CRP4

cobas®

Tina-quant C-Reactive Protein IV

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
07876033 190	Tina-quant C-Reactive Protein IV (250 tests)	System-ID 07 7607 6	**cobas c** 311, **cobas c** 501/502
11355279 216	Calibrator f.a.s. Proteins (5 × 1 mL)	Code 656	
11355279 160	Calibrator f.a.s. Proteins (5 × 1 mL, for USA)	Code 656	
20766321 322	CRP T Control N (5 × 0.5 mL)	Code 235	
10557897 122	Precinorm Protein (3 × 1 mL)	Code 302	
10557897 160	Precinorm Protein (3 × 1 mL, for USA)	Code 302	
11333127 122	Precipath Protein (3 × 1 mL)	Code 303	
11333127 160	Precipath Protein (3 × 1 mL, for USA)	Code 303	
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	Code 391	
05947626 160	PreciControl ClinChem Multi 1 (4 × 5 mL, for USA)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	Code 392	
05947774 160	PreciControl ClinChem Multi 2 (4 × 5 mL, for USA)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

For **cobas c** 311/501 analyzers:

CRP4: ACN 256

For **cobas c** 502 analyzer:

CRP4: ACN 8256

Intended use

Immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on **cobas c** systems.

Summary[1,2,3,4,5,6,7,8]

C-reactive protein is the classic acute phase protein in inflammatory reactions. It is synthesized by the liver and consists of five identical polypeptide chains that form a five-membered ring having a molecular weight of 105000 daltons. CRP is the most sensitive of the acute phase reactants and its concentration increases rapidly during inflammatory processes. Complexed CRP activates the classical complement pathway. The CRP response frequently precedes clinical symptoms, including fever. In normal healthy individuals CRP is a trace protein with a range up to 5 mg/L. After onset of an acute phase response the serum CRP concentration rises rapidly and extensively. The increase begins within 6 to 12 hours and the peak value is reached within 24 to 48 hours. Levels above 100 mg/L are associated with severe stimuli such as major trauma and severe infection (sepsis). CRP response may be less pronounced in patients suffering from liver disease. CRP assays are used to detect systemic inflammatory processes; to assess treatment of bacterial infections with antibiotics; to detect intrauterine infections with concomitant premature amniorrhexis; to differentiate between active and inactive forms of disease with concurrent infection, e.g. in patients suffering from SLE or Colitis ulcerosa; to therapeutically monitor rheumatic disease and assess anti-inflammatory therapy; to determine the presence of post-operative complications at an early stage, such as infected wounds, thrombosis and pneumonia, and to distinguish between infection and bone marrow rejection. Postoperative monitoring of CRP levels of patients can aid in the recognition of unexpected complications (persisting high or increasing levels). Measuring changes in the concentration of CRP provides useful diagnostic information about how acute and how serious a disease is. It also allows judgements about the disease genesis. Persistence of a high serum CRP concentration is usually a grave prognostic sign which generally indicates the presence of an uncontrolled infection.

Test principle[9,10]

Particle-enhanced immunoturbidimetric assay

Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The aggregates are determined turbidimetrically.

Reagents - working solutions

R1 TRIS[a)] buffer with bovine serum albumin; preservatives

R2 Latex particles coated with anti-CRP (mouse) in glycine buffer; immunoglobulins (mouse); preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

R1 is in position B and R2 is in position C.

Precautions and warnings

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

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

This kit contains components classified as follows in accordance with the European directive 1999/45/EC:

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

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

Reagent handling

Ready for use

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

Storage and stability

CRP4

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation

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

Elecsys Anti-SARS-CoV-2 S

cobas®

REF		Σ	SYSTEM
			cobas e 411
09289267190	09289267500	200	**cobas e** 601
			cobas e 602

English

System information

For **cobas e** 411 analyzer: test number 2550
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 71

Intended use

Immunoassay for the in vitro quantitative determination of antibodies (including IgG) to the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) spike (S) protein receptor binding domain (RBD) in human serum and plasma. The test is intended as an aid to assess the adaptive humoral immune response to the SARS-CoV-2 S protein.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

SARS-CoV-2, the causative agent of Coronavirus Disease 2019 (COVID-19), is an enveloped, single-stranded RNA Betacoronavirus. 7 coronaviruses have been identified as agents of human infection, causing disease ranging from mild common cold to severe respiratory failure.[1]

SARS-CoV-2 is transmitted primarily from person-to-person through respiratory droplets and aerosols.[2,3] The incubation period from infection to detectable viral load in the host commonly ranges from 2 to 14 days.[4,5] Detection of viral load can be associated with the onset of clinical signs and symptoms, although a considerable proportion of individuals remains asymptomatic or mildly symptomatic.[6,7,8] The interval during which an individual with COVID-19 is infectious has not yet been clearly established, however, transmission from symptomatic, asymptomatic, and pre-symptomatic individuals has been well described.[9,10,11]

Coronavirus genomes encode 4 main structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). The S protein is a very large transmembrane protein that assembles into trimers to form the distinctive surface spikes of coronaviruses. Each S monomer consists of an N-terminal S1 subunit and a membrane-proximal S2 subunit. The virus gains entry to the host cell through binding of the S protein to the angiotensin-converting enzyme 2 (ACE2), which is present on the surface of numerous cell types including the alveolar type II cells of the lung and epithelial cells of the oral mucosa.[12,13] Mechanistically, ACE2 is engaged by the receptor-binding domain (RBD) on the S1 subunit.[14,15]

Upon infection with SARS-CoV-2, the host mounts an immune response against the virus, typically including production of specific antibodies against viral antigens. IgM and IgG antibodies against SARS-CoV-2 appear to arise nearly simultaneously in blood.[16] There is significant inter-individual difference in the levels and chronological appearance of antibodies in COVID-19 patients, but median seroconversion has been observed at approximately 2 weeks.[17,18,19,20] Antibodies against SARS-CoV-2 with strong neutralizing capacity, especially potent if directed against the RBD, have been identified.[21,22,23,24] Numerous vaccines for COVID-19 are in development, many of which focus on eliciting an immune response to the RBD.[25,26,27]

Serologic assays can play an important role in understanding viral epidemiology in the general population and identifying individuals who are apparently naive and thus presumably susceptible to the virus.

The Elecsys Anti-SARS-CoV-2 S assay uses a recombinant protein representing the RBD of the S antigen in a double-antigen sandwich assay format, which favors the quantitative determination of high affinity antibodies against SARS-CoV-2. Quantification of the antibody response can help to determine the specific antibody titer and aid in longitudinal monitoring of the dynamics of the antibody response in individual patients.

Test principle

Double-antigen sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 20 µL of sample, biotinylated SARS-CoV-2 S-RBD-specific recombinant antigen and SARS-CoV-2 S-RBD-specific recombinant antigen labeled with a ruthenium complex[a)] form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Reagents - working solutions

The reagent rackpack is labeled as ACOV2S.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 SARS-CoV-2 S-Ag~biotin (gray cap), 1 bottle, 16 mL: Biotinylated RBD domain of SARS-CoV-2 S as recombinant antigen < 0.4 mg/L; HEPES[b)] buffer 50 mmol/L, pH 7.4; preservative.

R2 SARS-CoV-2 S-Ag~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 16 mL: RBD domain of SARS-CoV-2 S as recombinant antigen labeled with ruthenium complex < 0.4 mg/L; HEPES buffer 50 mmol/L, pH 7.4; preservative.

b) HEPES = [4-(2-hydroxyethyl)-piperazine]-ethane sulfonic acid

Precautions and warnings

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

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 dust/fume/gas/mist/vapours/spray.

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.

FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04885317 190	Tina-quant Ferritin Gen.4 250 tests	System-ID 07 6966 5	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
11355279 216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
10557897 122	Precinorm Protein (3 x 1 mL)	Code 302	
11333127 122	Precipath Protein (3 x 1 mL)	Code 303	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

For **cobas c** 311/501 analyzers:

FERR4: ACN 692

For **cobas c** 502 analyzer:

FERR4: ACN 8692

Intended use

In vitro test for the quantitative determination of ferritin in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6,7,8,9]

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon the iron content, and consists of a protein shell (apoferritin) of 24 subunits and an iron core containing an average of approx. 2500 Fe^{3+} ions (in the basic isoforms). Common to all isoforms is their construction from two separate subunits, the acidic H (heavy)-type subunit and the weakly basic L (light)-type subunit. The basic isoferritins are responsible for the long-term iron storage function and are mainly detectable in the liver, spleen and bone marrow. Acid isoferritins are found mainly in the myocardium, placenta, tumor tissue and - to a lesser extent - in the depot organs.

The determination of ferritin is necessary above all in iron metabolism diagnosis, monitoring iron therapy, ascertaining the iron reserves in groups at risk and in the differential diagnosis of anemias. It encompasses prelatent and latent iron deficiency as well as iron overloading. It is also used to distinguish between hypoferric anemia and hypochromic anemia (chronic infection and tumor anemias, sideroblastic anemia or thalassemia).

Ferritin determinations are particularly suitable for monitoring renal anemia when iron utilization and distribution disorders are present during therapy with erythropoietin. The ferritin detectable in blood is in equilibrium with the body's depot iron and hence acts as an indicator for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

The automated Roche ferritin assay is based on the immunological agglutination principle with enhancement of the reaction by latex.

Test principle[9]

Particle enhanced immunoturbidimetric assay

Human ferritin agglutinates with latex particles coated with anti-ferritin antibodies. The precipitate is determined turbidimetrically at 570/800 nm.

Reagents - working solutions

R1 TRIS buffer, pH 7.5; immunoglobulins (rabbit); preservative, stabilizers

R3 Aqueous matrix containing latex particles coated with anti-human ferritin antibodies (rabbit); preservative, stabilizers

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

Precautions and warnings

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

Reagent handling

Ready for use

Mix **cobas c** pack well before placing on the analyzer.

Storage and stability

FERR4

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 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- or K_3-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; with K_3-EDTA tubes pay particular attention that the tubes are adequately filled.

Centrifuge samples containing precipitates before performing the assay.

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

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[10]

Stability:[11]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-25) °C

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- See "Order information" section

General laboratory equipment

LDHI2

cobas®

Lactate Dehydrogenase acc. to IFCC ver.2

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03004732 122	Lactate Dehydrogenase acc. to IFCC ver.2 (300 tests)	System-ID 07 6607 0	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
10759350 190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
10759350 360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401	
12149435 122	Precinorm U plus (10 x 3 mL)	Code 300	
12149435 160	Precinorm U plus (10 x 3 mL, for USA)	Code 300	
12149443 122	Precipath U plus (10 x 3 mL)	Code 301	
12149443 160	Precipath U plus (10 x 3 mL, for USA)	Code 301	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947626 160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05947774 160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

For **cobas c** 311/501 analyzers:

LDHI2: ACN 080

LDIP2: ACN 147 (with automatic sample pre-dilution)[a)]

For **cobas c** 502 analyzer:

LDHI2: ACN 8080

LDIP2: ACN 8147 (with automatic sample pre-dilution)[a)]

a) Not available in the US

Intended use

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

Summary[1,2,3,4,5,6]

The lactate dehydrogenase (LDH) enzyme is widely distributed in tissue, particularly in the heart, liver, muscles and kidneys. The 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.

Elevated serum levels of LDH have been observed in a variety of disease states. The highest levels are seen in patients with megaloblastic anemia, disseminated carcinoma and shock. 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.

The method described here is derived from the formulation recommended by the IFCC[5,6] 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

R2 NAD: 62 mmol/L; stabilizers; preservatives

R1 is in position B and R2 is in position C.

Precautions and warnings

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

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

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

Hydroxylamine hydrochloride

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

Reagent handling

Ready for use

Storage and stability

LDHI2, LDIP2

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 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.

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 147/ACN 8147). 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

MG2

cobas®

Magnesium Gen.2

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
06481647 190	Magnesium Gen.2 (250 tests)	System-ID 07 7486 3	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
10759350 190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
10759350 360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401	
12149435 122	Precinorm U plus (10 x 3 mL)	Code 300	
12149435 160	Precinorm U plus (10 x 3 mL, for USA)	Code 300	
12149443 122	Precipath U plus (10 x 3 mL)	Code 301	
12149443 160	Precipath U plus (10 x 3 mL, for USA)	Code 301	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947626 160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05947774 160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

For **cobas c** 311/501 analyzers:

MG-2: ACN 701 (serum and plasma)

MGU-2: ACN 704 (urine)

SMG2: ACN 688 (STAT, serum and plasma, reaction time: 4)

SMG2U: ACN 689 (STAT, urine, reaction time: 4)

For **cobas c** 502 analyzer:

MG-2: ACN 8701 (serum and plasma)

MGU-2: ACN 8704 (urine)

SMG2: ACN 8688 (STAT, serum and plasma, reaction time: 4)

SMG2U: ACN 8689 (STAT, urine, reaction time: 4)

Intended use

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

Summary[1,2,3,4,5]

Magnesium along with potassium is a major intracellular cation. Mg^{2+} is a cofactor of many enzyme systems. Thus, all ATP-dependent enzymatic reactions require Mg^{2+} as a cofactor in the ATP-magnesium complex. Approximately 69 % of magnesium ions are stored in bone. The rest are part of the intermediary metabolism, about 70 % being present in free form while the other 30 % is bound to proteins (especially albumin), citrates, phosphate, and other complex formers. The Mg^{2+} serum level is kept constant within very narrow limits (0.65-1.05 mmol/L). Regulation takes place mainly via the kidneys, especially via the ascending loop of Henle.

This assay is used for diagnosing and monitoring hypomagnesemia (magnesium deficiency) and hypermagnesemia (magnesium excess). Numerous studies have shown a correlation between magnesium deficiency and changes in calcium-, potassium- and phosphate-homeostasis which are associated with cardiac disorders such as ventricular arrhythmias that cannot be treated by conventional therapy, increased sensitivity to digoxin, coronary artery spasms, and sudden death. Additional concurrent symptoms include neuromuscular and neuropsychiatric disorders. Hypermagnesemia is found in acute and chronic renal failure, magnesium excess, and magnesium release from the intracellular space.

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

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.

Urine magnesium levels are determined in magnesium depletion tests.

Test principle[5]

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

R2 Xylidyl blue: 0.28 mmol/L; detergent; preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

R1 is in position B and R2 is in position C.

Precautions and warnings

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

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

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.

03004899500V11.0

PreClean M

cobas®

REF 03004899190 **5 x 600 mL**

For USA: Elecsys PreClean M

English

Intended use

Wash solution for the removal of substances which potentially interfere with the detection of signals.

PreClean M is used in the MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers in conjunction with Elecsys assay reagents.

PreClean M can be used with all reagent lots.

Summary

PreClean M is used to remove potentially interfering substances before signal generation - the final step of the analytical procedure.

PreClean M is required when performing certain Elecsys assays. If required, its use is indicated in the "Materials required (but not provided)" section of the respective assay reagent Method Sheet.

Reagents - working solutions

5 x 600 mL detection wash solution

Phosphate buffer 10 mmol/L; sodium chloride 20 mmol/L; detergent ≤ 0.1 %; preservative; pH 7.0.

Precautions and warnings

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

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

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

PreClean M is ready for use. Avoid foam formation!

Storage and stability

Store at 15-25 °C. Store protected from light.

Stability:	
unopened	up to the stated expiration date
on the analyzer	4 weeks

Materials provided

- PreClean M

Materials required (but not provided)

- **cobas e** 601 or **cobas e** 602 analyzer. See appropriate operator's manual for additionally required materials.
- Elecsys assay reagents

Assay

Place bottles in the position provided in the analyzer (door) such that the dispensor (piercing) needle installed in the analyzer will pierce the front cap. Slightly open the lid to ensure circulation of air.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

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

Symbols

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

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
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.

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

CE

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www.roche.com

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

Roche

ms_04880340190V4.0

ProCell M

cobas®

REF **04880340** 190 **2 x 2 L**

For USA: Elecsys ProCell M

English

Intended use

System solution for generating electrochemical signals in MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 immunoassay analyzers.

ProCell M is used in conjunction with Elecsys assay reagents.

ProCell M can be used with all reagent lots.

Summary

ProCell M is used to perform the following tasks:[1,2,3,4]

- Conditioning of the electrodes
- Transport of the assay reactant mixture
- Washing of the streptavidin-coated microparticles
- Signal generation

Reagents - working solutions

2 x 2 L system buffer

Phosphate buffer 300 mmol/L, tripropylamine 180 mmol/L; detergent ≤ 0.1 %; preservative, pH 6.8.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.

Do not dispose undiluted reagent together with strong alkaline solution, e.g. Elecsys CleanCell M.

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.

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, USA: 1-800-428-2336

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The contents are ready for use. **Avoid foam formation.**

Storage and stability

Store at 15-25 °C.

Stability:	
unopened at 15-25 °C	up to the stated expiration date
on the analyzers	5 days

Materials provided

- ProCell M

Materials required (but not provided)

- MODULAR ANALYTICS E170, **cobas e** 601 or **cobas e** 602 immunoassay analyzers. See appropriate operator's manual for additionally required materials.

Assay

Place the ProCell M bottle in the appropriate position on the analyzer and insert the system's aspiration tube into the opening until the cap rests on the opening. There is no temperature adjustment required for ProCell M before use.

References

1 Blackburn GF, Shah HP, Kenten JH, et al. Electrochemiluminescence detection for development of immunoassays and DNA probe assays for clinical diagnostics. Clin Chem 1991;37(9):1534-1539.

2 Kenten JH, Casadei J, Link J, et al. Rapid electrochemiluminescence assays of polymerase chain reaction products. Clin Chem 1991;37(9):1626-1632.

3 Kenten JH, Gudibande S, Link J, et al. Improved electrochemiluminescent label for DNA probe assays: rapid quantitative assays of HIV-1 polymerase chain reaction products. Clin Chem 1992;38(6):873-879.

4 Leland JK, Powell MJ. Electrogenerated chemiluminescence: an oxidative-reduction type ECL reaction sequence using tripropyl amine. J Electrochem Soc 1990;137(10):3127-3131.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

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

Symbols

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

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
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.

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

CleanCell M

cobas®

REF **04880293** 190 **2 x 2 L**

For USA: Elecsys CleanCell M

English

Reagent handling: Ready for use. Avoid foam formation.

Storage and stability: on the MODULAR ANALYTICS E170 and **cobas e** analyzers: 21 days

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

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.

Prevention:

P234	Keep only in original packaging.
P264	Wash skin thoroughly after handling.
P280	Wear protective gloves/ eye protection/ face protection.

Response:

P332 + P313	If skin irritation occurs: Get medical advice/attention.
P337 + P313	If eye irritation persists: Get medical advice/attention.
P390	Absorb spillage to prevent material damage.

Product safety labeling follows EU GHS guidance.

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

For US users: Warning. Bottles contain potassium hydroxide solution; corrosive. In case of contact, flush areas with copious amounts of water. Get immediate medical attention for eyes, or if ingested.

Deutsch

Reagenz-Handhabung: Gebrauchsfertig. Schaumbildung vermeiden.

Lagerung und Haltbarkeit: auf MODULAR ANALYTICS E170 und **cobas e** Geräten: 21 Tage

Für USA: Achtung: Gemäß USA Bundesgesetz ist der Verkauf dieses Produktes nur auf Anforderung eines Arztes gestattet.

Die Packung enthält Bestandteile, die gemäß der Verordnung (EG) Nr. 1272/2008 wie folgt klassifiziert sind:

Warnung

H290	Kann gegenüber Metallen korrosiv sein.
H315	Verursacht Hautreizungen.
H319	Verursacht schwere Augenreizung.

Prävention:

P234	Nur in Originalverpackung aufbewahren.
P264	Nach Gebrauch Haut gründlich waschen.
P280	Schutzhandschuhe / Augenschutz / Gesichtsschutz tragen.

Reaktion:

P332 + P313	Bei Hautreizung: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen.
P337 + P313	Bei anhaltender Augenreizung: Ärztlichen Rat einholen/ärztliche Hilfe hinzuziehen.
P390	Verschüttete Mengen aufnehmen, um Materialschäden zu vermeiden.

Die Produktsicherheitskennzeichnung folgt den in der EU gültigen GHS-Regularien.

Kontakt: Tel.-Nr.: +49-621-7590 für alle Länder; 1-800-428-2336 für USA

Für US-Anwender: Warnung. Die Flaschen enthalten Kaliumhydroxidlösung; ätzend. Bei Kontakt die betroffenen Stellen mit reichlich fließendem Wasser abspülen. Bei Kontamination der Augen oder beim Verschlucken sofort einen Arzt aufsuchen.

Français

Préparation des réactifs: Prêt à l'emploi. Éviter la formation de mousse.

Conservation et stabilité sur les analyseurs MODULAR ANALYTICS E170 et **cobas e**: 21 jours

Pour les USA: Attention: Selon la législation US, ce produit ne peut être vendu que sur ordre d'un médecin.

Ce coffret contient des substances classées de la manière suivante selon le Règlement (CE) No. 1272/2008 :

Mise en garde

H290	Peut être corrosif pour les métaux.
H315	Provoque une irritation cutanée.
H319	Provoque une sévère irritation des yeux.

Prévention:

P234	Conserver uniquement dans l'emballage d'origine.
P264	Se laver la peau soigneusement après manipulation.
P280	Porter des gants de protection/ un équipement de protection des yeux/ du visage.

Réponse:

P332 + P313	En cas d'irritation cutanée: consulter un médecin.
P337 + P313	Si l'irritation oculaire persiste: consulter un médecin.
P390	Absorber toute substance répandue pour éviter qu'elle attaque les matériaux environnants.

L'étiquetage de sécurité du produit est conforme à la réglementation EU GHS.

Contact tél.: tous pays: +49-621-7590, USA: 1-800-428-2336

Pour les USA: Mise en garde. Les flacons contiennent de l'hydroxyde de potassium. Corrosif. En cas de contact, rincer abondamment avec de l'eau. En cas de contact avec les yeux, ou d'ingestion, consulter immédiatement un médecin.

Español

Preparación de los reactivos: Los reactivos están listos para el uso. Evitar la formación de espuma.

Conservación y estabilidad en los analizadores MODULAR ANALYTICS E170 y **cobas e**: 21 días

Para los EE.UU.: ¡Atención! Según la ley federal estadounidense, este producto puede ser vendido exclusivamente por facultativos o por prescripción médica.

El presente estuche contiene componentes que han sido clasificados por la directiva CE No. 1272/2008 de la siguiente manera:

CleanCell M

cobas®

¡Atención!

H290	Puede ser corrosivo para los metales.
H315	Provoca irritación cutánea.
H319	Provoca irritación ocular grave.

Prevención:

P234	Conservar únicamente en el recipiente original.
P264	Lavarse la piel concienzudamente tras la manipulación.
P280	Llevar guantes/gafas/máscara de protección.

Respuesta:

P332 + P313	En caso de irritación cutánea: Consultar a un médico.
P337 + P313	Si persiste la irritación ocular: Consultar a un médico.
P390	Absorber el vertido para que no dañe otros materiales.

Las indicaciones de seguridad del producto corresponden a los criterios del sistema globalmente armonizado de clasificación y etiquetado de productos químicos (GHS por sus siglas en inglés) válidas en la UE.

Contacto telefónico internacional: +49-621-7590, en los EE.UU.: 1-800-428-2336

Usuarios estadounidenses: ¡Atención! Los frascos contienen una solución corrosiva de hidróxido de potasio. En caso de contacto, enjuagar las áreas afectadas con abundantes cantidades de agua. Consultar de inmediato a un médico en caso de ingestión o contacto con los ojos.

Italiano

Utilizzo dei reattivi: pronti all'uso. Evitare la formazione di schiuma.

Conservazione e stabilità: sugli analizzatori MODULAR ANALYTICS E170 e **cobas e**: 21 giorni

Per gli USA: attenzione: secondo la legge federale, la vendita di questo prodotto deve avvenire solo dietro richiesta di un medico.

Questa confezione contiene componenti classificati, secondo il Regolamento (CE) N. 1272/2008, come segue:

Avvertenza

H290	Può essere corrosivo per i metalli.
H315	Provoca irritazione cutanea.
H319	Provoca grave irritazione oculare.

Prevenzione:

P234	Conservare soltanto nell'imballaggio originale.
P264	Lavare accuratamente la pelle dopo l'uso.
P280	Indossare guanti protettivi/Proteggere gli occhi/il viso.

Reazione:

P332 + P313	In caso di irritazione della pelle: consultare un medico.
P337 + P313	Se l'irritazione degli occhi persiste, consultare un medico.
P390	Assorbire la fuoriuscita per evitare danni materiali.

L'etichettatura relativa alla sicurezza del prodotto è conforme al regolamento GHS UE.

Contatto telefonico: per tutti i paesi: +49-621-7590;
per gli USA: 1-800-428-2336

Per gli utilizzatori negli USA: avvertenza: i flaconi contengono una soluzione di idrossido di potassio; corrosivo. In caso di contatto, sciacquare abbondantemente le aree affette. In caso di contatto con gli occhi, oppure se ingerito, consultare subito un medico.

Português

Preparação dos reagentes: Pronto a ser utilizado. Evite a formação de espuma.

Armazenamento e estabilidade: nos analisadores MODULAR ANALYTICS E170 e **cobas e**: 21 dias

Nos EUA: Atenção: Segundo a lei federal norte-americana, a venda deste dispositivo é restrita a médicos ou por prescrição destes.

Este dispositivo contém componentes que estão classificados da seguinte forma, de acordo com o Regulamento (CE) N.º 1272/2008:

Aviso

H290	Pode ser corrosivo para os metais.
H315	Provoca irritação cutânea.
H319	Provoca irritação ocular grave.

Prevenção:

P234	Conservar unicamente na embalagem de origem.
P264	Lavar a pele cuidadosamente após manuseamento.
P280	Usar luvas de protecção/protecção ocular/protecção facial.

Resposta:

P332 + P313	Em caso de irritação cutânea: consulte um médico.
P337 + P313	Caso a irritação ocular persista: consulte um médico.
P390	Absorver o produto derramado a fim de evitar danos materiais.

A rotulagem de segurança do produto cumpre as directivas EU GHS.

Telefone de contacto: todos os países: +49-621-7590, EUA: +1-800-428-2336

Para os utilizadores dos EUA: Aviso Os frascos contêm uma solução de hidróxido de potássio; corrosivo. Em caso de contacto, lavar as zonas afectadas imediata e abundantemente com água. Em caso de contacto com os olhos ou ingestão, contactar imediatamente um médico.

Dansk

Reagenshåndtering: Klar til brug. Undgå skumdannelse.

Opbevaring og holdbarhed: på MODULAR ANALYTICS E170 og **cobas e** analyseinstrumenter: 21 dage

I USA: Vigtigt: Lovgivningen påbyder, at salg af dette produkt kun må foretages af en læge eller efter lægelig ordination.

Dette kit indeholder komponenter, som i overensstemmelse med Europa-Parlamentets og Rådets forordning (EF) nr. 1272/2008 er klassificeret som følger:

Advarsel

H290	Kan ætse metaller.
H315	Forårsager hudirritation.
H319	Forårsager alvorlig øjenirritation.

Forebyggelse:

P234	Opbevares kun i den originale emballage.

P264	Vask huden grundigt efter brug.
P280	Bær beskyttelseshandsker/øjenbeskyttelse/ansigtsbeskyttelse.

Reaktion:

P332 + P313	Ved hudirritation: Søg lægehjælp.
P337 + P313	Ved vedvarende øjenirritation: Søg lægehjælp.
P390	Absorber udslip for at undgå materielskade.

Produktets sikkerhedsmærkning følger EUs GHS-retningslinjer.

Ved alvorlige tilfælde: Visiterende læge kan henvise til arbejds- og miljømedicinsk afdeling på Bispebjerg Hospital, tlf. 35 31 60 60.

Amerikanske brugere: Advarsel. Flaskerne indeholder kaliumhydroxidopløsning, ætsende. Kommer stoffet på huden, vaskes straks med store mængder vand. Kontakt omgående læge ved kontakt med øjnene eller ved indtagelse.

Svenska

Reagenshantering: Bruksfärdigt. Undvik skumbildning.

Förvaring och hållbarhet på analysinstrumenten MODULAR ANALYTICS E170 och **cobas e**: 21 dagar

För USA: Försiktighet: Amerikansk lag påbjuder att försäljning av denna produkt endast får ske av eller på uppmaning av en läkare.

Detta kit innehåller komponenter klassificerade som följer, i enlighet med Europaparlamentets och rådets förordning (EG) nr 1272/2008:

Varning

H290	Kan vara korrosivt för metaller.
H315	Irriterar huden.
H319	Orsakar allvarlig ögonirritation.

Förebyggande:

P234	Förvaras endast i originalförpackningen.
P264	Tvätta huden grundligt efter användning.
P280	Använd skyddshandskar/skyddsglasögon/ansiktsskydd.

Reaktion:

P332 + P313	Vid hudirritation: Sök läkarhjälp.
P337 + P313	Vid bestående ögonirritation: Sök läkarhjälp.
P390	Sug upp spill för att undvika materiella skador.

Produktsäkerhetsmärkningen följer EU GHS-riktlinjer.

Kontakttelefon, alla länder: +49-621-7590, USA: 1-800-428-2336

För användare i USA: Varning. Flaskorna innehåller kaliumhydroxidlösning, frätande. Vid eventuell kontakt, spola angripna områden med mycket stora mängder vatten. Sök omedelbart läkarhjälp för ögonen eller om substansen intagits.

Norsk

Reagenshåndtering: Klar til bruk. Unngå skumdannelse.

Oppbevaring og holdbarhet: På MODULAR ANALYTICS E170 og **cobas e**-analyseinstrumenter: 21 dager

For USA: Forsiktig: Amerikansk lov påbyr at salg av dette produktet kun kan rekvireres av en lege.

Dette kittet inneholder komponenter, som i overensstemmelse med forordning (EF) nr. 1272/2008 EF, er klassifisert som beskrevet:

Advarsel

H290	Kan etse metaller.
H315	Irriterer huden.
H319	Forårsaker alvorlig øyeirritasjon.

Forebygging:

P234	Oppbevares kun i originalpakningen.
P264	Vask huden grundig etter bruk.
P280	Bruk vernehansker/ vernebriller/ ansiktsskjerm.

Respons:

P332 + P313	Ved hudirritasjon: Kontakt lege.
P337 + P313	Ved vedvarende øyeirritasjon: Kontakt lege.
P390	Tørk opp søl for å forhindre materiell skade.

Produktsikkerhetsmerkingen følger retningslinjene til EU GHS.

Kontakttelefon: Giftinformasjonen 22 59 13 00. Kontakttelefon alle land: +49-621-7590, USA: 1-800-428-2336

For brukere i USA: Advarsel. Flaskene inneholder kaliumhydroksidløsning; etsende. Ved kontakt, skyll områdene med rikelige mengder vann. Søk legehjelp omgående hvis stoffet kommer i øynene eller svelges.

Česky

Zacházení s reagenciemi: Připraveno k použití. Zabraňte tvorbě pěny.

Uskladnění a stabilita: na analyzátorech MODULAR ANALYTICS E170 a **cobas e**: 21 dní

Pro USA: Varování: Federální zákon omezuje prodej tohoto přístroje pouze lékařem nebo na jeho pokyn.

Tato souprava obsahuje složky klasifikované v souladu s nařízením (ES) č. 1272/2008 takto:

Varování

H290	Může být korozivní pro kovy.
H315	Dráždí kůži.
H319	Způsobuje vážné podráždění očí.

Prevence:

P234	Uchovávejte pouze v původním obalu.
P264	Po manipulaci důkladně omyjte kůži.
P280	Používejte ochranné rukavice/ ochranné brýle/ obličejový štít.

Reakce:

P332 + P313	Při podráždění kůže: Vyhledejte lékařskou pomoc/ošetření.
P337 + P313	Přetrvává-li podráždění očí: Vyhledejte lékařskou pomoc/ošetření.
P390	Uniklý produkt absorbujte, aby se zabránilo materiálním škodám.

Bezpečnostní značky výrobku se řídí pokyny EU GHS.

Kontaktní telefon: všechny země: +49-621-7590, USA: 1-800-428-2336

Pro uživatele v USA: Varování. Nádobky obsahují roztok hydroxidu draselného; žíravý. V případě kontaktu, opláchněte zasažené místo proudem vody. Při zasažení očí nebo při požití vyhledejte okamžitou lékařskou pomoc.

CleanCell M

cobas®

Slovensky

Zaobchádzanie s reagenciou: Pripravené na použitie. Vyhnite sa napeneniu.

Skladovanie a stabilita: v analyzátoroch MODULAR ANALYTICS E170 a **cobas e**: 21 dní

Pre USA: Pozor: Americký federálny zákon umožňuje predaj tohto zariadenia len na základe objednávky od lekára.

Táto súprava obsahuje zložky klasifikované nasledovne podľa Smernice (EC) č. 1272/2008:

Varovanie

H290	Môže by korozívna pre kovy.
H315	Dráždi kožu.
H319	Spôsobuje vážne podráždenie očí.

Prevencia:

P234	Uchovávajte iba v pôvodnom balení.
P264	Po zaobchádzaní s produktom si dôkladne umyte ruky.
P280	Používajte vhodné ochranné rukavice a ochranu očí/tváre.

Reakcia:

P332 + P313	Ak sa objaví podráždenie pokožky, vyhľadajte lekársku pomoc/starostlivosť.
P337 + P313	Ak podráždenie očí pretrváva: vyhľadajte lekársku pomoc/starostlivosť.
P390	Absorbujte uniknutý produkt, aby sa zabránilo materiálnym škodám.

Bezpečnostné označenie výrobku sa riadi smernicami EU GHS.

Kontaktný telefón pre všetky krajiny: +49-621-7590, USA: 1-800-428-2336

Pre používateľov v USA: Varovanie. Fľašky obsahujú roztok hydroxidu draselného, žieravinu. V prípade kontaktu opláchnite postihnuté miesto veľkým množstvom vody. Pri postihnutí očí alebo prehltnutí vyhľadajte okamžite lekársku pomoc.

Polski

Postępowanie z odczynnikiem: Gotowe do użycia. Unikać tworzenia się piany.

Przechowywanie i stabilność: analizatory MODULAR ANALYTICS E170 i **cobas e**: 21 dni

Dla USA: Uwaga: Prawo federalne zezwala na sprzedaż niniejszego urządzenia wyłącznie na podstawie recepty lekarskiej.

Zestaw zawiera składniki sklasyfikowane zgodnie z Wytyczną (UE) nr 1272/2008, w następujący sposób:

Ostrzeżenie

H290	Może powodować korozję metali.
H315	Działa drażniąco na skórę.
H319	Działa drażniąco na oczy.

Zapobieganie:

P234	Przechowywać w oryginalnym opakowaniu.
P264	Po użyciu dokładnie umyć ręce.
P280	Należy nosić rękawice ochronne/ okulary/ zabezpieczenie twarzy.

W razie kontaktu:

P332 + P313	W przypadku wystąpienia podrażnienia skóry: Zasięgnąć porady/zgłosić się pod opiekę lekarza.
P337 + P313	W przypadku utrzymywania się działania drażniącego na oczy: Zasięgnąć porady/zgłosić się pod opiekę lekarza.
P390	Usunąć wyciek, aby zapobiec szkodom materialnym.

Oznakowanie wyrobu dotyczące bezpieczeństwa wg. wytycznych EU GHS.

Telefon kontaktowy dla wszystkich krajów: +49-621-7590; USA: 1-800-428-2336

Dla użytkowników w USA: Uwaga! Zawiera wodorotlenek potasu; żrący. W razie kontaktu spłukać dużą ilością wody. W przypadku kontaktu z oczami lub połknięcia natychmiast zgłosić się po pomoc lekarską.

Magyar

A reagens kezelése: Használatra kész. Kerülni kell a habképződést.

Tárolás és eltarthatóság: MODULAR ANALYTICS E170 és **cobas e** analizátorokon: 21 nap

USA-felhasználás esetén: Figyelem! Jelen anyag orvos által történő eladása vagy felírása szövetségi törvényi korlátozás alá esik.

A készlet olyan összetevőket tartalmaz, amelyek az 1272/2008 (EK) rendelet szerint az alábbi minősítésűek:

Figyelmeztetés

H290	Fémekre korrozív hatású lehet.
H315	Bőrirritáló hatású.
H319	Súlyos szemirritációt okoz.

Megelőzés:

P234	Az eredeti csomagolásban tárolandó.
P264	A használatot követően a bőrt alaposan meg kell mosni.
P280	Védőkesztyű / szemvédő / arcvédő használata kötelező.

Ellenintézkedés:

P332 + P313	Bőrirritáció esetén: orvosi ellátást kell kérni.
P337 + P313	Ha a szemirritáció nem múlik el: orvosi ellátást kell kérni.
P390	A kiömlött anyagot fel kell itatni a körülvevő anyagok károsodásának megelőzése érdekében.

A termékbiztontonsági feliratozás az EU GHS irányelveket követi.

Ügyfélszolgálati telefonszám: nemzetközi: +49-621-7590, USA: 1-800-428-2336

USA-felhasználás esetén: Vigyázat! A fiolák káliumhidroxid oldatot tartalmaznak; maró hatású. Bőrrel történő érintkezés esetén az érintett területeket öblítsék le bő vízzel. Szembe kerülése vagy lenyelése esetén forduljanak orvoshoz!

Ελληνικά

Χειρισμός του αντιδραστηρίου: Έτοιμο προς χρήση. Αποφύγετε το σχηματισμό αφρού.

Φύλαξη και σταθερότητα: στους αναλυτές MODULAR ANALYTICS E170 και **cobas e**: 21 ημέρες

Για τις Η.Π.Α.: Προσοχή: Η ομοσπονδιακή νομοθεσία περιορίζει την πώληση του προϊόντος αυτού μόνο σε ιατρούς ή κατόπιν εντολής ιατρού.

Το κιτ περιέχει συστατικά ταξινομημένα ως εξής σύμφωνα με την οδηγία (ΕΚ) αρ. 1272/2008:

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Προειδοποίηση

H290	Μπορεί να διαβρώσει μέταλλα.
H315	Προκαλεί ερεθισμό του δέρματος.
H319	Προκαλεί σοβαρό οφθαλμικό ερεθισμό.

Πρόληψη:

P234	Να διατηρείται μόνο στην αρχική συσκευασία.
P264	Πλύνετε το δέρμα σχολαστικά μετά τον χειρισμό.
P280	Να φοράτε προστατευτικά γάντια / μέσα ατομικής προστασίας για τα μάτια/πρόσωπο.

Ανταπόκριση:

P332 + P313	Εάν παρατηρηθεί ερεθισμός του δέρματος: Συμβουλευθείτε/Επισκεφθείτε γιατρό.
P337 + P313	Εάν δεν υποχωρεί ο οφθαλμικός ερεθισμός: Συμβουλευθείτε/Επισκεφθείτε γιατρό.
P390	Σκουπίστε τη χυμένη ποσότητα για να προλάβετε υλικές ζημιές.

Η επισήμανση ασφάλειας του προϊόντος τηρεί τις οδηγίες GHS της Ε.Ε.

Τηλέφωνο επικοινωνίας: για όλες τις χώρες: +49-621-7590, για τις Η.Π.Α.: 1-800-428-2336

Για χρήση στις Η.Π.Α.: Προειδοποίηση. Τα φιαλίδια περιέχουν διάλυμα υδροξειδίου του καλίου. Διαβρωτικό. Σε περίπτωση επαφής, ξεπλύνετε τις προσβεβλημένες περιοχές με άφθονο νερό. Εάν έλθει σε επαφή με τα μάτια ή καταποθεί, αναζητήστε άμεσα ιατρική φροντίδα.

Türkçe

Reaktif kullanımı: Kullanıma hazır. Köpük oluşmasından kaçının.

Saklama ve stabilite: MODULAR ANALYTICS E170 ve **cobas e** analizörlerinde: 21 gün

ABD için: Dikkat: Federal yasa bu cihazın satışına bir hekim tarafından veya hekim istemiyle yapılması yönünde bir kısıtlama getirmiştir.

Bu kit 1272/2008 sayılı Düzenlemeye (EC) göre aşağıdaki şekilde sınıflandırılan bileşenler içerir:

Uyarı

H290	Metallerde aşındırıcı olabilir.
H315	Deride tahrişe neden olur.
H319	Gözde ciddi tahrişe neden olur.

Önleme:

P234	Sadece orijinal ambalajında saklayın.
P264	Elleçlemeden sonra cildi iyice yıkayın.
P280	Koruyucu eldiven/ göz koruyucu/yüz koruyucu kullanın.

Yanıt:

P332 + P313	Deride tahriş olursa: Tıbbi tavsiye/yardım alın.
P337 + P313	Gözde tahriş devam ederse: Tıbbi tavsiye/yardım alın.
P390	Materyal hasarını önlemek için dökülmeyi emdirin.

Ürün güvenlik etiketi AB GHS kılavuzlarına tabidir.

İletişim telefon numarası: tüm ülkeler: +49-621-7590, ABD: 1-800-428-2336

Yalnızca ABD kullanıcıları için: Uyarı. Şişeler potasyum hidroksit solüsyonu içerir; aşındırıcıdır. Temas etmesi durumunda, etkilenen alanları bol miktarda su ile yıkayın. Gözlere temas etmesi veya yutulması durumunda derhal tıbbi yardım alın.

Български

Работа с реактивите: Готови за употреба. Да се избягва образуването на пяна.

Съхранение и годност: в анализатори MODULAR ANALYTICS E170 и **cobas e**: 21 дни

За САЩ: Внимание: Според федералния закон, този продукт трябва да се продава от лекар или с рецепта.

Този кит съдържа компоненти, класифицирани, както следва съгласно Регламент (ЕО) № 1272/2008:

Предупреждение

H290	Може да бъде корозивно за металите.
H315	Предизвиква дразнене на кожата.
H319	Предизвиква сериозно дразнене на очите.

Превенция:

P234	Да се съхранява само в оригиналната опаковка.
P264	Кожата да се измие старателно след употреба.
P280	Използвайте предпазни ръкавици/ защита за очите/ лицето.

Отговор:

P332 + P313	При поява на кожно дразнене: Потърсете медицински съвет/помощ.
P337 + P313	При продължително дразнене на очите: Потърсете медицински съвет/помощ.
P390	Попийте разлятото, за да се предотвратят материални вреди.

Етикетирането за безопасност на продуктите основно следва насоките GHS на ЕС.

Телефон за контакти: всички страни: +49-621-7590, САЩ: 1-800-428-2336

За потребителите в САЩ: Предупреждение. Шишетата съдържат разтвор на калиев хидроксид; корозивно. В случай на контакт, измийте засегнатите зони с обилни количества вода. Потърсете незабавна медицинска помощ за очите или при поглъщане.

Eesti keel

Reaktiivide käsitsemine: Valmis kasutamiseks. Vältige vahu teket.

Säilitamine ja stabiilsus: MODULAR ANALYTICS E170 ja **cobas e** analüsaatoril: 21 päeva

USA jaoks: Ettevaatust: Föderaalseaduse alusel on selle toote müük lubatud ainult arsti poolt või arsti korraldusel.

Komplekt sisaldab komponente, mida klassifitseeritakse kooskõlas Euroopa Parlamendi ja nõukogu määrusega (EÜ) nr 1272/2008 järgmiselt:

Hoiatus

H290	Võib söövitada metalle.
H315	Põhjustab nahaärritust.
H319	Põhjustab tugevat silmade ärritust.

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Ennetamine:

P234 Hoida üksnes originaalpakendis.

P264 Pärast käsitsemist peske nahk põhjalikult.

P280 Kanda kaitsekindaid/kaitserõivastust/kaitseprille/kaitsemaski.

Reageerimine:

P332 + P313 Nahaärrituse korral: pöörduda arsti poole.

P337 + P313 Kui silmade ärritus ei möödu: pöörduda arsti poole.

P390 Mahavoolanud toode absorbeerida, et see ei kahjustaks teisi materjale.

Toote ohutusmärgistus järgib EL-i GHS juhiseid.

Kontakttelefon: kõik riigid: +49-621-7590, USA: 1-800-428-2336

USA kasutajatele: Hoiatus. Pudelid sisaldavad kaaliumhüdroksiidi lahust, mis on söövitav. Kokkupuute korral loputage kahjustatud piirkondi rohke jooksva veega. Silma sattumisel või allaneelamise korral pöörduge kohe arsti poole.

Lietuvių

Reagentų paruošimas: Paruošti naudojimui. Venkite putų susidarymo.

Laikymo sąlygos ir stabilumas: MODULAR ANALYTICS E170 ir **cobas e** analizatoriuose: 21 diena

Skirta JAV: DĖMESIO: Federaliniai įstatymai leidžia šį prietaisą parduoti tik gydytojui arba gydytojo paskyrimu.

Šiame rinkinyje yra komponentų, kurie pagal reglamentą (EB) Nr. 2008/1272 skirstomi į šias klases:

Įspėjimas

H290 Gali esdinti metalus.

H315 Dirgina odą.

H319 Sukelia smarkų akių dirginimą.

Prevencija:

P234 Laikyti tik originalioje pakuotėje.

P264 Po naudojimo kruopščiai nuplauti odą.

P280 Mūvėti apsaugines pirštines/naudoti akių (veido) apsaugos priemones.

Veiksmai, kurių reikia imtis:

P332 + P313 Jeigu sudirginama oda: kreiptis į gydytoją.

P337 + P313 Jei akių dirginimas nepraeina: kreiptis į gydytoją.

P390 Absorbuoti išsiliejusią medžiagą, siekiant išvengti materialinės žalos.

Produktų saugumo žymėjimas parengtas vadovaujantis ES GHS gairėmis.

Kontaktinis telefono numeris: visos šalys: +49-621-7590, JAV: 1-800-428-2336

JAV vartotojams: Įspėjimas. Buteliukuose yra kalio hidroksido tirpalo; ardantis (ėsdinantis). Kontakto atveju plauti paveiktą sritį gausiu kiekiu vandens. Patekus į akis ar nurijus, nedelsiant ieškoti medicininės pagalbos.

Latviešu

Darbs ar reaģentiem: gatavs lietošanai. Nepieļaujiet putu veidošanos.

Glabāšana un stabilitāte: MODULAR ANALYTICS E170 un **cobas e** analizatoros: 21 diena

ASV: Uzmanību! saskaņā ar federālajiem tiesību aktiem šo ierīci ir atļauts iegādāties tikai no ārsta vai ar ārsta rīkojumu.

Šis komplekts satur sastāvdaļas, kurām saskaņā ar Regulu (EK) Nr. 1272/2008 ir šāda klasifikācija:

Brīdinājums

H290 Var kodīgi iedarboties uz metāliem.

H315 Kairina ādu.

H319 Izraisa nopietnu acu kairinājumu.

Novēršana:

P234 Turēt tikai oriģinālā iepakojumā.

P264 Pēc izmantošanas kārtīgi nomazgāt ādu.

P280 Izmantot aizsargcimdus/acu aizsargus/sejas aizsargus.

Reakcija:

P332 + P313 Ja rodas ādas iekaisums: lūdziet medicīnisku palīdzību.

P337 + P313 Ja acu iekaisums nepāriet: lūdziet medicīnisku palīdzību.

P390 Uzsūkt izšļakstījumus, lai novērstu materiālus zaudējumus.

Produkta drošības marķējums atbilst ES GHS prasībām.

Kontakttālrunis: visām valstīm: +49-621-7590, ASV: 1-800-428-2336

Lietotājiem ASV: brīdinājums. Pudelītēs ir kālija hidroksīda šķīdums; korozīvs. Šai vielai nokļūstot uz ādas, skalojiet skartās vietas ar lielu daudzumu ūdens. Ja pudelītes saturs iekļūst acīs vai tiek norīts, nekavējoties vērsieties pēc medicīniskas palīdzības.

Русский

Приготовление рабочего раствора: готов к применению. Избегайте образования пены.

Хранение и стабильность: на анализаторах MODULAR ANALYTICS E170 и **cobas e**: 21 день

Для США: Внимание: Федеральный закон ограничивает данного устройства, разрешена продажа только врачу или по его указанию.

Этот набор содержит компоненты, классифицируемые следующим образом в соответствии с Регламентом (ЕС) № 1272/2008:

Предупреждение

H290 Может вызывать коррозию металлов.

H315 Вызывает раздражение кожи.

H319 Вызывает серьезное раздражение глаз.

Меры предосторожности:

P234 Хранить только в оригинальном контейнере.

P264 После работы с реагентом тщательно вымыть кожу.

P280 Рекомендуется использовать защитные перчатки/средства защиты для глаз/лица.

Ответные действия:

P332 + P313 При возникновении раздражения кожи: Обратиться за медицинской консультацией / помощью.

P337 + P313 При длительном раздражении глаз: Обратиться за медицинской консультацией / помощью.

P390 Собрать пролитую жидкость, для предотвращения материального ущерба.

Маркировка о безопасности продукта соответствует руководству EU GHS.

Контактный телефон: для всех стран: +49-621-7590, США: 1-800-428-2336

Для пользователей в США: Предупреждение. Флаконы содержат раствор гидроксида калия; едкое вещество. В случае попадания на кожу промыть пораженные участки большим количеством воды. При попадании в глаза или проглатывании вещества немедленно обратиться к врачу.

Symbols / Symbole / Symboles / Símbolos / Simboli / Símbolos / Symboler / Symboler / Symboler / Symboly / Symboly / Symbole / Szimbólumok / Σύμβολα / Semboller / Символи / Sümbolid / Simboliai / Simboli / Символы

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see https://usdiagnostics.roche.com for definition of symbols used): / In Erweiterung zur ISO 15223-1 werden von Roche Diagnostics folgende Symbole und Zeichen verwendet (für USA: Definition der verwendeten Symbole, siehe https://usdiagnostics.roche.com): / Roche Diagnostics utilise les signes et les symboles suivants en plus de ceux de la norme ISO 15223-1 (pour les USA : voir https://usdiagnostics.roche.com pour la définition des symboles utilisés) : / Roche Diagnostics emplea los siguientes símbolos y signos adicionalmente a los indicados en la norma ISO 15223-1 (para los EE.UU.: consulte https://usdiagnostics.roche.com para la definición de los símbolos usados). / Oltre a quelli indicati nello standard ISO 15223-1, Roche Diagnostics impiega i seguenti simboli (per gli USA: per la definizione dei simboli impiegati, vedere https://usdiagnostics.roche.com): / A Roche Diagnostics utiliza os seguintes símbolos e sinais além dos listados na norma ISO 15223-1 (nos EUA: visite https://usdiagnostics.roche.com para consultar a definição dos símbolos utilizados): / Roche Diagnostics anvender nedenstående tegn og symboler ud over dem, der er angivet i ISO 15223-1-standarden (for USA: se https://usdiagnostics.roche.com for definition af de anvendte symboler): / Roche Diagnostics använder följande symboler och tecken utöver de som anges i ISO 15223-1-standarden (för USA: se https://usdiagnostics.roche.com för definition av symbols som används): / Roche Diagnostics bruker følgende symboler og tegn i tillegg til de som er listet opp i ISO standarden 15223-1 (for USA: se https://usdiagnostics.roche.com for definisjon av brukte symboler): / Roche Diagnostics používá kromě symbolů a znaků uvedených v normě ISO 15223-1 následující znaky (pro USA: pro definici použitých symbolů navštivte stránku https://usdiagnostics.roche.com): / Okrem znakov a symbolov uvedených v norme ISO 15223-1 používa Roche Diagnostics aj nasledujúce symboly a znaky (pre USA: pozri https://usdiagnostics.roche.com pre definíciu použitých symbolov: / Oprócz znaków zawartych w standardzie ISO 15223-1 (dla USA definicje używanych symboli, zob.: https://usdiagnostics.roche.com), firma Roche Diagnostics używa następujących symboli i znaków: / Az ISO 15223-1 szabványban feltüntetetteken kívül a Roche Diagnostics az alábbi szimbólumokat és jelöléseket alkalmazza (USA-felhasználás esetén: az alkalmazott szimbólumok definícióját lásd https://usdiagnostics.roche.com): / Η Roche Diagnostics χρησιμοποιεί τα ακόλουθα σύμβολα και σήματα πέραν αυτών που παρατίθενται στο πρότυπο ISO 15223-1 (για τις Η.Π.Α.: βλέπε https://usdiagnostics.roche.com για τον ορισμό των συμβόλων που χρησιμοποιούνται): / Roche Diagnostics, ISO 15223-1 standardında listelenenlerin yanı sıra aşağıdaki sembol ve işaretleri kullanmaktadır (ABD için: kullanılan sembollerin açıklaması için bkz. https://usdiagnostics.roche.com): / Roche Diagnostics използва следните символи и знаци, освен посочените в ISO 15223-1 стандарт (за САЩ: вижте https://usdiagnostics.roche.com за дефиниция на използваните символи): / Roche Diagnostics kasutab järgmisi märke ja sümboleid lisaks loetelule ISO 15223-1 standardis (USAs: kasutatud sümbolite selgitust vt https://usdiagnostics.roche.com): / Roche Diagnostics papildomai naudoja šiuos simbolius ir ženklus, be išvardytų standarte ISO 15223-1 (skirta JAV: naudojamų simbolių apibūdinimo ieškokite https://usdiagnostics.roche.com): / Papildus standartā ISO 15223-1 norādītajiem Roche Diagnostics izmanto šādus simbolus un apzīmējumus (ASV: izmantoto simbolu skaidrojumu skatīt vietnē https://usdiagnostics.roche.com): / В дополнение к перечисленным в стандарте ISO 15223-1, Roche Diagnostics применяет следующие символы и знаки (для США: см. https://usdiagnostics.roche.com для определения используемых символов):

CONTENT	Contents of kit / Inhalt der Packung / Contenu du coffret / Contenido del estuche / Contenuto della confezione / Conteúdo do dispositivo / Indhold i pakning / Innehåll i förpackning / Pakningsinnhold / Obsah soupravy / Obsah súpravy / Zawartość zestawu / A csomag tartalma / Περιεχόμενα του κιτ / Kit içeriği / Съдържание на кита / Komplekti sisu / Rinkinio turinys / Iepakojuma saturs / Состав набора
SYSTEM	Analyzers/Instruments on which reagents can be used / Geräte, auf denen die Reagenzien verwendet werden können / Analyseurs/appareils compatibles avec les réactifs / Analizadores/instrumentos adecuados para los reactivos / Analizzatori/strumenti su cui i reagenti possono essere usati / Analisadores/equipamentos em que os reagentes podem ser utilizados / Instrumenter, hvor reagenserne kan anvendes / Analysinstrument på vilka reagensen kan användas / Analyseinstrumenter hvor reagensene kan brukes / Analyzátory/přístroje, na kterých lze reagencie použít / Analyzátory/Prístroje, na ktorých môžu byť reagencie použité / Analizatory/aparaty, w których można zastosować odczynniki / Olyan analizátorok/készülékek, amelyeken a reagensek felhasználhatók / Αναλυτές στους οποίους μπορούν να χρησιμοποιηθούν τα αντιδραστήρια / Reaktiflerin kullanılabileceği analizörler/cihazlar / Анализатори/апарати, в които могат да се използват реактивите / Analüsaatorid/aparaadid, millel saab reaktiive kasutada / Analizatoriai/instrumentai, su kuriais gali būti naudojami reagentai / Analizatori/iekārtas, kurās var izmantot reaģentus / Анализаторы/Приборы, для которых предназначен данный набор реагентов
REAGENT	Reagent / Reagenz / Réactif / Reactivo / Reattivo / Reagente / Reagens / Reagens / Reagens / Reagencie / Reagencia / Odczynnik / Reagens / Αντιδραστήριο / Reaktif / Реактив / Reaktiiv / Reagentas / Reaģents / Реагент
CALIBRATOR	Calibrator / Kalibrator / Calibrateur / Calibrador / Calibratore / Calibrador / Kalibrator / Kalibrator / Kalibrator / Kalibrátor / Kalibrátor / Kalibrator / Kalibratór / Βαθμονομητής / Kalibratör / Калибратор / Kalibraator / Kalibratorius / Kalibrators / Калибратор

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	Volume after reconstitution or mixing / Volumen nach Rekonstitution oder Mischen / Volume après reconstitution ou homogénéisation / Volumen tras reconstitución o mezcla / Volume dopo ricostituzione o mescolamento / Volume após reconstituição ou mistura / Mængde efter rekonstituering eller blanding / Volym efter spädning eller blandning / Volum etter rekonstitusjon eller blanding / Objem po rekonstituci nebo smíchání / Objem po rekonštitúcii alebo zmiešaní / Objętość po rekonstytucji lub wymieszaniu / Elkészítés illetve keverés utáni térfogat / Όγκος μετά την ανασύσταση ή την ανάμιξη / Sulandırıldıktan veya karıştırıldıktan sonraki hacim / Обем след разтваряне или миксиране / Maht pärast lahustamist või segamist / Tūris po atskiedimo arba maišymo / Tilpums pēc atšķaidīšanas vai samaisīšanas / Объем после растворения или смешивания
GTIN	Global Trade Item Number / Globale Artikelnummer GTIN / Code article international / Número mundial de artículo comercial / Global Trade Item Number / Global Trade Item Number / Global Trade Item Number / Globalt artikelnummer / Artikkelnummer for global handel / Globální číslo obchodní položky / Globálne identifikačné číslo obchodnej jednotky / Globalny handlowy numer elementu / Globális Kereskedelmi Áruazonosító Szám / Διεθνής Κωδικός Μονάδας Εμπορίας / Küresel Ticari Ürün Numarası / Глобален търговски артикулен номер / Globaalne kaubaartikli number / Visuotinis prekės numeris / Globālais tirdzniecības identifikācijas numurs / Международный Торговый Идентификационный Номер
	UK: +808 100 1920 / IE: +1800 409 564 / USA: +1 1800 4282336 / DE: +49 621 7594747 / AT: +43 1 2778770 / CH: +41 0800806680 / FR: +33 476763088 / BE: + 2 247 4516 (NL), +2 247 45 46 (FR) / ES: +34 900300705 / IT: +39 800 610619 / CH: +41 0800806680 / PT: +351 800 202414 / DK: +45 70 20 05 05 / SE: +46 8 404 88 70 / NO: +47 23 37 33 33 / FI: +358 800 155 655 / NL: +31 800 2882882 / SI: +386 0808887 / SK: +421 257103680 / PL: +48 224815454 / HU: +36 80 200089 / GR: +30 8011161008 / TR: +90 800 2113636 / RO: +40 0800030234 / EE: +372 6460660 / LT: +370 52526692 / LV: +371 67840380 / RU: +8 800 1006896

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

CE

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ProCell M

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www.roche.com

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US Customer Technical Support 1-800-428-2336

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Reagent handling

Ready for use

Storage and stability

MG

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

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 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.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability in *serum/plasma*:[6]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-25) °C

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.[3] Urine samples are automatically prediluted with 0.9 % NaCl by the instrument.

Stability in *urine*:[6]	3 days at 15-25 °C
	3 days at 2-8 °C
	1 year at (-15)-(-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

cobas c 311 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 6-17 (STAT 4 / 6-17)	
Wavelength (sub/main)	505/600 nm	
Reaction direction	Decrease	
Units	mmol/L (mg/dL, mval/L)	
Reagent pipetting		Diluent (H_2O)
R1	97 µL	–
R2	97 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	9 µL	20 µL	100 µL
Increased	3 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-25 (STAT 4 / 10-25)	
Wavelength (sub/main)	505/600 nm	
Reaction direction	Decrease	
Units	mmol/L (mg/dL, mval/L)	
Reagent pipetting		Diluent (H_2O)
R1	97 µL	–
R2	97 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	9 µL	20 µL	100 µL
Increased	3 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-25 (STAT 4 / 10-25)	
Wavelength (sub/main)	505/600 nm	
Reaction direction	Decrease	
Units	mmol/L (mg/dL, mval/L)	
Reagent pipetting		Diluent (H_2O)
R1	97 µL	–
R2	97 µL	–

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

Normal	3 µL	–	–
Decreased	9 µL	20 µL	100 µL
Increased	6 µL	–	–

Application for urine

cobas c 311 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 6-17 (STAT 4 / 6-17)
Wavelength (sub/main)	505/600 nm
Reaction direction	Decrease
Units	mmol/L (mg/dL, mval/L)
Reagent pipetting	Diluent (H_2O)
R1	97 µL -
R2	97 µL -

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6 µL	14 µL	140 µL
Decreased	3 µL	14 µL	140 µL
Increased	6 µL	14 µL	140 µL

cobas c 501 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-25 (STAT 4 / 10-25)
Wavelength (sub/main)	505/600 nm
Reaction direction	Decrease
Units	mmol/L (mg/dL, mval/L)
Reagent pipetting	Diluent (H_2O)
R1	97 µL -
R2	97 µL -

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6 µL	14 µL	140 µL
Decreased	3 µL	14 µL	140 µL
Increased	6 µL	14 µL	140 µL

cobas c 502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-25 (STAT 4 / 10-25)
Wavelength (sub/main)	505/600 nm
Reaction direction	Decrease
Units	mmol/L (mg/dL, mval/L)
Reagent pipetting	Diluent (H_2O)
R1	97 µL -
R2	97 µL -

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6 µL	14 µL	140 µL
Decreased	3 µL	14 µL	140 µL
Increased	12 µL	14 µL	140 µL

Calibration

Calibrators	S1: H_2O S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration • after reagent lot change • 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 atomic absorption spectrometry.

For the USA, this method has been standardized against SRM 956.

Quality control

Serum/plasma

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

In addition, other suitable control material can be used.

Urine

Quantitative urine controls are recommended for routine quality control.

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

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

Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Conversion factors:	mmol/L x 2.43 = mg/dL
	mg/dL x 0.411 = mmol/L
	mval/L x 0.5 = mmol/L
	mval/L x 1.22 = mg/dL
	mval/L = mEq/L

Note: If the unit is changed from the primary unit mmol/L to mg/dL or mval/L in the serum/plasma applications MG-2 ACN (8)701 and SMG2 ACN (8)688 the corresponding field for the lower sensitivity limit has to be modified from "-99999" to one of the following values:

2. Unit mg/dL "Sensitivity Limit" low = -5967
3. Unit mval/L "Sensitivity Limit" low = -7250

No manual modification is required for the urine applications MGU-2 ACN (8)704 and SMG2U ACN (8)689.

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:[7] 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:[7] 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):[7] 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.[8,9]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[10]

Urine

Drugs: No interference was found at therapeutic concentrations using common drug panels.[9]

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

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 Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

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

Limits and ranges

Measuring range

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 and Limit of Detection

Serum/plasma

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

Urine

Limit of Blank	= 0.28 mmol/L (0.680 mg/dL)
Limit of Detection	= 0.56 mmol/L (1.36 mg/dL)

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

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

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

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

Expected values[11]

Serum/plasma:

Newborn:	0.62-0.91 mmol/L	(1.5-2.2 mg/dL)
5 months-6 years:	0.70-0.95 mmol/L	(1.7-2.3 mg/dL)
6-12 years:	0.70-0.86 mmol/L	(1.7-2.1 mg/dL)
12-20 years:	0.70-0.91 mmol/L	(1.7-2.2 mg/dL)
Adults:	0.66-1.07 mmol/L	(1.6-2.6 mg/dL)
60-90 years:	0.66-0.99 mmol/L	(1.6-2.4 mg/dL)
> 90 years:	0.70-0.95 mmol/L	(1.7-2.3 mg/dL)
Urine (24 h):		
	3.0-5.0 mmol/d	(72.9-121.5 mg/d)

Roche has not evaluated reference ranges in a pediatric population.

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. Results obtained in individual laboratories may differ.

Precision

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

Serum/plasma

Repeatability	*Mean*	*SD*	*CV*
	mmol/L (mg/dL)	*mmol/L (mg/dL)*	*%*
Precinorm U	0.891 (2.17)	0.008 (0.02)	0.9
Precipath U	1.73 (4.20)	0.01 (0.02)	0.8
Human serum 1	0.588 (1.43)	0.006 (0.01)	1.1
Human serum 2	0.797 (1.94)	0.007 (0.02)	0.8
Human serum 3	1.35 (3.3)	0.01 (0.0)	0.7
Intermediate precision	*Mean*	*SD*	*CV*
	mmol/L (mg/dL)	*mmol/L (mg/dL)*	*%*
Precinorm U	0.891 (2.17)	0.009 (0.02)	1.0
Precipath U	1.73 (4.20)	0.02 (0.05)	1.0
Human serum 1	0.588 (1.43)	0.008 (0.02)	1.3
Human serum 2	0.797 (1.94)	0.009 (0.02)	1.1
Human serum 3	1.35 (3.3)	0.01(0.0)	0.9

Urine

Repeatability	*Mean*	*SD*	*CV*
	mmol/L (mg/dL)	*mmol/L (mg/dL)*	*%*
Liquicheck 1	2.16 (5.25)	0.03 (0.07)	1.4
Liquicheck 2	5.16 (12.5)	0.04 (0.1)	0.8
Human urine 1	1.50 (3.65)	0.03 (0.07)	1.8
Human urine 2	6.29 (15.3)	0.05 (0.1)	0.8
Human urine 3	9.59 (23.3)	0.06 (0.2)	0.6
Intermediate precision	*Mean*	*SD*	*CV*
	mmol/L (mg/dL)	*mmol/L (mg/dL)*	*%*
Liquicheck 1	2.16 (5.25)	0.03 (0.07)	1.5
Liquicheck 2	5.16 (12.5)	0.06 (0.2)	1.1
Human urine 1	1.50 (3.65)	0.03 (0.07)	2.1
Human urine 2	6.29 (15.3)	0.06 (0.2)	0.9
Human urine 3	9.59 (23.3)	0.07 (0.2)	0.8

MG2

Magnesium Gen.2

cobas®

Method comparison

Magnesium values for human serum/plasma and urine samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Serum/plasma

Sample size (n) = 75

Passing/Bablok[12]	Linear regression
y = 1.029x - 0.015 mmol/L	y = 1.031x - 0.019 mmol/L
τ = 0.985	r = 0.999

The sample concentrations were between 0.308 and 1.67 mmol/L (0.748 and 4.06 mg/dL).

Urine

Sample size (n) = 57

Passing/Bablok[12]	Linear regression
y = 1.025x + 0.043 mmol/L	y = 1.025x + 0.038 mmol/L
τ = 0.994	r = 1.00

The sample concentrations were between 0.630 and 10.5 mmol/L (1.53 and 25.5 mg/dL).

References

1 Külpmann WR, Stummvoll HK, Lehmann P, eds. Elektrolyte, Klinik und Labor, 2nd ed. Vienna/New York: Springer-Verlag 1997.

2 Zumkley H, Spieker C, eds. Die Magnesiumfibel. Einhorn-Presse-Verlag, Reinbek, 1991.

3 Ehrhardt V, Paschen K, Vogt W, et al. Magnesium-Bestimmung im Serum und Urin mit einer verbesserten Xylidyl-Blau-Methode. Workshop Kaiserslautern. Workshop Report Magnesium 1989.

4 Ehrhardt V, Appel W, Paschen K, et al. Evaluierung eines Xylidyl-Blau-Reagenz zur Bestimmung von Magnesium. Wien Klin Wschr 1992;104:5-11.

5 Mann CK, Yoe JH. Spectrophotometric determination of magnesium with sodium 1-azo-2-hydroxy-3-(2,4-dimethyl-carboxanilido)-napthalene-1'-(2-hydroxy-benzene-5-sulfonate) Anal Chem 1956;28:202-205.

6 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.

7 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

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

9 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.

10 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

11 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests, 4th ed. Philadelphia, PA: WB Saunders Company 2006:706-709.

12 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.

Symbols

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

CONTENT	Contents of kit
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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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.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability:[7] 7 days at 15-25 °C

The sample may be stored for 4 days at 2-8 °C or 6 weeks at -20 °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.

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

cobas c 311 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 20-33		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	20 µL	–	
Sample volumes LDHI2	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	2.8 µL	–	–
Decreased	1.1 µL	–	–
Increased	2.8 µL	–	–
Sample volumes LDIP2	*Sample*	*Sample dilution*	
		Sample	Diluent (NaCl)
Normal	14 µL	20 µL	80 µL
Decreased	5.6 µL	20 µL	80 µL
Increased	14 µL	20 µL	80 µL

cobas c 501 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 28-47		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	20 µL	–	
Sample volumes LDHI2	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	2.8 µL	–	–
Decreased	1.1 µL	–	–
Increased	2.8 µL	–	–
Sample volumes LDIP2	*Sample*	*Sample dilution*	
		Sample	Diluent (NaCl)
Normal	14 µL	20 µL	80 µL
Decreased	5.6 µL	20 µL	80 µL
Increased	14 µL	20 µL	80 µL

cobas c 502 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 28-47		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	20 µL	–	
Sample volumes LDHI2	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	2.8 µL	–	–
Decreased	1.1 µL	–	–
Increased	5.6 µL	–	–
Sample volumes LDIP2	*Sample*	*Sample dilution*	
		Sample	Diluent (NaCl)
Normal	14 µL	20 µL	80 µL
Decreased	5.6 µL	20 µL	80 µL
Increased	20 µL	20 µL	80 µL

Calibration

Calibrators	S1: H_2O S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration • after reagent lot change • 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[6] 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.

LDHI2

Lactate Dehydrogenase acc. to IFCC ver.2

In addition, other suitable control material can be used.

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

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

Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte activity of each sample.

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

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a lactate dehydrogenase activity of 200 U/L (3.34 µkat/L).

Icterus:[8] 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:[8] 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):[8] 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.[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 Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

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

Limits and ranges

Measuring range

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

Lower detection limit of the test

10 U/L (0.17 µkat/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values

Acc. to IFCC measured at 37 °C:[12]

Females	135-214 U/L	(2.25-3.55 µkat/L)
Males	135-225 U/L	(2.25-3.75 µkat/L)
Children (2-15 y)	120-300 U/L	(2.00-5.00 µkat/L)
Newborns (4-20 d)	225-600 U/L	(3.75-10.0 µkat/L)

Consensus values:[13]

Males & Females	up to 250 U/L	(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.

Roche has not evaluated reference ranges in a pediatric population.

Specific performance data

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

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

LDHI2

Repeatability	*Mean*	*SD*	*CV*
	U/L (µkat/L)	*U/L (µkat/L)*	*%*
Precinorm U	164 (2.74)	1 (0.02)	0.8
Precipath U	263 (4.39)	2 (0.03)	0.7
Human serum 1	122 (2.04)	2 (0.03)	1.3
Human serum 2	396 (6.61)	4 (0.07)	0.9
Intermediate precision	*Mean*	*SD*	*CV*
	U/L (µkat/L)	*U/L (µkat/L)*	*%*
Precinorm U	159 (2.66)	2 (0.03)	1.0
Precipath U	260 (4.34)	2 (0.03)	0.9
Human serum 3	117 (1.95)	3 (0.05)	2.7
Human serum 4	323 (5.39)	4 (0.07)	1.1

LDIP2

Repeatability	*Mean*	*SD*	*CV*
	U/L (µkat/L)	*U/L (µkat/L)*	*%*
Precinorm U	166 (2.77)	1 (0.02)	0.6
Precipath U	268 (4.48)	1 (0.02)	0.4
Human serum 1	125 (2.09)	1 (0.02)	1.1
Human serum 2	402 (6.71)	3 (0.05)	0.7
Intermediate precision	*Mean*	*SD*	*CV*
	U/L (µkat/L)	*U/L (µkat/L)*	*%*
Precinorm U	168 (2.81)	2 (0.03)	1.1
Precipath U	272 (4.54)	3 (0.05)	0.9
Human serum 3	124 (2.07)	3 (0.05)	2.7
Human serum 4	340 (5.68)	4 (0.07)	1.2

Method comparison

LDH values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

LDHI2

Sample size (n) = 86

Passing/Bablok[14]	Linear regression
y = 1.000x + 4.40 U/L	y = 0.988x + 7.72 U/L
τ = 0.982	r = 1.000

The sample activities were between 100 and 935 U/L (1.67 and 15.6 µkat/L).

LDIP2

Sample size (n) = 86

Passing/Bablok[14]	Linear regression
y = 1.000x + 6.82 U/L	y = 0.983x + 11.0 U/L
τ = 0.975	r = 0.999

The sample activities were between 89.8 and 950 U/L (1.50 and 15.9 µkat/L).

References

1 Thomas L, ed. Labor und Diagnose, 4th ed. Marburg: Die Medizinische Verlagsgesellschaft 1992.

2 Moss DW, Henderson AR, Kachmar JF. Enzymes. In: Tietz NW, ed. Fundamentals of Clinical Chemistry, 3rd ed. Philadelphia, PA: WB Saunders 1987;346-421.

3 Zimmerman HJ, Henry JB In: Henry JB, ed. Clinical Diagnosis and Management by Laboratory Methods. 17th ed.Philadelphia, PA: WB Saunders 1984;251-282.

4 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;384-387.

5 van der Heiden C, Bais R, Gerhardt W, et al. Approved recommendation on IFCC methods for the measurement of catalytic concentration of enzymes. Part 8. IFCC method for lactate dehydrogenase. Eur J Clin Chem Clin Biochem 1994;32:639-655.

6 Schumann G, Bonora R, Ceriotti F, et al. IFCC Primary Reference Procedures for the Measurement of Catalytic Activity Concentrations of Enzymes at 37 °C – Part 3. Reference Procedures for the Measurement of Catalytic Concentrations of Lactate Dehydrogenase. Clin Chem Lab Med 2002;40(6):643-648.

7 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.

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 Lorentz K, Röhle G. Einführung der neuen Standardmethoden 1994 zur Bestimmung der katalytischen Enzymkonzentration bei 37 °C. Klin Chem Mitt 1995;26:290-293.

13 Thomas L, Müller M, Schumann G, et al. Consensus of DGKL and VDGH for interim reference intervals on enzymes in serum. J Lab Med 2005; 29(5):301-308.

14 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.

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 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.

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

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

FERR4

Tina-quant Ferritin Gen.4

cobas®

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

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 24-57		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Units	µg/L (pmol/L, ng/mL)		
Reagent pipetting		Diluent (H_2O)	
R1	80 µL	–	
R3	80 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	140 µL
Increased	10 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 36-70		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Units	µg/L (pmol/L, ng/mL)		
Reagent pipetting		Diluent (H_2O)	
R1	80 µL	–	
R3	80 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	140 µL
Increased	10 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 36-70		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Units	µg/L (pmol/L, ng/mL)		
Reagent pipetting		Diluent (H_2O)	
R1	80 µL	–	
R3	80 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	140 µL
Increased	–	–	–

Calibration

Calibrators	S1: H_2O	
	S2-6: C.f.a.s. Proteins	
	Multiply the lot-specific C.f.a.s. Proteins calibrator value by the factors below to determine the standard concentrations for the 6-point calibration curve:	
	S2: 0.0270	S5: 0.5000
	S3: 0.1120	S6: 1.3000
	S4: 0.2300	
Calibration mode	Spline	
Calibration frequency	Full calibration • after reagent lot change • 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 Elecsys Ferritin assay (immunological method) which is traceable to NIBSC (WHO).

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. 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

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Conversion factors:[12]	µg/L = ng/mL
	µg/L × 2.247 = pmol/L
	µmol/L × 445000 = ng/mL

Limitations - interference

Criterion: Recovery within ± 4 µg/L (≤ 8.99 pmol/L, ≤ 4 ng/mL) of initial values for samples ≤ 40 µg/L (≤ 89.9 pmol/L, ≤ 40 ng/mL) and within ± 10 % for samples > 40 µg/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).

Hemolysis:[13] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[13] No significant interference up to an L index of 1000 (approximate intralipid concentration: 1000 mg/dL). There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors: No significant interference from rheumatoid factors up to a concentration of 1200 IU/mL.

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

High-dose hook effect: Using prozone check, no false result without a flag was observed up to a ferritin concentration of 80000 µg/L (80000 ng/mL).

The polyclonal antibodies used in this assay are specific for ferritin from human liver and also recognize ferritin from human spleen. The antibodies show no cross reactivity to the human ferritin H subunit, which is the major component of human heart ferritin.

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 Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

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

Limits and ranges

Measuring range

5-1000 µg/L (11.2-2247 pmol/L, 5-1000 ng/mL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:8 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 8.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 3 µg/L (6.7 pmol/L, 3 ng/mL)
Limit of Detection	= 5 µg/L (11.2 pmol/L, 5 ng/mL)
Limit of Quantitation	= 5 µg/L (11.2 pmol/L, 5 ng/mL)

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

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

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

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

Values below the Limit of Detection (< 5 µg/L (11.2 pmol/L, 5 ng/mL)) will not be flagged by the instrument.

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a between-run coefficient of variation of ≤ 20 %. It has been determined using low concentration ferritin samples.

Expected values[17]

Adults: Expected values for ferritin concentrations in clinically healthy subjects are strongly dependent upon age and sex.

Results of a study with Tina-quant Ferritin on samples from 224 healthy test subjects (104 women, mainly premenopausal, and 120 men) are given below. These values correspond to the 5th and 95th percentiles.

Men (20-60 years)	30-400 µg/L (67-899 pmol/L, 30-400 ng/mL)
Women (17-60 years)	15-150 µg/L (34-337 pmol/L, 15-150 ng/mL)

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. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements with repeatability (n = 84) and intermediate precision (4 aliquots per run, 1 run per day, one lot of reagent, 21 days, on a Roche/Hitachi **cobas c** 501 analyzer). The following results were obtained:

Repeatability	*Mean*	*SD*	*CV*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	125 (281, 125)	1 (2, 1)	0.8
Precipath Protein	306 (688, 306)	2 (4, 2)	0.6
Human serum 1	8.76 (19.7, 8.76)	0.83 (1.9, 0.83)	9.5
Human serum 2	26.1 (58.7, 26.1)	0.7 (1.6, 0.7)	2.8
Human serum 3	223 (501, 223)	1 (2, 1)	0.7
Human serum 4	568 (1276, 568)	5 (11, 5)	0.9
Human serum 5	781 (1755, 781)	7 (16, 7)	0.8

Intermediate precision	*Mean*	*SD*	*CV*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	125 (281, 125)	1 (2, 1)	1.1
Precipath Protein	306 (688, 306)	4 (9, 4)	1.3
Human serum 1	8.76 (19.7, 8.76)	1.14 (2.6, 1.14)	13.0
Human serum 2	26.1 (58.7, 26.1)	0.7 (1.6, 0.7)	2.8
Human serum 3	223 (501, 223)	3 (7, 3)	1.2
Human serum 4	568 (1276, 568)	10 (22, 10)	1.7
Human serum 5	781 (1755, 781)	14 (31, 14)	1.8

Method comparison

Ferritin values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer using the Tina-quant Ferritin Gen.4 assay (y) were compared with those determined on a Roche/Hitachi 917 analyzer using the Tina-quant Ferritin assay (x).

Sample size (n) = 87

Passing/Bablok[18]	Linear regression
y = 0.904x + 7.73 µg/L	y = 0.901x + 8.68 µg/L
τ = 0.983	r = 0.998

The sample concentrations were between 19.5 and 775 µg/L (43.8 and 1741 pmol/L, 19.5 and 775 ng/mL).

In addition a comparison of the Tina-quant Ferritin Gen.4 assay on a Roche/Hitachi **cobas c** 501 analyzer (y) with the Tina-quant Ferritin Gen.3 assay on the same analyzer (x) using human serum and plasma samples gave the following correlations:

Sample size (n) = 88

Passing/Bablok[18]	Linear regression
y = 0.949x + 5.96 µg/L	y = 0.950x + 5.10 µg/L
τ = 0.989	r = 1.000

The sample concentrations were between 13.5 and 762 µg/L (30.3 and 1712 pmol/L, 13.5 and 762 ng/mL).

References

1 Wick M, Pinggera W, Lehmann P, eds. Iron Metabolism, Diagnosis and Therapy of Anemias. Clinical Aspects and Laboratory, 5th ed. Vienna/New York: Springer-Verlag 2003.

2 Kaltwasser IP, Werner E, eds. Serumferritin: Methodische und klinische Aspekte. Berlin/Heidelberg/New York: Springer-Verlag 1980.

3 Williams WJ, Beutler E, Ersler AJ, et al. eds. Hematology, 7th ed. New York: McGraw-Hill 2005.

4 Albertini A, Arosio P, Chiancone E, et al. eds. Ferritins and isoferritins as biochemical markers. Amsterdam/New York/Oxford: Elsevier 1984.

5 San Diego Declaration, Erythropoietin use and response in end-stage renal disease. The American Society of Nephrology, Annual meeting, San Diego. J Am Soc Nephrol 1995;3:35.

6 Finlayson NDC. Hereditary (primary) haemochromatosis. BMJ 1990;301:350-351.

7 Franco RS. Ferritin. In: Pesce AJ, Kaplan LA, eds. Methods in clinical chemistry. St. Louis/Washington/Toronto: CV Mosby Company 1987:1240-1242.

8 Dati F, Sauder U. Immunchemische Methoden im klinischen Labor. GIT Labor-Medizin 1990;7-8:357-372.

9 Dubois S, McGovern M, Ehrhardt V. Eisenstoffwechsel-Diagnostik mit Boehringer Mannheim/Hitachi-Analysensystemen: Ferritin, Transferrin und Eisen. GIT Labor-Medizin 1988;9:468-471.

10 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests. 4th ed. Philadelphia: WB Saunders; 2006:392.

11 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.

12 Young DS, Huth EJ. SI Units For Clinical Measurement. American College of Physicians 1998.

13 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

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

15 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.

16 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

17 Lotz J, Hafner G, Prellwitz W. Reference Study for Ferritin Assays. Kurzmitteilung Clin Lab 1997;43:993-994.

18 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.

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 after reconstitution or mixing

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Elecsys Anti-SARS-CoV-2 S

cobas®

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

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

For professional use.

The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.

All information required for correct operation is read in from the respective reagent barcodes.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	28 days (4 weeks)
on the analyzers	14 days

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes.

Li-heparin, EDTA and sodium citrate plasma.

Criterion: Slope 1.00 ± 0.10 + bias at 0.8 U/mL ± 20 %.

For native samples collected in sodium citrated plasma: Slope 0.84 ± 0.10.

Sampling devices containing liquid anticoagulants have a dilution effect resulting in lower values (U/mL) for individual patient specimens. In order to minimize dilution effects it is essential that respective sampling devices are filled completely according to manufacturer's instructions.

Stable for 3 days at 15-25 °C, 14 days at 2-8 °C, 3 months at -20 °C (± 5 °C). The samples may be frozen 3 times.

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.

Specimens should not be subsequently altered with additives (e.g. biocides, anti-oxidants or substances that could possibly change the pH or ionic strength of the sample) in order to avoid erroneous findings.

Centrifuge samples containing precipitates and thawed samples before performing the assay.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

The performance of the Elecsys Anti-SARS-CoV-2 S assay has not been established with cadaveric samples or body fluids other than serum and plasma.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 09289291190, CalSet Anti-SARS-CoV-2 S, for 4 x 1.0 mL
- REF 09289313190, PreciControl Anti-SARS-CoV-2 S, 4 x 1.0 mL
- REF 11732277122, Diluent Universal, 2 x 16 mL sample diluent or REF 03183971122, Diluent Universal, 2 x 36 mL sample diluent or REF 05192943190, Diluent Universal 2, 2 x 36 mL sample diluent
- General laboratory equipment
- **cobas e** analyzer

Additional materials for the **cobas e** 411 analyzer:

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, AssayCup, 60 x 60 reaction cups
- REF 11706799001, AssayTip, 30 x 120 pipette tips
- REF 11800507001, Clean-Liner

Additional materials for **cobas e** 601 and **cobas e** 602 analyzers:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Additional materials for all analyzers:

- REF 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

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.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibration

Traceability: This method has been standardized against the internal Roche standard for anti-SARS-CoV-2-S. This standard consists of an equimolar mixture of 2 monoclonal antibodies that bind Spike-1 RBD at 2 different epitopes. 1 nM of these antibodies correspond to 20 U/mL of the Elecsys Anti-SARS-CoV-2 S assay. No international standard is available for anti-SARS-CoV-2-S.

Note: the defined unit is specific for the Elecsys Anti-SARS-CoV-2 S assay and must not be used interchangeably with units of other assays.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the same reagent kit was registered on the analyzer).

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

Renewed calibration is recommended as follows:

- after 31 days when using the same reagent lot
- after 14 days when using the same reagent kit on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Anti-SARS-CoV-2 S.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per **cobas e** pack, and following each 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.

If necessary, repeat the measurement of the samples concerned.

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

Calculation

The analyzer automatically calculates the analyte concentration of each sample in U/mL.

Interpretation of the results

Result	Interpretation
< 0.80 U/mL	Negative for anti-SARS-CoV-2-S
≥ 0.80 U/mL	Positive for anti-SARS-CoV-2-S

Note: Due to the diversity of the antibodies, the measured anti-SARS-CoV-2-S value can vary depending on the testing procedure used and the applied standard. Results obtained from a single sample using tests from different manufacturers can therefore differ. If there is a change in the assay procedure used during the monitoring of antibody titers, then the anti-SARS-CoV-2-S values obtained upon changing over to the new procedure must be confirmed by parallel measurements with both methods. For citrated plasma (1 part citrate solution + 9 parts blood), the dilution effect must be taken into account.

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	≤ 1129 µmol/L or ≤ 66 mg/dL
Hemoglobin	≤ 1000 mg/dL or ≤ 10 g/L
Intralipid	≤ 2000 mg/dL
Biotin	≤ 4912 nmol/L or ≤ 1200 ng/mL
Rheumatoid factors	≤ 1200 IU/mL
IgG	≤ 7.0 g/dL or ≤ 70 g/L
IgA	≤ 1.6 g/dL or ≤ 16 g/L
IgM	≤ 1.0 g/dL or ≤ 10 g/L

Criterion: For concentrations of 1.0-20 U/mL, the deviation is ≤ 20 %. For concentrations > 20 U/mL, the deviation is ≤ 30 %. For concentrations < 1.0 U/mL, the deviation is ≤ 0.2 U/mL.

No false negative results due to a high-dose hook effect were found with the Elecsys Anti-SARS-CoV-2 S assay but occurrence of high-dose hook effect cannot be completely excluded.

Pharmaceutical substances

In vitro tests were performed on 17 commonly used pharmaceuticals. No interference with the assay was found except for itraconazole.

Interference of itraconazole was tested up to the listed concentration and no impact on results was observed.

Drug	Concentration tested
Itraconazole	15 mg/L

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

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

A negative test result does not completely rule out the possibility of an infection with SARS-CoV-2. Serum or plasma samples from the very early (pre-seroconversion) phase can yield negative findings. Therefore, this test cannot be used to diagnose an acute infection. It has also been reported that certain patients with confirmed infection do not develop SARS-CoV-2 antibodies.[24] Furthermore, waning of antibody titers has been reported in some individuals within a range of months after infection, a feature which has also been reported for other coronaviruses.[28,29,30]

Limits and ranges

Measuring range

0.40-250 U/mL (defined by the Limit of Quantitation and the maximum of the master curve). Values below the Limit of Quantitation are reported as < 0.40 U/mL. Values above the measuring range are reported as > 250 U/mL (or up to 2500 U/mL for 10-fold diluted samples).

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 0.30 U/mL

Limit of Detection = 0.35 U/mL

Limit of Quantitation = 0.40 U/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 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is defined as the lowest amount of analyte in a sample that can be accurately quantified with a CV ≤ 20 %. It has been determined using samples with low concentration of anti-SARS-CoV-2-S.

Dilution

Samples with anti-SARS-CoV-2-S concentrations above the measuring range can be diluted with Diluent Universal or Diluent Universal 2. The recommended dilution is 1:10. The concentration of the diluted sample must be ≥ 20 U/mL.

After dilution by the analyzers, the software automatically takes the dilution into account when calculating the sample concentration.

Note: Antibodies to SARS-CoV-2 are heterogeneous. In some isolated cases, this may lead to non-linear dilution behavior.

Specific performance data

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

Precision

Precision was determined using Elecsys reagents, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 1 run per day with 5 replicates of each sample for 5 days (n = 25). The following results were obtained:

cobas e 411 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
HSP[c)] 1	0.483	0.014	2.8	0.016	3.4
HSP 2	0.826	0.023	2.8	0.023	2.8
HSP 3	5.74	0.131	2.3	0.150	2.6
HSP 4	12.3	0.266	2.2	0.304	2.5
HSP 5	54.6	1.58	2.9	1.58	2.9
HSP 6	77.9	1.78	2.3	2.07	2.7
HSP 7	190	3.03	1.6	3.69	1.9
PC[d)] ACOV2S 1	< 0.40	-	-	-	-

Elecsys Anti-SARS-CoV-2 S

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cobas e 411 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
PC ACOV2S 2	10.8	0.207	1.9	0.230	2.1

c) HSP = human specimen (serum/plasma)

d) PC = PreciControl: PC ACOV2S 1 is free of analyte and therefore consistently resulted below measuring range (< 0.40 U/mL) throughout the experiment, standard deviation and coefficient of variance could therefore not be determined.

cobas e 601 and **cobas e** 602 analyzers					
		Repeatability		**Intermediate precision**	
Sample	Mean U/mL	SD U/mL	CV %	SD U/mL	CV %
HSP 1	0.441	0.007	1.6	0.016	3.7
HSP 2	0.933	0.014	1.5	0.022	2.3
HSP 3	5.60	0.102	1.8	0.181	3.2
HSP 4	12.0	0.189	1.6	0.334	2.8
HSP 5	53.2	0.761	1.4	1.46	2.7
HSP 6	75.5	1.55	2.1	2.70	3.6
HSP 7	183	3.31	1.8	5.13	2.8
PC ACOV2S 1	< 0.40	-	-	-	-
PC ACOV2S 2	10.5	0.118	1.1	0.341	3.3

Analytical specificity

1100 samples containing potentially cross-reacting analytes were tested with the Elecsys Anti-SARS-CoV-2 S assay. All samples were obtained before October 2019. No cross-reactivity was found. The resulting overall specificity was 100 %. Results are shown in the following tables:

SARS-CoV-2 related

Indication	**N**	**Reactive**	**Specificity %**
MERS CoV (anti-S1 IgG+)	7	0	100
Common Coronavirus panel[e)]	94	0	100

e) 100 pre-pandemic samples were screened for reactivity to Coronavirus HKU1, NL63, 229E, or OC43. 94 out of 100 samples showed serologic reactivity to antigens of at least 1, typically several of these viruses. These 94 samples were assessed for reactivity in the Elecsys Anti-SARS-CoV-2 S assay.

Infectious respiratory diseases

Indication	**N**	**Reactive**	**Specificity %**
Bordetella pertussis	34	0	100
Chlamydia pneumoniae	33	0	100
Common cold panel[f)]	21	0	100
Enterovirus	17	0	100
Haemophilus influenzae B	40	0	100
Influenza A	25	0	100
Influenza B	25	0	100
Influenza vaccinees	25	0	100
Mycoplasma pneumoniae	3	0	100
Parainfluenza	31	0	100
Respiratory syncytial virus	23	0	100

f) 21 potentially cross-reactive samples from individuals with common cold symptoms, collected before October 2019

Other infectious diseases

Indication	**N**	**Reactive**	**Specificity %**
Borrelia	6	0	100
Candida albicans	13	0	100
Chlamydia trachomatis	10	0	100
CMV acute (IgM+, IgG+)	86	0	100
E. coli (anti-E. coli-reactive)	10	0	100
EBV acute (IgM+, VCA IgG+)	106	0	100
Gonorrhea (tripper)	5	0	100
HAV acute (IgM+)	10	0	100
HAV late (IgG+)	15	0	100
HAV vaccinees	15	0	100
HBV acute	12	0	100
HBV chronic	12	0	100
HBV vaccinees	15	0	100
HCV	50	0	100
HEV	12	0	100
HIV	10	0	100
HSV acute (IgM+)	24	0	100
HTLV	6	0	100
Listeria	6	0	100
Measles	10	0	100
Mumps	14	0	100
Parvovirus B19	30	0	100
Plasmodium falciparum (malaria)	8	0	100
Rubella acute (IgM+, IgG+)	12	0	100
Toxoplasma gondii (IgM+, IgG+)	8	0	100
Treponema pallidum (syphilis)	62	0	100
VZV (varicella-zoster virus)	30	0	100

Autoimmune diseases

Indication	**N**	**Reactive**	**Specificity %**
AMA (anti-mitochondrial antibodies)	30	0	100
ANA (anti-nuclear antibodies)	2	0	100
Hemophiliacs	15	0	100
RA (rheumatoid arthritis)	10	0	100
SLE (systemic lupus erythematosus)	10	0	100

Hepatic diseases

Indication	**N**	**Reactive**	**Specificity %**
Alcohol induced hepatitis/cirrhosis	13	0	100
Drug induced hepatitis/cirrhosis	10	0	100
Fatty liver	10	0	100

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Indication	N	Reactive	Specificity %
Liver cancer	10	0	100
Non-viral liver disease	15	0	100

Clinical specificity

A total of 5991 samples were tested with the Elecsys Anti-SARS-CoV-2 S assay. All samples were obtained before October 2019. 1 false positive sample was detected.

The resulting overall specificity in the internal study was 99.98 %. The 95 % lower confidence limit was 99.91 %.

Cohort	N	Reactive	Specificity %	95 % lower confidence limit, %	95 % upper confidence limit, %
Diagnostic routine (Europe)	2528	0	100	99.85	100
Blood donors (USA)	2713	1	99.96	99.79	100
Blood donors (Africa)	750	0	100	99.51	100
Overall	**5991**	**1**	**99.98**	**99.91**	**100**

Sensitivity

A total of 1610 samples from 402 symptomatic patients (including 297 samples from 243 hospitalized patients) with a PCR confirmed SARS-CoV-2 infection were tested with the Elecsys Anti-SARS-CoV-2 S assay. 1 or more sequential samples from these patients were collected at various time points after PCR confirmation.

1423 of the tested samples had a sampling date of 14 days or later after diagnosis with PCR. 1406 of these 1423 samples were determined with ≥ 0.8 U/mL in the Elecsys Anti-SARS-CoV-2 S assay and hence considered positive, resulting in a sensitivity of 98.8 % (95 % CI: 98.1-99.3 %) in this sample cohort.

U/mL	Days after diagnosis with positive PCR					
	0-6	7-13	14-20	21-27	28-34	> 35
< 0.4	4	16	7	3	0	0
0.4 - < 0.8	0	6	7	0	0	0
0.8 - < 1.5	2	3	4	1	0	0
1.5 - < 2.5	0	2	6	2	0	0
2.5 - < 5	3	10	9	12	10	40
5 - < 10	1	7	7	15	25	49
10 - < 20	0	11	19	32	25	62
20 - < 50	1	13	19	40	38	183
50 - < 100	3	9	11	34	48	232
100 - < 150	1	4	11	11	21	135
150 - < 200	2	4	2	5	11	95
200 - ≤ 250	3	8	0	1	5	47
> 250	15	59	28	20	14	77
≥ 0.8	31	130	116	173	197	920
Total	35	152	130	176	197	920
Sensitivity, %	88.6	85.5	89.2	98.3	100	100
CS[g], % 95 % CI[h], %	86.1 80.3 - 90.7		**98.8** **98.1 - 99.3**			

g) CS = Cumulated sensitivity

h) CI = confidence intervall

Titer development was investigated with sequential samples from individual patients ranging up to 126 days following a reactive PCR result. None of the samples showed a decline of titer below the reactive range.

Titer development over time for patient samples ranging ≥ 100 days following a reactive PCR result is shown below.

Donor	D* U/mL	D U/mL	D U/mL	D U/mL	D U/mL	D U/mL	D U/mL	D U/mL
1	20 20.4	23 22.2	27 30.5	33 47.4	36 51.7	61 73.5	82 87.7	103 114
2	21 36.1	24 44.3	31 32.4	34 48.5	37 51.4	62 63.1	83 73.2	104 71.9
3	26 139	34 223	38 186	41 153	45 150	67 198	87 147	106 155
4	21 32.3	30 95.3	33 151	36 315	41 374	62 293	83 244	107 214
5	30 33.0	35 29.5	38 31.2	42 41.2	112 59.9			
6	20 7.88	30 32.6	38 26.6	62 39.2	71 35.7	76 40.3	86 36.0	107 42.1
7	19 20.7	22 40.4	25 101	29 149	39 115	48 97.7	59 115	104 175
8	15 22.1	22 14.2	30 37.1	37 166	40 136	55 226	79 124	107 96.9
9	34 181	41 148	45 148	52 165	67 152	74 154	87 125	106 119
10	26 4.42	29 4.79	32 4.83	35 5.21	42 4.67	52 5.95	73 7.28	103 7.69
11	16 305	42 296	78 371	106 408				
12	28 139	31 162	40 114	44 166	47 141	62 93.0	86 69.5	103 59.1
13	24 33.9	31 45.6	38 63.7	46 53.4	59 47.4	74 41.8	92 41.9	102 42.8
14	25 79.8	28 86.4	33 120	41 117	47 103	59 108	76 97.1	109 105
15	36 255	52 165	68 126	77 94.8	92 122	96 107	106 141	126 162
16	30 425	44 246	51 379	58 298	73 215	85 169	90 173	104 147
17	29 220	32 205	40 177	48 141	55 136	76 122	95 116	101 101
18	31 63.6	39 66.9	43 53.4	53 43.4	64 57.3	68 48.9	92 69.7	102 58.8
19	32 94.5	46 79.5	53 84.3	60 71.8	68 92.1	74 73.6	94 78.9	102 75.8
20	38 56.4	46 84.2	68 104	74 106	82 114	99 141	106 152	110 146
21	31 9.4	38 10.1	48 8.7	52 9.0	57 8.0	71 8.8	92 10.4	106 10.4
22	44 54.3	49 51.0	61 59.2	70 56.9	117 99.8			
23	35 524	42 451	55 416	74 386	81 392	109 345		
24	44 669	48 685	51 584	58 605	63 582	73 562	90 591	104 570
25	36 64.0	49 83.5	56 78.6	69 83.9	82 100	89 103	105 121	

* Days after initial positive PCR

Correlation of assay results to serum neutralization capacity

The Elecsys Anti-SARS-CoV-2 S assay was compared to a VSV[i)]-based pseudo-neutralization assay.[31] The results for 15 clinical samples from individual patients are summarized in the following table:

		Pseudo-neutralization assay		
		Positive	Indeterminate	Negative
Elecsys Anti-SARS-CoV-2 S assay	≥ 0.8 U/mL	12	0	0
	< 0.8 U/mL	1	1	1

Positive agreement rate: 92.3 %

i) VSV = Vesicular Stomatitis Virus

References

1 Ye Z-W, Yuan S, Yuen K-S, et al. Zoonotic origins of human coronaviruses. Int J Biol Sci 2020 Mar 15;16(10):1686-1697.

2 Transmission of SARS-CoV-2: implications for infection prevention precautions [Internet]. 2020 [cited 2020 Jul 14]. Available from: https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions

3 Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020 20;382(8):727-733.

4 Chan JF-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020 15;395(10223):514-523.

5 Lauer SA, Grantz KH, Bi Q, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. Ann Intern Med 2020 Mar 10.

6 Zhou R, Li F, Chen F, et al. Viral dynamics in asymptomatic patients with COVID-19. International Journal of Infectious Diseases 2020 Jul 1;96:288-290.

7 He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nature Medicine 2020 May;26(5):672-675.

8 Mizumoto K, Kagaya K, Zarebski A, et al. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill 2020 Mar 12;25(10).

9 Gao M, Yang L, Chen X, et al. A study on infectivity of asymptomatic SARS-CoV-2 carriers. Respir Med 2020 Aug;169:106026.

10 Yu P, Zhu J, Zhang Z, et al. A Familial Cluster of Infection Associated With the 2019 Novel Coronavirus Indicating Possible Person-to-Person Transmission During the Incubation Period. J Infect Dis 2020 11;221(11):1757-1761.

11 Liu Z, Chu R, Gong L, et al. The assessment of transmission efficiency and latent infection period on asymptomatic carriers of SARS-CoV-2 infection. International Journal of Infectious Diseases 2020 Jun 13.

12 Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol 2020;5(4):562-569.

13 Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020 Feb 24;12(1):1-5.

14 Wrapp D, Wang N, Corbett KS, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 2020 13;367(6483):1260-1263.

15 Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell 2020 16;181(2):271-280.e8.

16 Centers for Disease Control and Prevention. Interim Guidelines for COVID-19 Antibody Testing [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2020 Jun 4]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html

17 Long Q-X, Liu B-Z, Deng H-J, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med 2020 Apr 29.

18 Lou B, Li T-D, Zheng S-F, et al. Serology characteristics of SARS-CoV-2 infection since exposure and post symptom onset. Eur Respir J 2020 May 19;2000763.

19 Zhao J, Yuan Q, Wang H, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clin Infect Dis 2020 Mar 28.

20 Tuaillon E, Bolloré K, Pisoni A, et al. Detection of SARS-CoV-2 antibodies using commercial assays and seroconversion patterns in hospitalized patients. Journal of Infection 2020 Jun 3.

21 Salazar E, Kuchipudi SV, Christensen PA, et al. Relationship between Anti-Spike Protein Antibody Titers and SARS-CoV-2 In Vitro Virus Neutralization in Convalescent Plasma [Internet]. Immunology; 2020 Jun [cited 2020 Jun 13]. Available from: http://biorxiv.org/lookup/doi/10.1101/2020.06.08.138990

22 Klasse P, Moore JP. Antibodies to SARS-CoV-2 and their potential for therapeutic passive immunization. Giamarellos-Bourboulis EJ, van der Meer JW, editors. eLife. 2020 Jun 23;9:e57877.

23 Premkumar L, Segovia-Chumbez B, Jadi R, Martinez DR, Raut R, Markmann AJ, et al. The receptor-binding domain of the viral spike protein is an immunodominant and highly specific target of antibodies in SARS-CoV-2 patients. Science Immunology 2020 Jun 11;5(48).

24 Luchsinger LL, Ransegnola B, Jin D, et al. Serological Analysis of New York City COVID19 Convalescent Plasma Donors [Internet]. Infectious Diseases (except HIV/AIDS); 2020 Jun [cited 2020 Jul 23]. Available from: http://medrxiv.org/lookup/doi/10.1101/2020.06.08.20124792

25 Mukherjee R. Global efforts on vaccines for COVID-19: Since, sooner or later, we all will catch the coronavirus. J Biosci 2020;45.

26 Graham BS. Rapid COVID-19 vaccine development. Science 2020 29;368(6494):945-946.

27 Hotez PJ, Corry DB, Bottazzi ME. COVID-19 vaccine design: the Janus face of immune enhancement. Nature Reviews Immunology 2020 Jun;20(6):347-348.

28 Liu A, Wang W, Zhao X, et al. Disappearance of antibodies to SARS-CoV-2 in a Covid-19 patient after recovery. Clinical Microbiology and Infection 2020 Jul 8;0(0).

29 Long Q-X, Tang X-J, Shi Q-L, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nature Medicine 2020 Jun 18;1-5.

30 Wu L-P, Wang N-C, Chang Y-H, et al. Duration of Antibody Responses after Severe Acute Respiratory Syndrome - Volume 13, Number 10 - October 2007 - Emerging Infectious Diseases journal - CDC. [cited 2020 Jul 16]; Available from: https://wwwnc.cdc.gov/eid/article/13/10/07-0576_article

31 Meyer B, Torriani G, Yerly S, et al. Validation of a commercially available SARS-CoV-2 serological Immunoassay. medRxiv. 2020. https://doi.org/10.1101/2020.05.02.20080879.

For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

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

Symbols

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

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing

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GTIN Global Trade Item Number

CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Roche

CRP4

Tina-quant C-Reactive Protein IV

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin, K_2-EDTA, K_3-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 and Li-heparin plasma:	2 weeks at 15-25 °C
	3 weeks at 2-8 °C
	12 months at –20 ± 5 °C
Stability in K_2- and K_3-EDTA plasma:	1 day at 15-25 °C
	3 weeks at 2-8 °C
	12 months at –20 ± 5 °C

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

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

cobas c 311 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 8-18	
Wavelength (sub/main)	800/570 nm	
Reaction direction	Increase	
Units	mg/L (nmol/L, mg/dL)	
Reagent pipetting		Diluent (H_2O)
R1	150 µL	
R2	48 µL	24 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	4 µL	25 µL	75 µL
Increased	2 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 13-29	
Wavelength (sub/main)	800/570 nm	
Reaction direction	Increase	
Units	mg/L (nmol/L, mg/dL)	
Reagent pipetting		Diluent (H_2O)
R1	150 µL	
R2	48 µL	24 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	4 µL	25 µL	75 µL
Increased	2 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 13-29	
Wavelength (sub/main)	800/570 nm	
Reaction direction	Increase	
Units	mg/L (nmol/L, mg/dL)	
Reagent pipetting		Diluent (H_2O)
R1	150 µL	
R2	48 µL	24 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	4 µL	25 µL	75 µL
Increased	2 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2: Calibrator f.a.s. Proteins
Calibration mode	Non-linear
Calibration frequency	Full calibration - after reagent lot change - after 3 weeks on-board the analyzer - after 6 months when using a single reagent lot - as required following quality control procedures

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

This method has been standardized against the certified reference material in human serum of the IRMM (Institute for Reference Materials and Measurements) ERM-DA474/IFCC.[11]

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. 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.

Conversion factors:	mg/L × 9.52 = nmol/L	mg/dL × 95.2 = nmol/L
	mg/L × 0.1 = mg/dL	mg/dL × 10 = mg/L
	mg/dL × 0.01 = g/L	g/L × 100 = mg/dL

Limitations - interference

Criterion: Recovery within ± 0.5 mg/L (4.76 nmol/L) of initial values of samples ≤ 5.0 mg/L (47.6 nmol/L) and within ± 10 % for samples > 5 mg/L.

Icterus:[12] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 60 mg/dL or 1026 µmol/L).

Hemolysis:[12] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 622 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[12] No significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors: No significant interference from rheumatoid factors up to a concentration of 1200 IU/mL.

Immunoglobulins: No significant interference from immunoglobulins up to a concentration of 50 g/L (334 µmol/L) (simulated by human immunoglobulin G).

High-dose hook effect: No false result occurs up to a CRP concentration of 1200 mg/L (11424 nmol/L).

In vitro tests were performed on commonly used pharmaceuticals. In addition, special pharmaceuticals were tested. Among them the following substance caused interference:

Substance	No significant interference up to
Ticarcillin	225 mg/L

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

As with any assay employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample, which could cause falsely lowered results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[13]

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. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

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

Limits and ranges

Measuring range

0.6-350 mg/L (5.7-3332 nmol/L)

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	= 0.2 mg/L (1.9 nmol/L)
Limit of Detection	= 0.3 mg/L (2.9 nmol/L)
Limit of Quantitation	= 0.6 mg/L (5.7 nmol/L)

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

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

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

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

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration C-reactive protein samples.

Expected values

Consensus reference interval for adults:[14] < 5 mg/L (< 47.6 nmol/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. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

Repeatability	*Mean mg/L (nmol/L)*	*SD mg/L (nmol/L)*	*CV %*
CRP T Control N	3.63 (34.6)	0.0608 (0.579)	1.7
Precinorm Protein	9.69 (92.2)	0.128 (1.22)	1.3
Precipath Protein	55.8 (531)	1.09 (10.4)	2.0
Human serum 1	1.27 (12.1)	0.0294 (0.280)	2.3
Human serum 2	4.56 (43.4)	0.0702 (0.668)	1.5
Human serum 3	88.4 (842)	2.06 (19.6)	2.3
Human serum 4	186 (1771)	3.76 (35.8)	2.0
Human serum 5	337 (3208)	5.79 (55.1)	1.7

Intermediate precision	*Mean mg/L (nmol/L)*	*SD mg/L (nmol/L)*	*CV %*
CRP T Control N	3.63 (34.6)	0.0620 (0.590)	1.7
Precinorm Protein	9.65 (91.9)	0.165 (1.57)	1.7
Precipath Protein	55.8 (531)	1.21 (11.5)	2.2
Human serum 1	1.27 (12.1)	0.0310 (0.295)	2.4
Human serum 2	4.56 (43.4)	0.0735 (0.700)	1.6
Human serum 3	88.4 (842)	2.21 (21.0)	2.5
Human serum 4	186 (1771)	4.39 (41.8)	2.4
Human serum 5	337 (3208)	6.87 (65.4)	2.0

Method comparison

CRP values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using the C-Reactive Protein Gen.3 assay on a **cobas c** 501 analyzer (x).

Sample size (n) = 120

Passing/Bablok[15]	Linear regression
y = 0.988x + 0.222 mg/L	y = 0.923x + 1.94 mg/L
τ = 0.988	r = 0.999

The sample concentrations were between 0.670 and 347 mg/L (6.38 and 3303 nmol/L).

CRP values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using the C-Reactive Protein Gen.2 assay on a **cobas c** 501 analyzer (x).

CRP4

Tina-quant C-Reactive Protein IV

Sample size (n) = 112

Passing/Bablok[15]	Linear regression
y = 1.015x – 0.224 mg/L	y = 0.946x + 1.58 mg/L
τ = 0.989	r = 0.997

The sample concentrations were between 1.16 and 243 mg/L (11.0 and 2313 nmol/L).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995:234-236.

2 Thomas L. Labor und Diagnose, 7. Auflage, TH-Books Verlagsgesellschaft mbH, Frankfurt/Main 2008;1010-1021.

3 Burtis CA, Ashwood ER, eds. Tietz Fundamentals of Clinical Chemistry, 5th ed. Pa: WB Saunders Co 2001;332-333.

4 Thomas L, Messenger M. Pathobiochemie und Labordiagnostik der Entzündung. Lab med 1993;17:179–194.

5 Young B, Gleeson M, Cripps AW. C-reactive protein: A critical review. Pathology 1991;23:118-124.

6 Wasunna A, Whitelaw A, Gallimore R, et al. C-reactive protein and bacterial infection in preterm infants. Eur J Pediatr 1990 Mar;149(6):424-427.

7 Vergis N. Should CRP be used as a marker of infection in patients with liver cirrhosis? Clin Lab Int 2007;6:12-13.

8 Mackenzie I, Woodhouse J. C-reactive protein concentrations during bacteraemia: a comparison between patients with and without liver dysfunction. Intensive Care Medicine 2006;32:1344-1351.

9 Price CP, Trull AK, Berry D, et al. Development and validation of a particle-enhanced turbidimetric immunoassay for C-reactive protein. J Immunol Methods 1987;99:205-211.

10 Eda S, Kaufmann J, Roos W, et al. Development of a New Microparticle-Enhanced Turbidimetric Assay for C-reactive Protein with Superior Features in Analytical Sensitivity and Dynamic Range. J Clin Lab Anal 1998;12:137-144.

11 Auclair G, Zegers I, Charoud-Got J, et al. CERTIFICATION REPORT. The Certification of the Mass Concentration of C-Reactive Protein in Human Serum. Publications Office of the European Union, 2011. http://www.jrc.ec.europa.eu/

12 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

13 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

14 Dati F, Schumann G, Thomas L, et al. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardization against the IFCC/BCR/CAP reference material (CRM 470). Eur J Clin Chem Clin Biochem 1996;34:517-520.

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.

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

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