TP2

cobas®

Total Protein Gen.2

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
05171385 190*	Total Protein Gen.2 (700 tests)	System-ID 05 6827 8	Roche/Hitachi **cobas c** 701/702
05171385 214*	Total Protein Gen.2 (700 tests)	System-ID 05 6827 8	Roche/Hitachi **cobas c** 701/702
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	
10557897 122	Precinorm Protein (3 x 1 mL)	Code 302	
10557897 160	Precinorm Protein (3 x 1 mL, for USA)	Code 302	
11333127 122	Precipath Protein (3 x 1 mL)	Code 303	
11333127 160	Precipath Protein (3 x 1 mL, for USA)	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	
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	
05172152 190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3	

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

English

System information

TP2: ACN 8678 (serum, plasma)

S-TP2: ACN 8679 (STAT, reaction time: 6)

Intended use

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

Summary[1]

Plasma proteins are synthesized predominantly in the liver, plasma cells, lymph nodes, the spleen and in bone marrow. In the course of disease the total protein concentration and also the percentage represented by individual fractions can significantly deviate from normal values. Hypoproteinemia can be caused by diseases and disorders such as loss of blood, sprue, nephrotic syndrome, severe burns, salt retention syndrome and Kwashiorkor (acute protein deficiency).

Hyperproteinemia can be observed in cases of severe dehydration and illnesses such as multiple myeloma. Changes in the relative percentage of plasma proteins can be due to a change in the percentage of one plasma protein fraction. Often in such cases the amount of total protein does not change. The A/G ratio is commonly used as an index of the distribution of albumin and globulin fractions. Marked changes in this ratio can be observed in cirrhosis of the liver, glomerulonephritis, nephrotic syndrome, acute hepatitis, lupus erythematosus as well as in certain acute and chronic inflammations. Total protein measurements are used in the diagnosis and treatment of a variety of diseases involving the liver, kidney, or bone marrow, as well as other metabolic or nutritional disorders.

Test principle[2]

Colorimetric assay

Divalent copper reacts in alkaline solution with protein peptide bonds to form the characteristic purple-colored biuret complex. Sodium potassium tartrate prevents the precipitation of copper hydroxide and potassium iodide prevents autoreduction of copper.

$$\text{protein} + Cu^{2+} \xrightarrow{\text{alkaline solution}} \text{Cu-protein complex}$$

The color intensity is directly proportional to the protein concentration which can be determined photometrically.

Reagents - working solutions

R1	Sodium hydroxide: 400 mmol/L; potassium sodium tartrate: 89 mmol/L; pH 13.4
R3 (STAT R2)	Sodium hydroxide: 400 mmol/L; potassium sodium tartrate: 89 mmol/L; potassium iodide: 61 mmol/L; copper sulfate: 24.3 mmol/L; pH 13.2

R1 is in position B and R3 (STAT 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

H290	May be corrosive to metals.
H315	Causes skin irritation.
H319	Causes serious eye irritation.
H411	Toxic to aquatic life with long lasting effects.

Prevention:

P264	Wash skin thoroughly after handling.
P273	Avoid release to the environment.

P280	Wear protective gloves/ eye protection/ face protection.

Response:

P337 + P313	If eye irritation persists: Get medical advice/attention.
P390	Absorb spillage to prevent material damage.
P391	Collect spillage.

Product safety labeling follows EU GHS guidance.

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

Reagent handling

Ready for use

Storage and stability

TP2

Shelf life at 15-25 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	2 weeks
On-board on the Reagent Manager:	24 hours

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:	4 weeks
On-board on the Reagent Manager:	24 hours

Specimen collection and preparation

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

Only the specimens listed below were tested and found acceptable.
Serum.
Plasma: Li-heparin and K_2-EDTA plasma

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

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

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:[3]	6 days at 20-25 °C
	4 weeks at 4-8 °C
	1 year at -20 °C

The total protein concentration is 4 to 8 g/L lower when the sample is collected from a patient situated in the recumbent position rather than upright.[4]

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 701/702 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 18-33 (STAT 6 / 6-22)		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	g/L (g/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	28 µL	
R3 (STAT R2)	32 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	6 µL	15 µL	120 µL
Increased	4 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration • after 7 days • 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 SRM 927.

Quality control

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

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory’s individual requirements. 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 factor:	g/L x 0.1 = g/dL

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a total protein concentration of 66 g/L (6.6 g/dL).

Icterus:[5] No significant interference up to an I index of 20 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 342 µmol/L or 20 mg/dL).

Hemolysis:[5] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 311 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[5] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Dextran: No significant interference from dextran up to a concentration of 30 mg/mL.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[6,7]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[8]

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

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

Limits and ranges

Measuring range

2.0-120 g/L (0.2-12 g/dL)

Determine samples having higher activities 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

2.0 g/L (0.2 g/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).

Values below the lower detection limit (< 2.0 g/L) will not be flagged by the instrument.

Expected values

Expected values according to Josephson[9]		
Adults	66-87 g/L	(6.6-8.7 g/dL)
Expected values according to Tietz[10]		
Umbilical cord	48-80 g/L	(4.8-8.0 g/dL)
Premature	36-60 g/L	(3.6-6.0 g/dL)
Newborn	46-70 g/L	(4.6-7.0 g/dL)
1 week	44-76 g/L	(4.4-7.6 g/dL)
7 months-1 year	51-73 g/L	(5.1-7.3 g/dL)
1-2 years	56-75 g/L	(5.6-7.5 g/dL)
> 3 years	60-80 g/L	(6.0-8.0 g/dL)
Adults (ambulatory)	64-83 g/L	(6.4-8.3 g/dL)
Expected values according to Australasian Association of Clinical Biochemists[11]		
Adults	60-80 g/L	

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 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:

TP2:

Repeatability	*Mean*	*SD*	*CV*
	g/L (g/dL)	*g/L (g/dL)*	*%*
Precinorm U	68.2 (6.82)	0.4 (0.04)	0.6
Precipath U	50.0 (5.00)	0.5 (0.05)	1.0
Human serum A	52.9 (5.29)	0.5 (0.05)	0.9
Human serum B	118 (11.8)	1 (0.1)	0.5
Human serum C	89.3 (8.93)	0.5 (0.05)	0.6

S-TP2:

Repeatability	*Mean*	*SD*	*CV*
	g/L (g/dL)	*g/L (g/dL)*	*%*
Precinorm U	68.0 (6.80)	0.2 (0.02)	0.4
Precipath U	50.1 (5.01)	0.2 (0.02)	0.4
Human serum A	52.8 (5.28)	0.3 (0.03)	0.6
Human serum B	117 (11.7)	0.4 (0.04)	0.4
Human serum C	89.0 (8.90)	0.5 (0.05)	0.6

TP2 / S-TP2:

Intermediate precision	*Mean*	*SD*	*CV*
	g/L (g/dL)	*g/L (g/dL)*	*%*
Precinorm U	67.9 (6.79)	1.6 (0.16)	2.4
Precipath U	50.7 (5.07)	0.9 (0.09)	1.7
Human serum 3	20.4 (2.04)	0.5 (0.05)	2.5
Human serum 4	87.8 (8.78)	1.5 (0.15)	1.7

Results for intermediate precision were obtained on the master system **cobas c** 501 analyzer.

Method comparison

Total protein values for human serum samples obtained on a Roche/Hitachi **cobas c** 701 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi **cobas c** 501 analyzer (x).

Sample size (n) = 101

TP2:

Passing/Bablok[12]	Linear regression
y = 1.019x - 1.26 g/L	y = 1.017x - 1.22 g/L
τ = 0.967	r = 0.999

The sample concentrations were between 2.50 and 116 g/L (0.250 and 11.6 g/dL).

S-TP2:

Passing/Bablok[12]	Linear regression
y = 1.008x - 0.832 g/L	y = 1.005x - 0.711 g/L
τ = 0.973	r = 0.999

The sample concentrations were between 2.30 and 117 g/L (0.230 and 11.7 g/dL).

References

1 Brobeck JR, ed. Physiological Basis of Medical Practice, 9th ed. Baltimore, MD: Wilkins and Wilkins 1973;4-7.

2 Weichselbaum TE. An accurate and rapid method for the determination of proteins in small amounts of blood serum and plasma. Am J Clin Pathol 1946;10:40-49.

3 WHO Publication: Use of anticoagulants in diagnostic laboratory investigations, WHO/DIL/LAB/99.1 Rev.2:Jan 2002.

4 Koller A. Total serum protein. In: Kaplan LA, Pesce AJ, eds. Clinical Chemistry, theory, analysis, and correlation St. Louis: Mosby Company 1984;1316-1319.

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

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

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

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

9 Josephson B, Gyllenswärd C. The Development of the Protein Fractions and of Cholesterol Concentration in the Serum of Normal Infants and Children. Scandinav J Clin Lab Investigation 1957;9:29.

10 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;518-523.

11 Tate JR, Sikaris KA, Jones GRD, et al. Harmonising adult and paediatric reference intervals in Australia and New Zealand: An evidence-based approach for establishing a first panel of chemistry analytes. Clin Biochem Rev 2014; Nov 35(4):213-35.

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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