Intended use**

PreciControl ClinChem Multi 2 is for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

**Summary**

PreciControl ClinChem Multi 2 is a lyophilized control based on human serum. The adjusted concentrations and activities of the control components are usually in the pathological range.

Some methods specified in the relevant value sheet may not be available in all countries.

**Reagents – working solutions**

*Reactive components in the lyophilizate:*

Human serum with chemical additives and material of biological origin as specified.

The origin of the biological additives is as follows:

| *Analyte* | *Origin* |
|---|---|
| ALT (GPT) | human, recombinant |
| AST (GOT) | human, recombinant |
| Aldolase | rabbit muscle |
| Alkaline phosphatase | human placenta (recombinant) |
| Amylase, total | human saliva / porcine pancreas |
| Amylase, pancreatic | porcine pancreas |
| Cholesterol | bovine plasma |
| Creatine kinase | human CK-MM / human CK-MB (recombinant) |
| CK-MB | human CK-MB (recombinant) |
| γ-GT | human, recombinant |
| GLDH | bacterial, recombinant |
| LDH | porcine heart |
| Lipase | human pancreas (recombinant) |
| Acid phosphatase | human prostate / potato |
| ASLO | sheep |
| CRP | human |
| Transferrin | human |
| Ferritin | human |

*Non-reactive components in the lyophilizate:*

Stabilizers

The concentrations and activities of the components are lot-specific. The exact target values are given in the electronically available or enclosed value sheets.

The values are also encoded in the enclosed control barcode sheets for COBAS INTEGRA and **cobas c** 111 analyzers.

For the **cobas c** analyzers (except for the **cobas c** 111 analyzer) the values are encoded in electronic files sent via the **cobas** link to the analyzers.

**Target values and ranges**

The target values were determined using the method stated in the electronically available or enclosed value sheets. Determinations for Roche methods were performed under strictly standardized conditions on Roche analyzers using Roche system reagents and the Roche master calibrator.

The target value specified is the mean of all values obtained. The corresponding control range is calculated as the target value ± 3 standard deviations (the standard deviation being the value obtained from several target value determinations). Results should be within the defined ranges. Each laboratory should establish corrective measures to be taken if values fall outside the range.

A clinically insignificant difference may be seen between the value(s) listed on the value sheet and the value(s) obtained from the instrument readable data. This is caused by:

- the rounding of value(s) during conversion from the unit in the instrument readable data to the unit that is being used.
- the calculation of the ranges by the analyzer using the percentage values for the ranges encoded in the barcodes.

The traceability of the target value is given in the respective Method Sheets for the system reagents to be used in combination with the recommended calibrator.

**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.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

**Handling**

Carefully open one bottle, avoiding the loss of lyophilizate, and pipette in exactly 5.0 mL of distilled/deionized water. Carefully close the bottle and dissolve the contents completely by occasional gentle swirling within 30 minutes. Avoid the formation of foam.

The enclosed barcoded labels are intended exclusively for the **cobas c** systems (except for the **cobas c** 513 analyzer) to identify the control. Attach the barcoded labels to the tubes carrying the sample cups containing the control material.

**Storage and stability**

Store at 2-8 °C.

Criterion for the stability data stated by Roche:

Recovery within ± 10 % of initial value.

Stability of the lyophilized control serum:

Up to the stated expiration date at 2-8 °C.

Stability of components after reconstitution*:

| | | |
|---|---|---|
| at | 15-25 °C | 12 hours |
| at | 2-8 °C | 5 days |
| at | (-15)-(-25) °C | 28 days (when frozen once) |

*Exceptions: see below

Stability of total bilirubin, acid phosphatase, prostatic acid phosphatase and UIBC in reconstituted control serum (stored protected from light):

| | | |
|---|---|---|
| at | 15-25 °C | 8 hours |

# PreciControl ClinChem Multi 2

| | | |
|---|---|---|
| at | 2-8 °C | 24 hours |
| at | (-15)-(-25) °C | 14 days (when frozen once) |

Stability of direct bilirubin in reconstituted control serum (stored protected from light):

| | | |
|---|---|---|
| at | 15-25 °C | 8 hours |
| at | 2-8 °C | 24 hours |
| at | (-15)-(-25) °C | 10 days (when frozen once) |

Stability of ALT in reconstituted control serum:

| | | |
|---|---|---|
| at | 15-25 °C | 12 hours |
| at | 2-8 °C | 5 days |
| at | (-15)-(-25) °C | 14 days (when frozen once) |

The possible appearance of a slight green coloration has no effect on the recovery of the values.

Store control tightly capped and protected from light when not in use.

**Materials provided**

- See “Reagents – working solutions” section
- Barcoded labels

**Materials required (but not provided)**

- Roche system reagents and clinical chemistry analyzers
- General laboratory equipment

**Assay**

Dispense the required volume into a sample cup and analyze in the same way as patient samples.

The controls should be run daily in parallel with patient samples and after every calibration. Control intervals must be adapted to individual laboratory’s requirements.

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

**References**

1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

**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 |

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www.roche.com
+800 5505 6606

# PreciControl HbA1c norm

cobas®

| | | |
|---|---|---|
| REF 05479207190 | 05479207500 | → 4 x 1 mL Control |
| REF 05991323922 | 05479207500 | → 4 x 1 mL Control (QCS) |

## English

### System information

For use on **cobas c** and COBAS INTEGRA analyzer systems, refer to the corresponding method sheet of the assay for the identification on the systems.

For use on the **cobas c** 513 analyzer the control codes can be found in the following table:

| PCA1N | |
|---|---|
| Code | Short name |
| 30001 | PCA1NWS1 |
| 30002 | PCA1NWS2 |
| 30003 | PCA1NHS1 |
| 30004 | PCA1NHS2 |

Different codes have been assigned to distinguish between whole blood (W) and hemolysate (H), and between S1 and S2 sample probe.

For use on the **cobas c** 303 and 503 analyzer the control codes can be found in the following table:

| PCA1N | | |
|---|---|---|
| Code | Short name | Sample type |
| 20002 | PCA1NWS2 | Whole blood |
| 20003 | PCA1NHS1 | Hemolysate |

### Intended use

PreciControl HbA1c norm is for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

### Summary

PreciControl HbA1c norm is a liquid control based on hemolyzed human blood.

The adjusted concentrations of the control components are usually in the normal range or at the normal/pathological threshold.

Some methods specified in the relevant value sheet may not be available in all countries.

### Reagents – working solutions

*Reactive components in the liquid controls:*

Hemolyzed human blood

The concentrations of the components are lot-specific. The exact target values are given in the electronically available or enclosed value sheets.

The values are also encoded in the enclosed control barcode sheets for COBAS INTEGRA and **cobas c** 111 analyzers.

For the **cobas c** analyzers (except for the **cobas c** 111 analyzer) the values are encoded in electronic files sent via the **cobas** link to the analyzers.

### Target values and ranges

The target values were determined using the method stated in the electronically available or enclosed value sheets. Determinations for Roche methods were performed under strictly standardized conditions on Roche analyzers using Roche system reagents and the Roche master calibrator. The target value specified is the mean of all values obtained. The corresponding control range is calculated as the target value ± 3 standard deviations (the standard deviation being the value obtained from several target value determinations). Results should be within the defined ranges. Each laboratory should establish corrective measures to be taken if values fall outside the range.

A clinically insignificant difference may be seen between the value(s) listed on the value sheet and the value(s) obtained from the instrument readable data. This is caused by:

- the rounding of value(s) during conversion from the unit in the instrument readable data to the unit that is being used.
- the calculation of the ranges by the analyzer using the percentage values for the ranges encoded in the barcodes.

The traceability of the target value is given in the respective Method Sheets for the system reagents to be used in combination with the recommended calibrator.

### Precautions and warnings

For in vitro diagnostic use for laboratory 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.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A). However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

### Handling

The product is ready-for-use. Mix carefully before use. Avoid the formation of foam.

Equilibrate the control to room temperature before use.

The enclosed barcoded labels are intended exclusively for the **cobas c** systems (except for the **cobas c** 513 analyzer) to identify the control. Attach the barcoded labels to the tubes carrying the sample cups containing the control material.

### Storage and stability

Store at 2-8 °C.

Criterion for the stability data stated by Roche:

Recovery within ± 10 % of initial value.

Stability:

| | |
|---|---|
| Unopened: | Up to the stated expiration date at 2-8 °C. |
| After opening: | 28 days at 2-8 °C or 12 weeks at (–15)-(–25) °C, provided that dispensing of the control occurs without microbial contamination, e.g. by pouring out. Freeze only once. |

Store control tightly capped when not in use.

### Materials provided

- See “Reagents – working solutions” section
- Barcoded labels

### Materials required (but not provided)

- Roche system reagents and clinical chemistry analyzers
- General laboratory equipment

### Assay

Dispense the required volume into a sample cup and analyze in the same way as patient samples.

The controls should be run daily in parallel with patient samples and after every calibration. Control intervals must be adapted to individual laboratory’s requirements.

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

# PreciControl HbA1c norm

cobas®

**References**

1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

**Symbols**

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



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Roche

05854237001V6.0

# PreciControl HbA1c path

cobas®

REF **05912504** 190 — 4 x 1 mL Control

REF **05991331** 922 — 4 x 1 mL Control (QCS)

**English**

**System information**

For use on Roche/Hitachi **cobas c** analyzers the control code is 209.

For use on COBAS INTEGRA analyzers the system ID is 07 7478 2.

For use on the Roche/Hitachi **cobas c** 513 analyzer the control codes can be found in the following table:

| PCA1P | |
|---|---|
| Code | Short name |
| 30011 | PCA1PWS1 |
| 30012 | PCA1PWS2 |
| 30013 | PCA1PHS1 |
| 30014 | PCA1PHS2 |

Different codes have been assigned to distinguish between whole blood (W) and hemolysate (H), and between S1 and S2 sample probe.

**Intended use**

PreciControl HbA1c path is for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

**Summary**

PreciControl HbA1c path is a liquid control based on hemolyzed human blood.

The adjusted concentrations of the control components are usually in the pathological range.

Some methods specified in the relevant value sheet may not be available in all countries.

**Reagents – working solutions**

*Reactive components in the liquid controls:*

Hemolyzed human blood, in vitro glycated HbA1c

The concentrations of the components are lot-specific. The exact target values are given in the electronically available or enclosed value sheets.

The values are also encoded in the enclosed control barcode sheets for COBAS INTEGRA and **cobas c** 111 analyzers.

For the **cobas c** analyzers (except for the **cobas c** 111 analyzer) the values are encoded in electronic files sent via the **cobas** link to the analyzers.

**Target values and ranges**

The target values were determined using the method stated in the electronically available or enclosed value sheets. Determinations for Roche methods were performed under strictly standardized conditions on Roche analyzers using Roche system reagents and the Roche master calibrator. The target value specified is the mean of all values obtained. The corresponding control range is calculated as the target value ± 3 standard deviations (the standard deviation being the value obtained from several target value determinations). Results should be within the defined ranges. Each laboratory should establish corrective measures to be taken if values fall outside the range.

A clinically insignificant difference may be seen between the value(s) listed on the value sheet and the value(s) obtained from the instrument readable data. This is caused by:

- the rounding of value(s) during conversion from the unit in the instrument readable data to the unit that is being used.
- the calculation of the ranges by the analyzer using the percentage values for the ranges encoded in the barcodes.

The traceability of the target value is given in the respective Method Sheets for the system reagents to be used in combination with the recommended calibrator.

**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.

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

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

**Handling**

The product is ready-for-use. Mix carefully before use. Avoid the formation of foam.

Equilibrate the control to room temperature before use.

The enclosed barcoded labels are intended exclusively for the **cobas c** systems (except for the **cobas c** 513 analyzer) to identify the control. Attach the barcoded labels to the tubes carrying the sample cups containing the control material.

**Storage and stability**

Store at 2-8 °C.

Criterion for the stability data stated by Roche:

Recovery within ± 10 % of initial value.

Stability:

| | |
|---|---|
| Unopened: | Up to the stated expiration date at 2-8 °C. |
| After opening: | 28 days at 2-8 °C or 12 weeks at (–15)-(–25) °C, provided that dispensing of the control occurs without microbial contamination, e.g. by pouring out. Freeze only once. |

Store control tightly capped when not in use.

**Materials provided**

- See “Reagents – working solutions” section
- Barcoded labels

**Materials required (but not provided)**

- Roche system reagents and clinical chemistry analyzers
- General laboratory equipment

**Assay**

Dispense the required volume into a sample cup and analyze in the same way as patient samples.

The controls should be run daily in parallel with patient samples and after every calibration. Control intervals must be adapted to individual laboratory’s requirements.

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

**References**

1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

# PreciControl HbA1c path

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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

**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 |

**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.



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Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

# Preciset RF

cobas®

REF **12172828** 322 5 x 1 mL Calibrator

**English**

**System information**

For use on Roche/Hitachi MODULAR analyzers and **cobas c** analyzers the calibrator codes are 725–729.

For use on COBAS INTEGRA analyzers the system ID is 07 7995 4.

**Intended use**

Preciset RF is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.

**Summary**

Preciset RF consists of 5 liquid ready-for-use calibrators based on a bovine serum albumin matrix.

The concentrations of the calibrator components have been adjusted to ensure optimal calibration of the appropriate Roche methods on clinical chemistry analyzers.

Some methods specified in the relevant value sheet may not be available in all countries.

**Reagents – working solutions**

*Reactive components:*

RF in human serum

*Non-reactive components:*

HEPES buffer, bovine serum albumin, sodium chloride, preservative

The concentrations of the components are lot-specific. The exact calibrator values are given in the electronically available or enclosed value sheets.

The values are also encoded in the enclosed calibrator barcode sheets for Roche/Hitachi MODULAR and COBAS INTEGRA analyzers.

For the **cobas c** analyzers (except for the **cobas c** 111 analyzer) the values are encoded in electronic files sent via the **cobas** link to the analyzers.

**Calibrator values**

The calibrator values were determined using the method stated in the electronically available or enclosed value sheets. Determinations were performed under strictly standardized conditions on Roche analyzers using Roche system reagents and the Roche master calibrator.

The calibrator values were obtained via single determinations performed in different laboratories, in several separate runs. The calibrator value specified is the median of all values obtained.

Traceability information is given in the relevant Method Sheets for the system reagents.

**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.

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

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

**Handling**

The product is ready-for-use. Mix carefully before use. Avoid the formation of foam.

The enclosed barcoded labels are intended exclusively for Roche/Hitachi MODULAR automated analyzers and **cobas c** systems to identify the calibrator. Attach the barcoded labels to the tubes carrying the sample cups containing the calibrator material.

**Storage and stability**

Store at 2-8 °C.

Criterion for the stability data stated by Roche:

Recovery within ± 10 % of initial value.

Stability:

| | |
|---|---|
| Unopened: | Up to the stated expiration date at 2-8 °C. |
| After opening: | 24 hours at 15-25 °C or 30 days at 2-8 °C, provided that dispensing of the calibrator occurs without microbial contamination, e.g. by pouring out. |

Do not freeze.

Store calibrators tightly capped when not in use.

**Materials provided**

- See “Reagents – working solutions” section
- Barcoded labels

**Materials required (but not provided)**

- Roche system reagents and clinical chemistry analyzers
- General laboratory equipment

**Assay**

Use Preciset RF as specified in the relevant Method Sheet for the system reagents.

**References**


1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.


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 |
| CALIBRATOR | Calibrator |
| → | Volume after reconstitution or mixing |
| GTIN | Global Trade Item Number |

**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.

12172895001V10.0

# Preciset RF

cobas®

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



CE 0123

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Roche

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

03149501001V1.0

# REF Electrode

cobas®

**ISE Reference Electrode**

**Order information**

| REF | CONTENT | Analyzer(s) on which the electrode can be used |
|---|---|---|
| 03149501001 | REF Electrode 1 (electrode) | **cobas c** 311 analyzer<br>**cobas** 6000 analyzer series: **cobas c** 501 module<br>**cobas** 8000 modular analyzer series: **cobas** 8000 ISE 900 / 1800 module<br>**cobas pure** integrated solutions: **cobas c** 303 analytical unit<br>**cobas pro** integrated solutions: **cobas** pro ISE analytical unit, **cobas** ISE neo 900 analytical unit, **cobas** ISE neo 1800 analytical unit |

**English**

**Intended use**

The REF Electrode is intended for closing the measurement circuit for the quantitative determination of sodium, potassium, and chloride in human origin serum, plama or urine.

**Precautions and warnings**

For in vitro diagnostic use for trained laboratory technicians.

**Warning**

- Samples containing material of human origin are potentially infectious. Wear personal protective equipment when replacing or installing electrodes at analyzers. If any biohazardous material is spilled, wipe it up immediately and apply a disinfectant.
- If sample or waste contacts with your skin, wash the affected area immediately with soap and water, then apply a disinfectant. Consult a physician.
- When disposing of used electrodes, treat them as biohazardous.

**Caution**

- Do not use electrodes after the shelf life or on-board stability period has expired. Otherwise, it may lead to unstable sodium, potassium, and chloride results due to the unstable potential reading of electrodes.

**NOTE:** Boric acid (CAS Registry No. 10043-35-3) is contained in the gel solution inside the electrode at 0.2 % of the total weight as a preservative.

**Storage and stability**

Store electrodes at 7-40 °C.

See labels for expiration dates.

**On-board stability**

After installation, the electrode is stable for the following time period:
6 months

The electrodes should be replaced after this time period has expired. For replacement refer to instructions in the operator's manual of the applicable analyzers.

**NOTE:** When replacing the electrode in **cobas pro** or **cobas pure**, the user should scan the barcode affixed on the rear side of the package instead of the barcode placed on the product's label.

**Materials provided**

See "Order information" section

**Materials required (but not provided)**

See "Order information" section

General laboratory equipment

**References**

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

| | |
|---|---|
| Cont. | Quantity contained in the package |
| CONTENT | Quantity contained in the package |
| GTIN | Global Trade Item Number |
| INSTALL BEFORE | Latest date by which the electrode has to be installed on the analyzer |
| RoHS | Directive for the restriction of the use of certain hazardous substances in electrical and electronic equipment |

**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.



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Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

# RF Control Set

cobas®

REF 03005496122 | 03005496500 | 2 x 1 mL Control Level I
2 x 1 mL Control Level II

## English

### System information

For use on **cobas c** and COBAS INTEGRA analyzer systems, refer to the corresponding method sheet of the assay for the identification on the systems.

### Intended use

RF Control Set is for use in quality control by monitoring accuracy and precision for the quantitative method as specified in the value sheets.

### Summary

RF Control Set consists of 2 liquid ready-for-use controls based on a diluted human serum.

The adjusted concentrations of the control components are in the low concentration range for Level I and in the high concentration range for Level II.

Some methods specified in the relevant value sheet may not be available in all countries.

### Reagents – working solutions

*Reactive components:*

Human serum with chemical additives and material of biological origin as specified. The origin of the biological additive is as follows:

| Analyte | Origin |
|---|---|
| RF | human |

*Non-reactive components:*

HEPES buffer, bovine serum albumin, sodium chloride, preservative

The concentrations of the controls are lot-specific. The exact target values are given in the electronically available or enclosed value sheets.

The values are also encoded in the enclosed control barcode sheets for COBAS INTEGRA analyzers.

For the **cobas c** analyzers (except for the **cobas c** 111 analyzer) the values are encoded in electronic files sent via the **cobas** link to the analyzers.

### Target values and ranges

The target values were determined using the method stated in electronically available or enclosed value sheets. Determinations for Roche methods were performed under strictly standardized conditions on Roche analyzers using Roche system reagents and the Roche master calibrator. The target value specified is the mean of all values obtained. The corresponding control range is calculated as the target value ± 20 % for the Level I and ± 15 % for the Level II control. Results should be within the defined ranges. Each laboratory should establish corrective measures to be taken if values fall outside the range.

A clinically insignificant difference may be seen between the value(s) listed on the value sheet and the value(s) obtained from the instrument readable data. This is caused by:

- the rounding of value(s) during conversion from the unit in the instrument readable data to the unit that is being used.
- the calculation of the ranges by the analyzer using the percentage values for the ranges encoded in the barcodes.

The traceability of the target value is given in the respective Method Sheets for the system reagents to be used in combination with the recommended calibrator.

### Precautions and warnings

For in vitro diagnostic use for laboratory 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.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A). However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[1,2]

### Handling

The product is ready-for-use. Mix carefully before use. Avoid the formation of foam.

The enclosed barcoded labels are intended exclusively for the **cobas c** systems to identify the control. Attach the barcoded labels to the tubes carrying the sample cups containing the control material.

### Storage and stability

Store at 2-8 °C.

Criterion for the stability data stated by Roche:
Recovery within ± 10 % of initial value.

Stability:

| | |
|---|---|
| Unopened: | up to the stated expiration date at 2-8 °C |
| After opening: | 24 hours at 15-25 °C or 30 days at 2-8 °C, provided that dispensing of the control occurs without microbial contamination, e.g. by pouring out. |

Store controls tightly capped when not in use.

### Materials provided

- See “Reagents – working solutions” section
- Barcoded labels

### Materials required (but not provided)

- Roche system reagents and clinical chemistry analyzers
- General laboratory equipment

### Assay

Dispense the required volume into a sample cup and analyze in the same way as patient samples.

The controls should be run daily in parallel with patient samples and after every calibration. Control intervals must be adapted to individual laboratory’s requirements.

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

### References


1 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

2 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.


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:

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

# RF Control Set

| | |
|---|---|
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |
| BTL LOT | Bottle lot |



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# RF-II

cobas®

**Rheumatoid Factors II**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08058628190* | 08058628500 | Rheumatoid Factors II (400 tests) | System-ID 2104 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08058628214* | 08058628500 | Rheumatoid Factors II (400 tests) | System-ID 2104 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 12172828322 | Preciset RF (5 x 1 mL) | Codes 20725-20729 | |
| 03005496122 | RF Control Set<br>Level I (2 x 1 mL)<br>Level II (2 x 1 mL) | <br>Code 20215<br>Code 20216 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

## English

### System information

**RF-II:** ACN 21040

### Intended use

In vitro test for the quantitative determination of Rheumatoid Factors (RF-II) in human serum and plasma on **cobas c** systems. Measurements may be used as an aid in the diagnosis of rheumatoid arthritis.

### Summary

Measurements of rheumatoid factors with this assay in human serum and plasma may be used as an aid in the diagnosis of rheumatoid arthritis.

Rheumatoid factors are a heterogeneous group of autoantibodies directed against the antigenic determinants on the Fc-region of IgG molecules.[1] They are important in the diagnosis of rheumatoid arthritis, but can also be found in other inflammatory rheumatic diseases and in various non-rheumatic diseases. They are also found in clinically healthy persons, however with low or moderate levels. Despite these restrictions, the detection of rheumatoid factors is a diagnostic criterion in several clinical guidelines for classifying rheumatoid arthritis.[1,2,3,4,5]

The autoantibodies occur in all the immunoglobulin classes, although the usual analytical methods are limited to the detection of rheumatoid factors of the IgM type. The classic procedure for the quantitation of rheumatoid factors is by agglutination with IgG-sensitized sheep erythrocytes or latex particles. Particular problems of these semiquantitative methods are the poor between-laboratory precision and reproducibility, together with standardization difficulties. For these reasons, new assay methods such as nephelometry, turbidimetry, enzyme-immunoassays and radioimmunoassays have been developed.[6,7,8] This assay is based on the immunological agglutination principle with enhancement of the reaction by latex.

### Test principle[1,9,10]

Immunoturbidimetric assay

Latex-bound heat-inactivated IgG (antigen) reacts with the RF-antibodies in the sample to form antigen/antibody complexes which, following agglutination, are measured turbidimetrically.

### Reagents - working solutions

**R1** Glycine buffer: 170 mmol/L, pH 8.0; polyethylene glycol: 0.05 %; bovine serum albumin; stabilizer; preservative

**R3** Latex particles coated with human IgG; glycine buffer: 170 mmol/L, pH 7.3; stabilizer; preservative

R1 is in position B and R3 is in position C.

### Precautions and warnings

For in vitro diagnostic use for laboratory 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.

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

Warning

H317 May cause an allergic skin reaction.

**Prevention:**

P261 Avoid breathing mist or vapours.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

**Response:**

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

**Disposal:**

P501 Dispose of contents/container to an approved waste disposal plant.

**Hazardous components:**

- 2-methyl-2H-isothiazol-3-one hydrochloride

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A). However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[11,12]

### Reagent handling

Ready for use

# RF-II

**Rheumatoid Factors II**

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 8 weeks |

**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
Plasma: Li-heparin and $K_2$-EDTA plasma

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.

| | |
|---|---|
| Stability:[13] | 1 day at 20-25 °C |
| | 8 days at 4-8 °C |
| | 3 months at -20 °C (±5 °C) |

Freeze only once.

**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.

**Application for serum and plasma**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 800/570 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 63 µL | – |
| R3 | 21 µL | – |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 2.1 µL | – | – |
| Decreased | 2.1 µL | 20 µL | 80 µL |
| Increased | 2.1 µL | – | – |

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

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2-6: Preciset RF |
| Calibration mode | Non-linear |
| Calibration frequency | Full calibration<br>- every 180 days during shelf life<br>- after reagent lot change<br>- as required following quality control procedures |

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

Traceability:[14] This method has been standardized using the WHO Standard 64/2.

**Quality control**

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

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 8 weeks. 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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit IU/mL.

**Limitations - interference**

Criterion: Recovery within ± 1.4 IU/mL of initial values of samples ≤ 14 IU/mL and within ± 10 % for samples > 14 IU/mL.

Icterus:[15] No significant interference up to an I index of 40 for conjugated and 60 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 624 µmol/L or 40 mg/dL and approximate unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[15] No significant interference up to an H index of 300 (approximate hemoglobin concentration: 186 µmol/L or 300 mg/dL).

Lipemia (Intralipid):[15] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[16,17]

High-dose hook effect: Using the prozone check automatically performed by the analyzer, no false result without a flag was observed up to an RF concentration of 6000 IU/mL.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[18]

There is the possibility that other substances and/or factors may interfere with the test and cause unreliable results.

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**

10-130 IU/mL

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from

samples diluted using the rerun function are automatically multiplied by a factor of 5.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

Limit of Blank = 10 IU/mL

Limit of Detection = 10 IU/mL

Limit of Quantitation = 10 IU/mL

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 95$^{th}$ 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 20 %. It has been determined using low concentration RF samples.

**Expected values**

< 14 IU/mL

This value is based on serum samples from 541 test subjects.

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

| *Repeatability* | *Mean* *IU/mL* | *SD* *IU/mL* | *CV* *%* |
|---|---|---|---|
| RF Control Level 1 | 21.8 | 0.509 | 2.3 |
| RF Control Level 2 | 51.3 | 0.329 | 0.6 |
| Human serum 1 | 15.0 | 0.704 | 4.7 |
| Human serum 2 | 30.2 | 0.295 | 1.0 |
| Human serum 3 | 37.9 | 0.250 | 0.7 |
| Human serum 4 | 63.0 | 0.286 | 0.5 |
| Human serum 5 | 109 | 0.707 | 0.6 |

| *Intermediate precision* | *Mean* *IU/mL* | *SD* *IU/mL* | *CV* *%* |
|---|---|---|---|
| RF Control Level 1 | 21.8 | 0.550 | 2.5 |
| RF Control Level 2 | 51.3 | 0.408 | 0.8 |
| Human serum 1 | 15.0 | 0.704 | 4.7 |
| Human serum 2 | 30.2 | 0.396 | 1.3 |
| Human serum 3 | 39.5 | 0.365 | 0.9 |
| Human serum 4 | 61.7 | 0.359 | 0.6 |
| Human serum 5 | 109 | 0.773 | 0.7 |

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

RF values for human serum and plasma samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 68

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 1.004x + 0.00648 IU/mL | y = 0.986x + 0.494 IU/mL |
| τ = 0.949 | r = 0.996 |

The sample concentrations were between 12.6 and 121 IU/mL.

RF values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 65

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 1.037x - 1.61 IU/mL | y = 1.016x - 0.990 IU/mL |
| τ = 0.942 | r = 0.995 |

The sample concentrations were between 11.8 and 125 IU/mL.

RF values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 66

| Passing/Bablok[19] | Linear regression |
|---|---|
| y = 1.026x - 1.70 IU/mL | y = 1.027x - 1.70 IU/mL |
| τ = 0.971 | r = 0.999 |

The sample concentrations were between 11.4 and 130 IU/mL.

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.

**References**

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**Symbols**

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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68305 Mannheim, Germany
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10394246001V10.0

# Sample Cup

cobas®

| REF | CONTENT | SYSTEM |
|---|---|---|
| | | COBAS INTEGRA® 400 plus analyzer |
| | | MODULAR *PRE-ANALYTICS* **EVO** |
| | | **cobas c** 111 analyzer |
| | | **cobas c** 303 analytical unit |
| | | **cobas c** 311 analyzer |
| | | **cobas e** 402 analytical unit |
| | | **cobas e** 411 analyzer |
| | | **cobas c** 501 module |
| | | **cobas c** 502 module |
| | | **cobas c** 503 analytical unit |
| 10394246001 | 5000 (20 x 250) | **cobas e** 601 module |
| | | **cobas e** 602 module |
| | | **cobas c** 701 module |
| | | **cobas c** 702 module |
| | | **cobas c** 703 analytical unit |
| | | **cobas e** 801 module |
| | | **cobas e** 801 analytical unit |
| | | **cobas** 8000 ISE 900 module |
| | | **cobas** 8000 ISE 1800 module |
| | | **cobas** ISE neo analytical unit |
| | | **cobas pro** ISE analytical unit |

**English**

**Intended use**

The Sample Cup is an IVD accessory intended to be used with the following systems:

- COBAS INTEGRA® 400 plus analyzer
- MODULAR *PRE-ANALYTICS* **EVO**
- **cobas c** 111 analyzer
- **cobas c** 303 analytical unit
- **cobas c** 311 analyzer
- **cobas e** 402 analytical unit
- **cobas e** 411 analyzer
- **cobas c** 501 module
- **cobas c** 502 module
- **cobas c** 503 analytical unit
- **cobas e** 601 module
- **cobas e** 602 module
- **cobas c** 701 module
- **cobas c** 702 module
- **cobas c** 703 analytical unit
- **cobas e** 801 module
- **cobas e** 801 analytical unit
- **cobas** 8000 ISE 900 module
- **cobas** 8000 ISE 1800 module
- **cobas** ISE neo analytical unit
- **cobas pro** ISE analytical unit

For professional use only.

**Combination of devices**

The Sample Cup is meant to be used only in combination with the following devices:

- COBAS INTEGRA® 400 plus analyzer
- MODULAR *PRE-ANALYTICS* **EVO**
- **cobas c** 111 analyzer
- **cobas c** 303 analytical unit
- **cobas c** 311 analyzer
- **cobas e** 402 analytical unit
- **cobas e** 411 analyzer
- **cobas c** 501 module
- **cobas c** 502 module
- **cobas c** 503 analytical unit
- **cobas e** 601 module
- **cobas e** 602 module
- **cobas c** 701 module
- **cobas c** 702 module
- **cobas c** 703 analytical unit
- **cobas e** 801 module
- **cobas e** 801 analytical unit
- **cobas** 8000 ISE 900 module
- **cobas** 8000 ISE 1800 module
- **cobas** ISE neo analytical unit
- **cobas pro** ISE analytical unit

**Summary**

A small container used for sample, calibrator and control material. Depending on the system, the Sample Cup will be loaded directly onto a rack or sample disk or in a primary sample container. The Sample Cup can be used on all systems listed.

Please check the respective Operators Manual for specific dead volume specifications.

# Sample Cup

cobas®

**Precautions and warnings**

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all biological samples. Do not re-use the product.

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.

**Storage and Stability**

Do not expose the Sample Cup to UV-light. Store the Sample Cup in the box. Store at 2 - 32 °C.

For further information, please refer to the appropriate Operators Manual for the analyzer concerned, and the Method Sheets of all necessary components.

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):

| | |
|---|---|
| SYSTEM | Analyzers/Instruments on which reagents can be used |
| CONTENT | Content of kit |
| GTIN | Global Trade Item Number |
| 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.



CE

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Roche

Distributed in USA by:
Roche Diagnostics, 9115 Hague Road
Indianapolis, Indiana USA
US Customer Technical Support 1-800-428-2336

# TP2

cobas®

**Total Protein Gen.2**

Order information

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack (s) can be used |
|---|---|---|---|---|
| 08058652190* | 08058652500 | Total Protein Gen.2 (1050 tests) | System-ID 2111 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08058652214* | 08058652500 | Total Protein Gen.2 (1050 tests) | System-ID 2111 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 10557897122 | Precinorm Protein (3 x 1 mL) | Code 20302 | |
| 11333127122 | Precipath Protein (3 x 1 mL) | Code 20303 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

## English

### System information

**TP2:** ACN 21110

### Intended use

In vitro test for the quantitative determination of total protein in human serum and plasma on **cobas c** systems.

### Summary

Measurements of total protein, performed with this assay in human serum or plasma, are used as aid in diagnosis and monitoring of a variety of diseases involving the liver, kidney, or bone marrow, as well as other metabolic or nutritional disorders.[1,2,3,4]

Plasma proteins are synthesized predominantly in the liver, plasma cells, lymph nodes, the spleen and bone marrow. In the course of disease the total protein concentration and also the percentage represented by individual fractions can significantly deviate from normal values. Hypoproteinemia can be caused by diseases and disorders such as loss of blood, sprue, nephrotic syndrome, severe burns, salt retention syndrome and Kwashiorkor (acute protein deficiency).

Hyperproteinemia can be observed in cases of severe dehydration and illnesses such as multiple myeloma. Changes in the relative percentage of plasma proteins can be due to a change in the percentage of 1 plasma protein fraction. Often in such cases the amount of total protein does not change. The albumin/globulin (A/G) ratio is commonly used as an index of the distribution of albumin and globulin fractions. Marked changes in this ratio can be observed in cirrhosis of the liver, glomerulonephritis, nephrotic syndrome, acute hepatitis, lupus erythematosus as well as in certain acute and chronic inflammations.[1,2,3,4]

### Test principle[5]

Colorimetric assay

Divalent copper reacts in alkaline solution with protein peptide bonds to form the characteristic purple-colored biuret complex. Sodium potassium tartrate prevents the precipitation of copper hydroxide and potassium iodide prevents autoreduction of copper.

$$\text{protein} + Cu^{2+} \xrightarrow{\text{alkaline solution}} \text{Cu-protein complex}$$

The color intensity is directly proportional to the protein concentration which can be determined photometrically.

### Reagents - working solutions

**R1** Sodium hydroxide: 400 mmol/L; potassium sodium tartrate: 89 mmol/L

**R3** Sodium hydroxide: 400 mmol/L; potassium sodium tartrate: 89 mmol/L; potassium iodide: 61 mmol/L; copper sulfate: 24.3 mmol/L

R1 is in position B and R3 is in position C.

### 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.

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

Warning

| | |
|---|---|
| H290 | May be corrosive to metals. |
| H315 | Causes skin irritation. |
| H319 | Causes serious eye irritation. |
| H412 | Harmful to aquatic life with long lasting effects. |

**Prevention:**

| | |
|---|---|
| P264 | Wash skin thoroughly after handling. |
| P273 | Avoid release to the environment. |
| P280 | Wear protective gloves/ eye protection/ face protection. |

**Response:**

| | |
|---|---|
| P337 + P313 | If eye irritation persists: Get medical advice/attention. |
| P390 | Absorb spillage to prevent material damage. |

**Disposal:**

| | |
|---|---|
| P501 | Dispose of contents/container to an approved waste disposal plant. |

Product safety labeling follows EU GHS guidance.

# TP2

**Total Protein Gen.2**

Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 15-25 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |

**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.

Plasma: Li-heparin and $K_2$-EDTA plasma

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.

| | |
|---|---|
| *Stability:*[6] | 6 days at 20-25 °C |
| | 4 weeks at 4-8 °C |
| | 1 year at -20 °C (± 5 °C) |

Freeze only once.

The total protein concentration is 4 to 8 g/L lower when the sample is collected from a patient situated in the recumbent position rather than upright.[7]

**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.

**Application for serum and plasma**

**Test definition**

| | | | |
|---|---|---|---|
| Reporting time | 10 min | | |
| Wavelength (sub/main) | 700/546 nm | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 59 µL | 18 µL | |
| R3 | 21 µL | – | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 1.3 µL | – | – |
| Decreased | 1.3 µL | 25 µL | 50 µL |
| Increased | 1.3 µL | – | – |

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

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. |
| Calibration mode | Linear |
| Calibration frequency | Automatic full calibration<br>- after reagent lot change |
| | Full calibration<br>- as required following quality control procedures |

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

Traceability: This method has been standardized against SRM 927.

**Quality control**

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

The control intervals and limits should be adapted to each laboratory’s individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit g/L (g/dL).

| | |
|---|---|
| Conversion factor: | g/L x 0.1 = g/dL |

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial value at a total protein concentration of 66 g/L (6.6 g/dL).

Icterus[8]: No significant interference up to an I index of 20 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 342 µmol/L or 20 mg/dL).

Hemolysis[8]: No significant interference up to an H index of 500 (approximate hemoglobin concentration: 311 µmol/L or 500 mg/dL).

Lipemia (Intralipid)[8]: No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Dextran: No significant interference from dextran up to a concentration of 30 mg/mL.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[9,10]

In very rare cases, gammopathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.[11]

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**

2.0-120 g/L (0.2-12 g/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from

samples diluted using the rerun function are automatically multiplied by a factor of 3.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

| | |
|---|---|
| Limit of Blank | = 2.0 g/L (0.2 g/dL) |
| Limit of Detection | = 2.0 g/L (0.2 g/dL) |
| Limit of Quantitation | = 3.0 g/L (0.3 g/dL) |

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 95$^{th}$ 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 20 %. It has been determined using low concentration total protein samples.

**Expected values**

**g/L**

*Expected values according to Josephson* [12]

| | |
|---|---|
| Adults | 66-87 g/L* |

* calculated by unit conversion factor

*Expected values according to Tietz*[13]

| | |
|---|---|
| Umbilical cord | 48-80 g/L |
| Premature | 36-60 g/L |
| Newborn | 46-70 g/L |
| 1 week | 44-76 g/L |
| 7 months-1 year | 51-73 g/L |
| 1-2 years | 56-75 g/L |
| > 3 years | 60-80 g/L |
| Adults (ambulatory) | 64-83 g/L |

*Expected values according to Australasian Association of Clinical Biochemists*[14]

| | |
|---|---|
| Adults | 60-80 g/L |

**g/dL**

*Expected values according to Josephson* [12]

| | |
|---|---|
| Adults | 6.6-8.7 g/dL |

*Expected values according to Tietz*[13]

| | |
|---|---|
| Umbilical cord | 4.8-8.0 g/dL |
| Premature | 3.6-6.0 g/dL |
| Newborn | 4.6-7.0 g/dL |
| 1 week | 4.4-7.6 g/dL |
| 7 months-1 year | 5.1-7.3 g/dL |
| 1-2 years | 5.6-7.5 g/dL |
| > 3 years | 6.0-8.0 g/dL |
| Adults (ambulatory) | 6.4-8.3 g/dL |

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *g/L* | *g/L* | *%* |
| PCCC1[a)] | 49.5 | 0.244 | 0.5 |
| PCCC2[b)] | 73.0 | 0.358 | 0.5 |
| Human serum 1 | 4.61 | 0.140 | 3.0 |
| Human serum 2 | 32.1 | 0.224 | 0.7 |
| Human serum 3 | 61.4 | 0.292 | 0.5 |
| Human serum 4 | 72.9 | 0.394 | 0.5 |
| Human serum 5 | 103 | 0.588 | 0.6 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *g/L* | *g/L* | *%* |
| PCCC1[a)] | 49.7 | 0.396 | 0.8 |
| PCCC2[b)] | 73.0 | 0.495 | 0.7 |
| Human serum 1 | 4.83 | 0.196 | 4.1 |
| Human serum 2 | 32.4 | 0.326 | 1.0 |
| Human serum 3 | 61.4 | 0.396 | 0.6 |
| Human serum 4 | 72.9 | 0.453 | 0.6 |
| Human serum 5 | 103 | 0.686 | 0.7 |

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Total protein values for human serum samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 74

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 1.010x - 0.0180 g/L | y = 1.010x - 0.0639 g/L |
| τ = 0.975 | r = 0.999 |

The sample concentrations were between 8.43 and 116 g/L.

Total protein values for human serum samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 74

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 1.012x - 0.536 g/L | y = 1.015x - 0.785 g/L |
| τ = 0.979 | r = 1.000 |

The sample concentrations were between 7.50 and 117 g/L.

Total Protein values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

# TP2

**Total Protein Gen.2**

Sample size (n) = 69

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 1.008x - 1.25 g/L | y = 1.017x - 1.86 g/L |
| τ = 0.987 | r = 0.999 |

The sample concentrations were between 7.66 and 115 g/L.

**References**


1 Brobeck JR, ed. Physiological Basis of Medical Practice, 9th ed. Baltimore, MD: Wilkins and Wilkins 1973;4-7.

2 Thomas L. Clinical Laboratory Diagnostics (Labor und Diagnose). [Internet] Frankfurt/Main, TH-Books Verlagsgesellschaft mbH;2016. Available from: https://www.clinical-laboratory-diagnostics.com/

3 Burtis CA, Ashwood ER, Bruns DE. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 5th ed. 2012.

4 Pagana KD, Pagana TJ. Mosby's manual of diagnostic and laboratory tests. 5th ed. St. Louis, Elsevier; 2014.

5 Weichselbaum TE. An accurate and rapid method for the determination of proteins in small amounts of blood serum and plasma. Am J Clin Pathol 1946;10:40-49.

6 WHO Publication: Use of anticoagulants in diagnostic laboratory investigations, WHO/DIL/LAB/99.1 Rev.2:Jan 2002.

7 Koller A. Total serum protein. In: Kaplan LA, Pesce AJ, eds. Clinical Chemistry, theory, analysis, and correlation St. Louis: Mosby Company 1984;1316-1319.

8 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

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

10 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.

11 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

12 Josephson B, Gyllenswärd C. The Development of the Protein Fractions and of Cholesterol Concentration in the Serum of Normal Infants and Children. Scandinav J Clin Lab Investigation 1957;9:29.

13 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;518-523.

14 Tate JR, Sikaris KA, Jones GRD, et al. Harmonising adult and paediatric reference intervals in Australia and New Zealand: An evidence-based approach for establishing a first panel of chemistry analytes. Clin Biochem Rev 2014; Nov 35(4):213-35.

15 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.


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

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

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



CE 0123


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# TRIGL

cobas®

**Triglycerides**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08058687190* | 08058687500 | Triglycerides (1000 tests) | System-ID 2113 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08058687214* | 08058687500 | Triglycerides (1000 tests) | System-ID 2113 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

**English**

**System information**

**TRIGL:** ACN 21130

**Intended use**

In vitro test for the quantitative determination of triglycerides in human serum and plasma on **cobas c** systems.

**Summary**

Triglyceride measurements, performed with this assay in human serum and plasma are used as an aid in identifying patients at risk of developing atherosclerosis and for the diagnosis of dyslipidemias.

Triglycerides are esters of the trihydric alcohol glycerol with 3 long-chain fatty acids.[1] They are partly synthesized in the liver and partly ingested in food. Triglycerides are water-insoluble molecules and are carried in the circulation in water-soluble complexes called lipoproteins. The plasma triglyceride level reflects the concentration of the triglyceride-carrying lipoproteins VLDL (very-low-density lipoproteins) and chylomicrons.[2] Chylomicrons are primarily involved in the absorption and delivery of dietary fat while VLDLs deliver endogenous lipids to other tissues.

Triglycerides are considered a risk factor for atherosclerotic cardiovascular disease.[3] Cardiovascular risk is increased when fasting triglycerides are > 1.7 mmol/L (> 150 mg/dL). Individuals with triglycerides > 2.3 mmol/L (> 200 mg/dL) are considered at high risk. The determination of triglycerides is utilized in the diagnosis of patients having diabetes mellitus, nephrosis, liver obstruction, lipid metabolism disorders and numerous other endocrine diseases.[4]

Elevated levels of plasma triglycerides are also associated with an increased risk of acute pancreatitis and aortic valve stenosis.[5]

The enzymatic triglycerides assay as described by Eggstein and Kreutz still required saponification with potassium hydroxide. Numerous attempts were subsequently made to replace alkaline saponification by enzymatic hydrolysis with lipase.[6] Bucolo and David tested a lipase/protease mixture; Wahlefeld used an esterase from the liver in combination with a particularly effective lipase from Rhizopus arrhizus for hydrolysis.[7, 8]

This method is based on the work by Wahlefeld using a lipoprotein lipase from microorganisms for the rapid and complete hydrolysis of triglycerides to glycerol followed by oxidation to dihydroxyacetone phosphate and hydrogen peroxide. The hydrogen peroxide produced then reacts with 4-aminophenazone and 4-chlorophenol under the catalytic action of peroxidase to form a red dyestuff (Trinder endpoint reaction). The color intensity of the red dyestuff formed is directly proportional to the triglyceride concentration and can be measured photometrically.[9,10]

**Test principle[10]**

Enzymatic colorimetric test.

$$\text{triglycerides} + 3\ H_2O \xrightarrow{\text{LPL}} \text{glycerol} + 3\ \text{RCOOH}$$

$$\text{glycerol} + \text{ATP} \xrightarrow[Mg^{2+}]{\text{GK}} \text{glycerol-3-phosphate} + \text{ADP}$$

$$\text{glycerol-3-phosphate} + O_2 \xrightarrow{\text{GPO}} \text{dihydroxyacetone phosphate} + H_2O_2$$

$$H_2O_2 + \text{4-aminophenazone} + \text{4-chlorophenol} \xrightarrow{\text{peroxidase}} \text{4-(p-benzoquinone-monoimino)-phenazone} + 2\ H_2O + HCl$$

**Reagents - working solutions**

**R1** PIPES buffer: 50 mmol/L, pH 6.8; $Mg^{2+}$: 40 mmol/L; sodium cholate: 0.20 mmol/L; ATP: ≥ 1.4 mmol/L; 4-aminophenazone: ≥ 0.13 mmol/L; 4-chlorophenol: 4.7 mmol/L; lipoprotein lipase (Pseudomonas spec.): ≥ 83 µkat/L; glycerol kinase (Bacillus stearothermophilus): ≥ 3 µkat/L; glycerol phosphate oxidase (E. coli): ≥ 41 µkat/L; peroxidase (horseradish): ≥ 1.6 µkat/L; preservative, stabilizers

R1 is in position B.

**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.

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |

**Specimen collection and preparation**

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

# TRIGL

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**Triglycerides**

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin and $K_2$-EDTA plasma.

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.

| | |
|---|---|
| Stability in serum: | 2 days at 20-25 °C[11] |
| | 10 days at 2-8 °C[12] |
| | 3 months at -20 °C (± 5 °C)[13] |
| | several years at -70 °C (± 5 °C)[13] |

Freeze only once.

| | |
|---|---|
| Stability in plasma: | 2 days at 20-25 °C[11] |
| | 15 days at 2-8 °C[14] |
| | 3 months at -20 °C (± 5 °C)[13] |
| | several years at -70 °C (± 5 °C)[13] |

Freeze only once.

**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.

**Application for serum and plasma**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 700/505 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 66 µL | 15 µL |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 1.1 µL | – | – |
| Decreased | 1.1 µL | 15 µL | 60 µL |
| Increased | 1.1 µL | – | – |

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

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. |
| Calibration mode | Linear |
| Calibration frequency | Full calibration<br>- after reagent lot change<br>- every 8 weeks on-board<br>- as required following quality control procedures |

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

Traceability: This method has been standardized against the ID/MS method.

**Quality control**

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

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, g/L).

| | |
|---|---|
| Conversion factors: | mmol/L x 88.5 = mg/dL |
| | mmol/L x 0.885 = g/L |

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial values at a triglyceride concentration of 2.3 mmol/L (203 mg/dL).

Icterus:[15] No significant interference up to an I index of 10 for conjugated bilirubin and 10 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 171 µmol/L or 10 mg/dL; approximate unconjugated bilirubin concentration: 171 µmol/L or 10 mg/dL).

Hemolysis:[15] No significant interference up to an H index of 700 (approximate hemoglobin concentration: 434 µmol/L or 700 mg/dL).

Lipemia:[15] The L index correlates with sample turbidity but not with triglycerides level. Extremely lipemic samples (triglycerides greater than 3000 mg/dL) can produce normal results[16].

Prozone Check: The flag > Kin is an indicator for extremely high triglyceride concentrations in the sample. False low results are due to oxygen depletion during assay reaction.

Endogenous unesterified glycerol in the sample will falsely elevate serum triglycerides.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[17,18]

Exception: Ascorbic acid and calcium dobesilate cause artificially low triglyceride results. Intralipid is directly measured as analyte in this assay and leads to high triglyceride results.

Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.[19]

Acetaminophen intoxications are frequently treated with N-Acetylcysteine. N-Acetylcysteine at a plasma concentration above 166 mg/L and the Acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low results.

Venipuncture should be performed prior to the administration of Metamizole. Venipuncture immediately after or during the administration of Metamizole may lead to falsely low results. A significant interference may occur at plasma Metamizole concentrations above 0.05 mg/mL.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[20]

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**

0.1-10.0 mmol/L (8.85-885 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

| | |
|---|---|
| Limit of Blank | = 0.1 mmol/L (8.85 mg/dL) |
| Limit of Detection | = 0.1 mmol/L (8.85 mg/dL) |
| Limit of Quantitation | = 0.1 mmol/L (8.85 mg/dL) |

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 95$^{th}$ 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 20 %. It has been determined using low concentration triglycerides samples.

**Expected values according to NCEP[21]**

**mmol/L**

Normal range: < 1.70 mmol/L

**Clinical interpretation** according to the recommendations of the European Atherosclerosis Society: [22]

| | mmol/L | Lipid metabolism disorder |
|---|---|---|
| Cholesterol<br>Triglycerides | < 5.18<br>< 2.26 | No |
| Cholesterol | 5.18-7.77 | Yes<br>if HDL-cholesterol<br>< 0.9 mmol/L |
| Cholesterol<br>Triglycerides | > 7.77<br>> 2.26 | Yes |

**mg/dL**

Normal range: < 150 mg/dL

**Clinical interpretation** according to the recommendations of the European Atherosclerosis Society: [22]

| | mg/dL | Lipid metabolism disorder |
|---|---|---|
| Cholesterol<br>Triglycerides | < 200<br>< 200 | No |
| Cholesterol | 200-300 | Yes<br>if HDL-cholesterol<br>< 35 mg/dL |
| Cholesterol<br>Triglycerides | > 300<br>> 200 | Yes |

**Note:** If the free glycerol is to be taken into account, then 0.11 mmol/L (10 mg/dL) must be subtracted from the triglycerides value obtained.[13]

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mmol/L* | *mmol/L* | *%* |
| PCCC1[a)] | 1.37 | 0.00824 | 0.6 |
| PCCC2[b)] | 2.50 | 0.0150 | 0.6 |
| Human serum 1 | 0.195 | 0.00414 | 2.1 |
| Human serum 2 | 1.73 | 0.0107 | 0.6 |
| Human serum 3 | 3.14 | 0.0229 | 0.7 |
| Human serum 4 | 5.25 | 0.0324 | 0.6 |
| Human serum 5 | 8.56 | 0.0476 | 0.6 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mmol/L* | *mmol/L* | *%* |
| PCCC1[a)] | 1.37 | 0.0104 | 0.8 |
| PCCC2[b)] | 2.51 | 0.0209 | 0.8 |
| Human serum 1 | 0.195 | 0.00443 | 2.3 |
| Human serum 2 | 1.73 | 0.0126 | 0.7 |
| Human serum 3 | 3.14 | 0.0250 | 0.8 |
| Human serum 4 | 5.23 | 0.0350 | 0.7 |
| Human serum 5 | 8.50 | 0.0555 | 0.7 |

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Triglycerides values for human serum and plasma samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 74

| Passing/Bablok[23] | Linear regression |
|---|---|
| y = 1.015x + 0.0125 mmol/L | y = 1.020x + 0.00786 mmol/L |
| τ = 0.983 | r = 0.999 |

The sample concentrations were between 0.300 and 9.19 mmol/L.

Triglycerides values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 74

| Passing/Bablok[23] | Linear regression |
|---|---|
| y = 1.019x - 0.00772 mmol/L | y = 1.021x - 0.0114 mmol/L |
| τ = 0.994 | r = 1.000 |

The sample concentrations were between 0.170 and 9.63 mmol/L.

# TRIGL

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**Triglycerides**

Triglycerides values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 75

| Passing/Bablok[23] | Linear regression |
|---|---|
| y = 1.018x - 0.0236 mmol/L | y = 1.022x - 0.0320 mmol/L |
| τ = 0.995 | r = 1.000 |

The sample concentrations were between 0.611 and 9.72 mmol/L.

**References**


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

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123


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Roche

# UA2

cobas®

**Uric Acid ver.2**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08058750190* | 08058750500 | Uric Acid ver.2 (1300 tests) | System-ID 2117 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08058750214* | 08058750500 | Uric Acid ver.2 (1300 tests) | System-ID 2117 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

## English

### System information

**UA2:** ACN 21170 (Serum/plasma)

**UA2U:** ACN 21171 (Urine)

### Intended use

In vitro test for the quantitative determination of uric acid in human serum, plasma and urine on **cobas c** systems.

### Summary

Uric acid measurements, performed with this assay, in human serum, plasma and urine are used as aid in diagnosis and treatment of numerous renal and metabolic disorders associated with hyper- or hypo-uricemia.

Uric acid is the major final product of purine metabolism in the human organism. Purines from dietary nucleic acids are converted in the liver and small intestine to uric acid.[1] Uric acid is present as a normal intracellular component and in biological fluids. Chemically, it is a reducing agent and accounts for nearly half of the antioxidant activity in blood. Uric acid production is balanced between purine ingestion, de novo synthesis, reabsorption, and degradation. Two-thirds of uric acid is excreted renally, while one-third is eliminated through the gastrointestinal system. Serum uric acid levels increase physiologically and gradually over the course of human life and are strongly influenced by the diet.[1,2]

High serum levels of uric acid can adversely affect organ systems. Overproduction of uric acid, insufficient excretion of uric acid, or often a combination of both can lead to hyperuricemia.[3] Primary causes of hyperuricemia include idiopathic and hereditary metabolic disorders. Secondary causes of increased uric acid formation include excessive dietary intake of purines and increased nucleic acid turnover (e.g. in myeloproliferative disorders, lymphoproliferative disorders, psoriasis, sarcoidosis, hemolytic anemia, cytotoxic drug treatments). Major causes of decreased uric acid excretion are: acute or chronic kidney disease, increased renal tubular reabsorption, reduced tubular secretion, lead poisoning, preeclampsia, low doses of salicylate, thiazide diuretics, Down syndrome.[1]

Hyperuricemia is mostly asymptomatic, but persistent hyperuricemia and uric acid precipitation may lead to the accumulation of urate crystals in many tissues, resulting in either acute painful conditions, such as gout/tophaceous gout/gouty arthritis, urolithiasis, or, in severe cases, in uric acid kidney diseases.[4]

Hypouricemia is much less common than hyperuricemia. Hypouricemia is often defined as serum uric acid levels ≤ 2.0 mg/dL (0.12 mmol/L). It may be secondary to any one of a number of underlying conditions, such as severe hepatocellular disease with reduced purine synthesis or xanthine oxidase activity, defective renal tubular reabsorption of uric acid (congenital or acquired), overtreatment of hyperuricemia, treatment with uricosuric drugs and cancer chemotherapy with 6-mercaptopurine or azathioprine.[1,5]

Phosphotungstic acid (PTA), uricase, and HPLC-based methods have been described for measuring uric acid. PTA methods are now rarely used.[1,6] The uricase-based method utilizes the enzyme uricase to oxidize uric acid.[7] Uricase can be employed in methods that involve the UV measurement of the consumption of uric acid or in combination with other enzymes to provide a colorimetric assay.[1]

The colorimetric method developed by Town, et al. involves initial sample incubation with a reagent mixture containing ascorbate oxidase and a clearing system. In this test system it is important that any ascorbic acid present in the sample is eliminated in the preliminary reaction; this precludes any ascorbic acid interference with the subsequent peroxidase (POD) indicator reaction. Upon addition of the starter reagent, oxidation of uric acid by uricase begins.[8]

The Roche assay described here is a slight modification of the colorimetric method described above. In this reaction, the peroxide reacts in the presence of peroxidase (POD), N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline (TOOS), and 4-aminophenazone to form a quinone-diimine dye. The intensity of the red color formed is proportional to the uric acid concentration and is determined photometrically.

### Test principle

Enzymatic colorimetric test.

Uricase cleaves uric acid to form allantoin and hydrogen peroxide.

$$\text{Uric acid} + 2\ H_2O + O_2 \xrightarrow{\text{Uricase}} \text{allantoin} + CO_2 + H_2O_2$$

In the presence of peroxidase, 4-aminophenazone is oxidized by hydrogen peroxide to a quinone-diimine dye.

$$2\ H_2O_2 + H^+ + \text{TOOS}^{a)} + \text{4-aminophenazone} \xrightarrow{\text{Peroxidase}} \text{quinone-diimine dye} + 4\ H_2O$$

a) N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline

The color intensity of the quinone-diimine formed is directly proportional to the uric acid concentration and is determined by measuring the increase in absorbance.

### Reagents - working solutions

**R1** Phosphate buffer: 0.05 mol/L, pH 7.8; TOOS: 7 mmol/L; fatty alcohol polyglycol ether: 4.8 %; ascorbate oxidase (EC 1.10.3.3; zucchini) ≥ 83.5 µkat/L (25 °C); stabilizers; preservative

**R3** Phosphate buffer: 0.1 mol/L, pH 7.8; potassium hexacyanoferrate (II): 0.3 mmol/L; 4-aminophenazone ≥ 3 mmol/L; uricase (EC 1.7.3.3; Arthrobacter protophormiae) ≥ 83.4 µkat/L (25 °C); peroxidase (POD) (EC 1.11.1.7; horseradish) ≥ 50 µkat/L (25 °C); stabilizers; preservative

R1 is in position B and R3 is in position C.

### 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.

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

Warning

| | |
|---|---|
| H319 | Causes serious eye irritation. |

**Prevention:**

| | |
|---|---|
| P264 | Wash skin thoroughly after handling. |
| P280 | Wear eye protection/ face protection. |

**Response:**

| | |
|---|---|
| P305 + P351 + P338 | IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. |
| P337 + P313 | If eye irritation persists: Get medical advice/attention. |

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 26 weeks |
| | 6 months at -20 °C (± 5 °C) |

Freeze only once.

| | |
|---|---|
| Stability in urine[9] (upon NaOH addition): | 4 days at 20-25 °C |

**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.
Plasma: Li-heparin and $K_2$-EDTA plasma.

EDTA plasma values are approximately 7 % lower than serum values.

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.

Urine: Assay urinary uric acid as soon as possible. Do not refrigerate.

To prevent ureate precipitation in urine samples, add sodium hydroxide to keep urine alkaline (pH > 8.0). To achieve stated uric acid stability, add NaOH prior to sample collection. Urine samples are diluted 1 + 10 with distilled/deionized water or 0.9 % NaCl. This dilution is taken into account in the calculation of the results. If stabilizers are added to the sample, the sample index feature must not be used.

Centrifuge samples containing precipitates before performing the assay.

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

| | |
|---|---|
| Stability in serum/plasma:[9] | 7 days at 4-8 °C |
| | 3 days at 20-25 °C |

**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.

**Application for serum and plasma**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 700/546 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 55 µL | 19 µL |
| R3 | 11 µL | 15 µL |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 2.3 µL | – | – |
| Decreased | 3.6 µL | 21 µL | 61 µL |
| Increased | 2.3 µL | – | – |

**Application for urine**

**Test definition**

| | | |
|---|---|---|
| Reporting time | 10 min | |
| Wavelength (sub/main) | 700/546 nm | |
| Reagent pipetting | | Diluent ($H_2O$) |
| R1 | 55 µL | 19 µL |
| R3 | 11 µL | 15 µL |

| *Sample volumes* | *Sample* | *Sample dilution* | |
|---|---|---|---|
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 2.3 µL | 10 µL | 100 µL |
| Decreased | 2.3 µL | 4 µL | 106 µL |
| Increased | 2.3 µL | 10 µL | 100 µL |

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

**Calibration**

*Application for serum/plasma (ACN 21170)*

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. |
| Calibration mode | Linear |

| | |
|---|---|
| Calibration frequency | Automatic full calibration<br>- after reagent lot change<br>Full calibration<br>- every 12 weeks on-board<br>- as required following quality control procedures |

*Application for urine (ACN 21171)*

Transfer of calibration from serum/plasma application (ACN 21170)

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

Traceability: This method has been standardized against ID/MS.[10]

**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 |
| Urine: | Quantitative urine controls are recommended for routine quality control. |

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit mg/dL (µmol/L, mg/L, mmol/L).

| | |
|---|---|
| Conversion factors: | mg/dL x 59.5 = µmol/L |
| | mg/dL x 10.0 = mg/L |
| | mg/dL x 0.0595 = mmol/L |

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial value at a uric acid concentration of 7 mg/dL (417 µmol/L) in serum/plasma and at a uric acid concentration of 92 mg/dL (5474 µmol/L) in urine. Recovery within ± 10 % for drug interference.

*Serum/plasma*

Icterus:[11] No significant interference up to an I index of 40 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 684 µmol/L or 40 mg/dL).

Hemolysis:[11] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[11] No significant interference up to an L index of 1500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[12,13] Exceptions: Calcium dobesilate causes artificially low uric acid results.

Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.[14]

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 0.17 mmol/L (3 mg/dL).

Uricase reacts specifically with uric acid. Other purine derivatives can inhibit the uric acid reaction.

Acetaminophen intoxications are frequently treated with N-Acetylcysteine. N-Acetylcysteine at the therapeutic concentration when used as an antidote and the Acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low results.

Venipuncture should be performed prior to the administration of Metamizole. Venipuncture immediately after or during the administration of Metamizole may lead to falsely low results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[15]

*Urine*

Drugs: No interference was found at therapeutic concentrations using common drug panels.[13] Exceptions: Calcium dobesilate, Levodopa and methyldopa can all cause artificially low uric acid results.

Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.

High homogentisic acid concentrations in urine samples lead to false results.

Acetaminophen, Acetylcysteine and Metamizole are metabolized quickly. Therefore, interference from these substances is unlikely but cannot be excluded.

Hemolysis: No significant interference up to an H index of 750 (approximate hemoglobin concentration: 466 µmol/L or 750 mg/dL).

Urea: No significant interference from urea up to a concentration of 2100 mmol/L (12612 mg/dL).

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**

*Serum/plasma*

0.2-25 mg/dL (11.9-1487 µmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

*Urine*

2.2-275 mg/dL (131-16362 µmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

*Serum/plasma*

| | |
|---|---|
| Limit of Blank | = 0.2 mg/dL |
| Limit of Detection | = 0.2 mg/dL |
| Limit of Quantitation | = 0.2 mg/dL |

*Urine*

| | |
|---|---|
| Limit of Blank | = 2.2 mg/dL |
| Limit of Detection | = 2.2 mg/dL |
| Limit of Quantitation | = 2.2 mg/dL |

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 95$^{th}$ 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 20 %. It has been determined using low concentration uric acid samples.

**Expected values**
**mg/dL**

*Serum/plasma*[16]

Males: 3.4-7.0 mg/dL

Females: 2.4-5.7 mg/dL

*Urine* (reference range according to Krieg and Colombo)

1st morning urine[17] 37-92 mg/dL*

24-hour urine[18] 200-1000 mg/day*

corresponding to 13-67 mg/dL

(calculated from a urine volume of 1.5 L/24 h)

**µmol/L**

*Serum/plasma*[16]

Males: 202.3-416.5 µmol/L*

Females: 142.8-339.2 µmol/L*

* calculated by unit conversion factor

*Urine* (reference range according to Krieg and Colombo)

1st morning urine[17] 2200-5475 µmol/L

24-hour urine[18] 1200-5900 µmol/day

corresponding to 773-3986 µmol/L

(calculated from a urine volume of 1.5 L/24 h)

*Urine* (reference range according to Tietz)[19]

| | | |
|---|---|---|
| Average diet | | 250-750 mg/24 hours |
| Low purine diet | | |
| | Females | < 400 mg/24 hours |
| | Males | < 480 mg/24 hours |
| High purine diet | | < 1000 mg/24 hours |

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

*Serum/plasma*

| *Repeatability* | *Mean mg/dL* | *SD mg/dL* | *CV %* |
|---|---|---|---|
| PCCC1[b)] | 4.60 | 0.0193 | 0.4 |
| PCCC2[c)] | 10.6 | 0.0655 | 0.6 |
| Human serum 1 | 0.430 | 0.00713 | 1.7 |
| Human serum 2 | 2.32 | 0.0147 | 0.6 |
| Human serum 3 | 6.66 | 0.0347 | 0.5 |
| Human serum 4 | 12.0 | 0.0756 | 0.6 |
| Human serum 5 | 21.4 | 0.129 | 0.6 |

| *Intermediate precision* | *Mean mg/dL* | *SD mg/dL* | *CV %* |
|---|---|---|---|
| PCCC1[b)] | 4.60 | 0.0467 | 1.0 |
| PCCC2[c)] | 10.6 | 0.0983 | 0.9 |
| Human serum 1 | 0.430 | 0.00880 | 2.0 |
| Human serum 2 | 2.32 | 0.0185 | 0.8 |
| Human serum 3 | 6.66 | 0.0400 | 0.6 |
| Human serum 4 | 12.0 | 0.0940 | 0.8 |
| Human serum 5 | 21.4 | 0.143 | 0.7 |

b) PreciControl ClinChem Multi 1
c) PreciControl ClinChem Multi 2

*Urine*

| *Repeatability* | *Mean mg/dL* | *SD mg/dL* | *CV %* |
|---|---|---|---|
| Control 1[d)] | 9.05 | 0.0780 | 0.9 |
| Control 2[d)] | 16.1 | 0.0957 | 0.6 |
| Human urine 1 | 2.91 | 0.0584 | 2.0 |
| Human urine 2 | 37.1 | 0.171 | 0.5 |
| Human urine 3 | 74.7 | 0.279 | 0.4 |
| Human urine 4 | 115 | 0.556 | 0.5 |
| Human urine 5 | 224 | 0.866 | 0.4 |

| *Intermediate precision* | *Mean mg/dL* | *SD mg/dL* | *CV %* |
|---|---|---|---|
| Control 1[d)] | 9.18 | 0.144 | 1.6 |
| Control 2[d)] | 16.1 | 0.159 | 1.0 |
| Human urine 1 | 3.06 | 0.576 | 18.8 |
| Human urine 2 | 37.1 | 0.615 | 1.7 |
| Human urine 3 | 74.9 | 1.93 | 2.6 |
| Human urine 4 | 115 | 4.34 | 3.8 |
| Human urine 5 | 224 | 1.39 | 0.6 |

d) commercially available control material

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Uric acid values for human serum, plasma and urine obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

**Serum/plasma**

Sample size (n) = 88

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.004x - 0.0207 mg/dL | y = 1.008x - 0.0265 mg/dL |
| τ = 0.985 | r = 1.000 |

The sample concentrations were between 0.290 and 24.6 mg/dL.

**Urine**

Sample size (n) = 81

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.002x - 0.168 mg/dL | y = 1.004x - 0.162 mg/dL |
| τ = 0.987 | r = 1.000 |

The sample concentrations were between 3.27 and 270 mg/dL.

Uric acid values for human serum, plasma and urine obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

**Serum/plasma**

Sample size (n) = 83

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.000x + 0.003 mg/dL | y = 1.023x - 0.141 mg/dL |
| τ = 0.979 | r = 0.998 |

The sample concentrations were between 0.200 and 23.7 mg/dL.

**Urine**

Sample size (n) = 102

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.038x - 0.0408 mg/dL | y = 1.057x - 0.990 mg/dL |
| τ = 0.991 | r = 1.000 |

The sample concentrations were between 2.45 and 243 mg/dL.

Uric acid values for human serum, plasma and urine samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

**Serum/plasma**

Sample size (n) = 76

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 1.009x - 0.0125 mg/dL | y = 0.999x + 0.0327 mg/dL |
| τ = 0.963 | r = 1.000 |

The sample concentrations were between 0.294 and 23.3 mg/dL.

**Urine**

Sample size (n) = 66

| Passing/Bablok[20] | Linear regression |
|---|---|
| y = 0.990x - 0.0957 mg/dL | y = 0.994x - 0.220 mg/dL |
| τ = 0.997 | r = 1.000 |

The sample concentrations were between 4.41 and 254 mg/dL.

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

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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# UREAL

cobas®

**Urea/BUN**

Order information

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 08058806190* | 08058806500 | Urea/BUN (600 tests) | System-ID 2119 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |
| 08058806214* | 08058806500 | Urea/BUN (600 tests) | System-ID 2119 001 | **cobas c** 303, **cobas c** 503, **cobas c** 703 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 10759350190 | Calibrator f.a.s. (12 x 3 mL) | Code 20401 | |
| 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 | |
| 08063494190 | Diluent NaCl 9 % (123 mL) | System-ID 2906 001 | |

* Some kits shown may not be available in all countries.

**English**

**System information**

**UREAL:** ACN 21191 (Serum/plasma)

**URELU:** ACN 21190 (Urine)

**U-BUN:** ACN 21192 (Serum/plasma)

**UBUNU:** ACN 21193 (Urine)

**Intended use**

In vitro test for the quantitative determination of urea/urea nitrogen in human serum, plasma and urine on **cobas c** systems.

**Summary**

Measurements of urea/urea nitrogen in human serum, plasma and urine, performed with this assay are used as screening tests and as an aid in diagnosis and monitoring of renal function.

Urea is the major end product of protein nitrogen metabolism. It is synthesized by the urea cycle in the liver from ammonia which is produced by amino acid deamination. Urea is excreted mostly by the kidneys but minimal amounts are also excreted in sweat and degraded in the intestines by bacterial action.[1]

Serum urea mass concentration is either specified for the complete urea molecule or for nitrogen equivalents [blood urea nitrogen (BUN)].[2] Determination of blood urea nitrogen is primarily used as a screening test for renal function. When used in conjunction with serum creatinine determinations it can aid in the differential diagnosis of the three types of azotemia: prerenal, renal, and postrenal. The urea to creatinine ratio has been proposed as a crude discriminator between prerenal and intrinsic azotemia.[1]

Elevations in blood urea nitrogen concentration are seen in inadequate renal perfusion, shock, diminished blood volume (prerenal causes), chronic nephritis, nephrosclerosis, tubular necrosis, glomerular-nephritis (renal causes), and urinary tract obstruction (postrenal causes). Transient elevations may also be seen during periods of high protein intake. Liver diseases may lead to unpredictable blood urea nitrogen concentrations, including abnormally low levels. Low blood urea nitrogen concentrations are not common, but can be found in cases such as malnutrition, lack of protein in the diet, or overhydration.[1,3]

**Test principle**

Kinetic test with urease and glutamate dehydrogenase.[4,5,6,7]

Urea is hydrolyzed by urease to form ammonium and carbonate.

$$\text{Urea} + 2\ H_2O \xrightarrow{\text{Urease}} 2\ NH_4^+ + CO_3^{2-}$$

In the second reaction 2-oxoglutarate reacts with ammonium in the presence of glutamate dehydrogenase (GLDH) and the coenzyme NADH to produce L-glutamate. In this reaction 2 moles of NADH are oxidized to $NAD^+$ for each mole of urea hydrolyzed.

$$NH_4^+ + \text{2-oxoglutarate} + \text{NADH} \xrightarrow{\text{GLDH}} \text{L-glutamate} + NAD^+ + H_2O$$

The rate of decrease in the NADH concentration is directly proportional to the urea concentration in the specimen and is measured photometrically.

**Reagents - working solutions**

**R1** NaCl 9 %

**R3** TRIS buffer: 220 mmol/L, pH 8.6; 2-oxoglutarate: 73 mmol/L; NADH: 2.5 mmol/L; ADP: 6.5 mmol/L; urease (jack bean): ≥ 300 µkat/L; GLDH (bovine liver): ≥ 80 µkat/L; preservative; nonreactive stabilizers

R1 is in position B and R3 is in position C.

**Precautions and warnings**

For in vitro diagnostic use for laboratory 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.

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| Shelf life at 2-8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 8 weeks |

**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
Plasma: Li-heparin and $K_2$-EDTA plasma. Do not use ammonium heparin.

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.

Urine

Bacterial growth in the specimen and high atmospheric ammonia concentrations as well as contamination by ammonium ions may cause

erroneously elevated results. If stabilizers are added to the sample, the sample index feature must not be used.

| | |
|---|---|
| Stability in *serum/plasma*:[8] | 7 days at 15-25 °C |
| | 7 days at 2-8 °C |
| | 1 year at (–15)-(–25) °C |

Freeze only once.

| | |
|---|---|
| Stability in *urine*:[8] | 2 days at 15-25 °C |
| | 7 days at 2-8 °C |
| | 1 month at (–15)-(–25) °C |

Freeze only once.

Centrifuge samples containing precipitates before performing the assay.

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

**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.

**Application for serum and plasma**

**Test definition**

| | | | |
|---|---|---|---|
| Reporting time | 10 min | | |
| Wavelength (sub/main) | 700/340 nm | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 8 µL | 66 µL | |
| R3 | 28 µL | 81 µL | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 1.5 µL | – | – |
| Decreased | 1.5 µL | 25 µL | 50 µL |
| Increased | 1.5 µL | – | – |

**Application for urine**

**Test definition**

| | | | |
|---|---|---|---|
| Reporting time | 10 min | | |
| Wavelength (sub/main) | 700/340 nm | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 8 µL | 66 µL | |
| R3 | 28 µL | 81 µL | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 1.5 µL | 2.0 µL | 98 µL |
| Decreased | 1.5 µL | 1.3 µL | 116 µL |
| Increased | 1.5 µL | – | – |

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

**Calibration**

*Application for serum/plasma (ACN 21191/21192)*

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2: C.f.a.s. |
| Calibration mode | Linear |
| Calibration frequency | Full calibration<br>- after reagent lot change<br>- every 4 weeks on-board<br>- as required following quality control procedures |

*Application for urine (ACN 21190/21193)*

Transfer of calibration from serum/plasma application (ACN 21191/21192)

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

Traceability: This method has been standardized against ID/MS.

**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 |
| Urine: | Quantitative urine controls are recommended for routine quality control. |

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 8 weeks.

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**

**cobas c** systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, g/L).

Conversion factors:

mmol/L urea x 6.006 = mg/dL urea

mmol/L urea x 0.06006 = g/L urea

mmol/L urea nitrogen x 2.801 = mg/dL urea nitrogen

mmol/L urea nitrogen x 0.02801 = g/L urea nitrogen

mg/dL urea x 0.467 = mg/dL urea nitrogen

When 24-hour urine is used as the specimen, multiply the result by the 24-hour volume to obtain values in g or mmol/24 hours.

**Limitations - interference**

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[9]

*Serum/plasma*

Criterion: Recovery within ± 0.83 mmol/L of initial values of samples ≤ 8.3 mmol/L and within ± 10 % for samples > 8.3 mmol/L.

Icterus:[10] 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).

Hemolysis:[10] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[10] No significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Ammonium ions may cause erroneously elevated results.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[11,12]

*Urine*

Criterion: Recovery within ± 15 mmol/L of initial values of samples ≤ 150 mmol/L and within ± 10 % for samples > 150 mmol/L.

Hemolysis: No significant interference up to an H index of 750 (approximate hemoglobin concentration: 466 µmol/L or 750 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[12]

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**

*Serum/plasma*

0.5-40 mmol/L (3.0-240 mg/dL urea, 1.4-112 mg/dL urea nitrogen)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

*Urine*

1-2000 mmol/L (6-12000 mg/dL urea, 2.8-5600 mg/dL urea nitrogen)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:1.8 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 1.8.

Determine samples having concentrations lower than the technical limit of 40 mmol/L (240 mg/dL urea and 112 mg/dL urea nitrogen) via the rerun function. Samples are measured undiluted.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

*Serum/plasma*

| | |
|---|---|
| Limit of Blank | = 0.5 mmol/L |
| Limit of Detection | = 0.5 mmol/L |
| Limit of Quantitation | = 0.5 mmol/L |

*Urine*

| | |
|---|---|
| Limit of Blank | = 1.0 mmol/L |
| Limit of Detection | = 1.0 mmol/L |
| Limit of Quantitation | = 1.0 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 95$^{th}$ 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 20 %. It has been determined using low concentration urea/urea nitrogen samples.

**Expected values**

**mmol/L**

Urea:

*Serum/plasma*[13]

| | |
|---|---|
| Adults | 2.76-8.07 mmol/L |
| *Urine* | |
| 24-hour urine[14] | 428-714 mmol/24 h, corresponding to 286-595 mmol/L[a)] |

a) Based on average urine output of 1.2-1.5 L/24 h

Urea nitrogen (BUN):

*Serum/plasma*[14]

| | |
|---|---|
| Adults (18-60 years) | 2.14-7.14 mmol/L |
| Adults (60-90 years) | 2.86-8.21 mmol/L |
| Infants (< 1 year) | 1.43-6.78 mmol/L |
| Infants/children | 1.79-6.43 mmol/L |
| *Urine* | |
| 24-hour urine[14] | 428-714 mmol/24 h, corresponding to 286-595 mmol/L[b)] |

b) Based on average urine output of 1.2-1.5 L/24 h

**mg/dL**

Urea:

*Serum/plasma*[13]

| | |
|---|---|
| Adults | 16.6-48.5 mg/dL |
| *Urine* | |
| 24-hour urine[14] | 25.7-42.9 g/24 h, corresponding to 1.71-3.57 g/dL[a)] |

a) Based on average urine output of 1.2-1.5 L/24 h

Urea nitrogen (BUN):

*Serum/plasma*[14]

| | |
|---|---|
| Adults (18-60 years) | 6-20 mg/dL |
| Adults (60-90 years) | 8-23 mg/dL |
| Infants (< 1 year) | 4-19 mg/dL |
| Infants/children | 5-18 mg/dL |
| *Urine* | |
| 24-hour urine[14] | 12-20 g/24 h, corresponding to 801-1666 mg/dL[b)] |

b) Based on average urine output of 1.2-1.5 L/24 h

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 analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

**Precision**

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 c** 503 analyzer.

*Serum/plasma*

# UREAL

cobas®

**Urea/BUN**

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mmol/L* | *mmol/L* | *%* |
| PCCC1[c)] | 6.53 | 0.0408 | 0.6 |
| PCCC2[d)] | 18.3 | 0.0690 | 0.4 |
| Human serum 1 | 1.31 | 0.0416 | 3.2 |
| Human serum 2 | 5.12 | 0.0441 | 0.9 |
| Human serum 3 | 7.67 | 0.0451 | 0.6 |
| Human serum 4 | 18.7 | 0.101 | 0.5 |
| Human serum 5 | 31.0 | 0.124 | 0.4 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mmol/L* | *mmol/L* | *%* |
| PCCC1[c)] | 6.50 | 0.0745 | 1.1 |
| PCCC2[d)] | 18.4 | 0.198 | 1.1 |
| Human serum 1 | 1.31 | 0.0459 | 3.5 |
| Human serum 2 | 5.12 | 0.0659 | 1.3 |
| Human serum 3 | 7.67 | 0.0931 | 1.2 |
| Human serum 4 | 18.7 | 0.226 | 1.2 |
| Human serum 5 | 31.0 | 0.350 | 1.1 |

c) PreciControl ClinChem Multi 1

d) PreciControl ClinChem Multi 2

*Urine*

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mmol/L* | *mmol/L* | *%* |
| Control 1[e)] | 143 | 2.86 | 2.0 |
| Control 2[e)] | 239 | 3.68 | 1.5 |
| Human urine 1 | 3.22 | 0.0435 | 1.4 |
| Human urine 2 | 73.2 | 2.50 | 3.4 |
| Human urine 3 | 407 | 3.28 | 0.8 |
| Human urine 4 | 922 | 5.03 | 0.5 |
| Human urine 5 | 1583 | 10.1 | 0.6 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mmol/L* | *mmol/L* | *%* |
| Control 1[e)] | 143 | 3.17 | 2.2 |
| Control 2[e)] | 239 | 4.32 | 1.8 |
| Human urine 1 | 3.22 | 0.0547 | 1.7 |
| Human urine 2 | 73.2 | 2.78 | 3.8 |
| Human urine 3 | 411 | 4.93 | 1.2 |
| Human urine 4 | 919 | 11.5 | 1.2 |
| Human urine 5 | 1583 | 19.7 | 1.2 |

e) commercially available control material

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

**Method comparison**

Urea values for human serum, plasma and urine samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

*Serum/plasma*

Sample size (n) = 94

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 1.009x + 0.0202 mmol/L | y = 1.006x + 0.0265 mmol/L |
| τ = 0.986 | r = 1.000 |

The sample concentrations were between 0.600 and 38.1 mmol/L.

*Urine*

Sample size (n) = 91

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 0.962x - 0.432 mmol/L | y = 0.960x + 0.586 mmol/L |
| τ = 0.982 | r = 1.000 |

The sample concentrations were between 71.0 and 1964 mmol/L.

Urea values for human serum, plasma and urine samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

*Serum/plasma*

Sample size (n) = 89

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 1.017x + 0.0905 mmol/L | y = 1.015x + 0.148 mmol/L |
| τ = 0.986 | r = 1.000 |

The sample concentrations were between 0.700 and 35.4 mmol/L.

*Urine*

Sample size (n) = 73

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 0.981x + 0.901 mmol/L | y = 0.973x + 4.74 mmol/L |
| τ = 0.960 | r = 0.999 |

The sample concentrations were between 41.0 and 1875 mmol/L.

Urea values for human serum, plasma and urine samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

*Serum/plasma*

Sample size (n) = 74

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 1.000x + 0.0800 mmol/L | y = 1.000x + 0.0683 mmol/L |
| τ = 0.983 | r = 1.000 |

The sample concentrations were between 0.821 and 39.5 mmol/L.

*Urine*

Sample size (n) = 74

| Passing/Bablok[15] | Linear regression |
|---|---|
| y = 0.948x - 1.68 mmol/L | y = 0.942x + 0.489 mmol/L |
| τ = 0.980 | r = 1.000 |

The sample concentrations were between 46.4 and 1912 mmol/L.

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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:

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123

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# Mixed-bed resin MBH 100

*Global: 11404954001*

*General laboratory equipment to fill the external water supply units (ion exchange resin for demineralized water).*

## Compatible instruments

COBAS INTEGRA® 400 plus, **cobas c** 111, **cobas c** 311, **cobas c** 501, **cobas c** 502, **cobas c** 503, **cobas c** 701, **cobas c** 702, **cobas c** 513, **cobas e** 411, **cobas e** 601, **cobas e** 602, **cobas e** 801, **cobas c** 303, **cobas e** 402

## Location for use

Exchange resin for the external water supply unit.

## Product registration on instrument

Not applicable.

## Replacement frequency

Depending on the throughput.

## Product labeling

No method sheet available for this product.

## Onboard stability

Not applicable.

## Pack size

1 bag with 25 L.

## Legal manufacturer

Applichem