CERU

cobas®

Ceruloplasmin

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
20764663 322	Ceruloplasmin 100 tests	System-ID 07 6466 3	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
03555941 190	Calibrator f.a.s. PAC (3 x 1 mL)	Code 589	
04567021 190	Prealbumin/Ceruloplasmin Control Set*		
	Precinorm PC (3 x 1 mL)	Code 102	
	Precipath PC (3 x 1 mL)	Code 103	
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	

*Not for use in the US; US customers should use a suitable commercially available control.

English

System information

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

CER: ACN 707

For **cobas c** 502 analyzer:

CER: ACN 8707

Intended use

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

Summary[1,2,3]

Ceruloplasmin is an acute phase protein and transport protein. The blue-colored glycoprotein belongs to the α2-globulin electrophoretic fraction and contains 8 copper atoms per molecule.

Incorporation of copper into the structure occurs during the synthesis of ceruloplasmin in the hepatocytes. After secretion from the liver, ceruloplasmin migrates to copper-requiring tissue where the copper is liberated during catabolism of the ceruloplasmin molecule. In addition to transporting copper, ceruloplasmin has a catalytic function in the oxidation of iron (Fe^{2+} to Fe^{3+}), polyamines, catecholamines, and polyphenols.

Decreased concentrations occur during recessive autosomal hepatolenticular degeneration (Wilson's disease). On a pathochemical level, the disease, which is accompanied by lower ceruloplasmin synthesis, occurs as a consequence of missing Cu^{2+} incorporation into the molecule due to defective metallothionine. This results in pathological deposits of copper in the liver (with accompanying development of cirrhosis), brain (with neurological symptoms), cornea (Kayser-Fleischer ring), and kidneys (hematuria, proteinuria, aminoaciduria). In homozygous carriers, ceruloplasmin levels are severely depressed. Heterozygous carriers exhibit either no decrease at all or just a mild decrease. The rare Menke's syndrome involves a genetically caused copper absorption disorder with concomitant lowering of the ceruloplasmin level. Protein loss syndromes and liver cell failures are the most important causes of acquired ceruloplasmin depressions. As ceruloplasmin is a sensitive reactant to the acute phase, increases occur during acute and chronic inflammatory processes. Great increases can lead to a green-blue coloration of the sera. Methods for assaying ceruloplasmin include immunodiffusion, nephelometry and turbidimetry.

Test principle[2]

Immunoturbidimetric assay.

Human ceruloplasmin forms a precipitate with a specific antiserum which is determined turbidimetrically.

Reagents - working solutions

R1 Accelerator
Polyethylene glycol (PEG): 50 g/L; phosphate buffer; preservative

R2 Anti-ceruloplasmin T antiserum (rabbit) specific for human ceruloplasmin: > 0.42 g/L; phosphate buffer; preservative

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.

Reagent handling

Ready for use

Storage and stability

CERU

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

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. 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.

Stability:[4]	3 days at 2-8 °C
	4 weeks at (-15)-(-25) °C

Materials provided

See “Reagents – working solutions” section for reagents.

CERU

Ceruloplasmin

cobas®

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	10/6-25		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	g/L (µmol/L, mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	11 µL	15 µL	150 µL
Decreased	11 µL	5 µL	160 µL
Increased	11 µL	15 µL	150 µL

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10/10-36		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	g/L (µmol/L, mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	11 µL	15 µL	150 µL
Decreased	11 µL	5 µL	160 µL
Increased	11 µL	15 µL	150 µL

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10/10-36		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	g/L (µmol/L, mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	11 µL	15 µL	150 µL
Decreased	11 µL	5 µL	160 µL
Increased	11 µL	20 µL	90 µL

Calibration

Calibrators	S1: H_2O	
	S2-S6: C.f.a.s. PAC	
	Multiply the lot-specific C.f.a.s. PAC calibrator value by the factors below to determine the standard concentrations for the 6-point calibration curve:	
	S2: 0.600	S5: 3.20
	S3: 1.25	S6: 4.00
	S4: 2.10	
Calibration mode	RCM2	
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 reference preparation of the IRMM (Institute for Reference Materials and Measurements) BCR470/CRM470 (RPPHS - Reference Preparation for Proteins in Human Serum).[5]

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:	mg/dL x 0.01 = g/L	g/L x 7.46 = µmol/L
	g/L x 100 = mg/dL	mg/dL x 0.0746 = µmol/L

Limitations - interference

Criterion: Recovery within ± 10 % of the initial value at a ceruloplasmin concentration of 0.2 g/L (1.49 µmol/L, 20 mg/dL).

Icterus:[6] 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:[6] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[6] No significant interference up to an L index of 200. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors up to 100 IU/mL do not interfere.

High dose hook-effect: No false result occurs up to a ceruloplasmin concentration of 5 g/L (37.3 µmol/L, 500 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[7,8]

Exception: Intralipid causes artificially high ceruloplasmin results.

In very rare cases, gammopathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.[9]

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

CERU

Ceruloplasmin

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 not required.

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

Limits and ranges

Measuring range

0.03-1.4 g/L (0.22-10.44 µmol/L, 3-140 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

Lower limits of measurement

Lower detection limit of the test

0.03 g/L (0.22 µmol/L, 3 mg/dL)

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[10]

Male:	0.15-0.30 g/L
Female:	0.16-0.45 g/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 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:

Repeatability	*Mean*	*SD*	*CV*
	g/L (µmol/L, mg/dL)	*g/L (µmol/L, mg/dL)*	*%*
Precinorm Protein	0.283 (2.11, 28.3)	0.004 (0.03, 0.4)	1.6
Precipath Protein	0.620 (4.62, 62.0)	0.007 (0.05, 0.7)	1.1
Human serum 1	0.298 (2.23, 29.8)	0.003 (0.02, 0.25)	0.8
Human serum 2	0.501 (3.74, 50.1)	0.004 (0.03, 0.4)	0.7
Human serum 3	1.30 (9.70, 130)	0.009 (0.07, 0.9)	0.7
Intermediate precision	*Mean*	*SD*	*CV*
	g/L (µmol/L, mg/dL)	*g/L (µmol/L, mg/dL)*	*%*
Precinorm Protein	0.293 (2.19, 293)	0.004 (0.03, 0.4)	1.4
Precipath Protein	0.413 (3.08, 41.3)	0.004 (0.03, 0.4)	1.0
Human serum 3	0.188 (1.40, 18.8)	0.005 (0.04, 0.5)	2.6
Human serum 4	0.436 (3.25, 436)	0.007 (0.05, 0.7)	1.5

Method comparison

Ceruloplasmin 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).

Sample size (n) = 82

Passing/Bablok[11]	Linear regression
y = 0.980x + 0.012 g/L	y = 1.015x – 0.001 g/L
τ = 0.934	r = 0.997

The sample concentrations were between 0.132 and 1.32 g/L (0.984 and 9.85 µmol/L, 13.2 and 132 mg/dL).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995:227-228.

2 Wolf PL. Ceruloplasmin: methods and clinical use. Crit Rev Clin Lab Sci 1982;17:229-245.

3 Sternlieb I. Copper and the liver. Gastroenterology 1980;78:1615-1628.

4 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;122-123.

5 Baudner S, Bienvenu J, Blirup-Jensen S, et al. The certification of a matrix reference material for immunochemical measurement of 14 human serum proteins CRM470. Report EUR 15243 EN 1993;1-186.

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

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

8 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.

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

10 Data on file at Roche Diagnostics.

11 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

0020764663322c501V9.0

CERU

Ceruloplasmin

CE

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