TP2

Total Protein Gen. 2

cobas®

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03183734190	03183734500	Total Protein Gen.2 (300 tests)	System-ID 07 6827 8	**cobas c** 311, **cobas c** 501/502, COBAS INTEGRA 400 plus

Materials required (but not provided):

		cobas c 311, **cobas c** 501/502	COBAS INTEGRA 400 plus
10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 401	System-ID 07 3718 6
12149435122	Precinorm U plus (10 x 3 mL)	Code 300	System-ID 07 7999 7
12149443122	Precipath U plus (10 x 3 mL)	Code 301	System-ID 07 8000 6
10557897122	Precinorm Protein (3 x 1 mL)	Code 302	System-ID 07 9105 9
11333127122	Precipath Protein (3 x 1 mL)	Code 303	System-ID 07 9106 7
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	System-ID 07 7469 3
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	System-ID 07 7469 3
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	System-ID 07 7470 7
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	System-ID 07 7470 7
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	n.a.

English

Intended use

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

Summary

Measurements of total protein, performed with this assay in human serum or plasma, are used as aid in diagnosis and monitoring of a variety of diseases involving the liver, kidney, or bone marrow, as well as other metabolic or nutritional disorders.[1,2,3,4]

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

Hyperproteinemia can be observed in cases of severe dehydration and illnesses such as multiple myeloma. Changes in the relative percentage of plasma proteins can be due to a change in the percentage of one plasma protein fraction. Often in such cases the amount of total protein does not change. The albumin/globulin (A/G) ratio is commonly used as an index of the distribution of albumin and globulin fractions. Marked changes in this ratio can be observed in cirrhosis of the liver, glomerulonephritis, nephrotic syndrome, acute hepatitis, lupus erythematosus as well as in certain acute and chronic inflammations.[1,2,3,4]

Test principle[5]

Colorimetric assay

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

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

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

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

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

Warning

H290	May be corrosive to metals.
H315	Causes skin irritation.
H319	Causes serious eye irritation.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P264	Wash skin thoroughly after handling.
P273	Avoid release to the environment.
P280	Wear protective gloves/ eye protection/ face protection.

Response:

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

Disposal:

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

Product safety labeling follows EU GHS guidance.

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

Reagent handling

Ready for use

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

TP2

Total Protein Gen. 2

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

Centrifuge samples containing precipitates before performing the assay.

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

Stability:[6]	6 days at 20-25 °C
	4 weeks at 4-8 °C
	1 year at -20 °C (± 5 °C)

Freeze only once.

The total protein concentration is 4 to 8 g/L lower when the sample is collected from a patient situated in the recumbent position rather than upright.[7]

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- See "Order information" section
- General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

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

Calculation

The systems automatically calculate the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help.

Conversion factor: g/L x 0.1 = g/dL

Expected values

Expected values according to Josephson [8]

Adults	66-87 g/L	(6.6-8.7 g/dL)

Expected values according to Tietz[9]

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[10]

Adults	60-80 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.

cobas c systems

System information

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

TP2: ACN 678

S-TP2: ACN 679 (STAT, reaction time: 5)

For **cobas c** 502 analyzer:

TP2: ACN 8678

S-TP2: ACN 8679 (STAT, reaction time: 5)

Reagents - working solutions

R1	Sodium hydroxide: 400 mmol/L; potassium sodium tartrate: 89 mmol/L
R2	Sodium hydroxide: 400 mmol/L; potassium sodium tartrate: 89 mmol/L; potassium iodide: 61 mmol/L; copper sulfate: 24.3 mmol/L

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

Storage and stability

Shelf life at 15-25 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	4 weeks

Application for serum and plasma

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 6-23 (STAT 5 / 6-23)		
Wavelength (sub/main)	700 / 546 nm		
Reaction direction	Increase		
Units	g/L (g/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	28 µL	
R2	32 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	6 µL	15 µL	120 µL
Increased	2 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 10-34 (STAT 5 / 10-34)		
Wavelength (sub/main)	700 / 546 nm		
Reaction direction	Increase		
Units	g/L (g/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	28 µL	
R2	32 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	6 µL	15 µL	120 µL
Increased	2 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End

TP2

Total Protein Gen. 2

Reaction time / Assay points	10 / 10-34 (STAT 5 / 10-34)		
Wavelength (sub/main)	700 / 546 nm		
Reaction direction	Increase		
Units	g/L (g/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	28 µL	
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 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.

Limitations - interference

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

Icterus:[11] 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:[11] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 311 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[11] No significant i nterference 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.[12,13]

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

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

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

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

Lower limits of measurement

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).

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 on the **cobas c** 501 analyzer:

Repeatability	*Mean*	*SD*	*CV*
	g/L (g/dL)	*g/L (g/dL)*	*%*
Precinorm U	49.6 (4.96)	0.7 (0.07)	1.4
Precipath U	48.8 (4.88)	0.5 (0.05)	1.0
Human serum 1	48.3 (4.83)	0.5 (0.05)	1.1
Human serum 2	83.0 (8.30)	0.8 (0.08)	0.9
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

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

Method comparison

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

Sample size (n) = 86

Passing/Bablok[15]	Linear regression
y = 0.985x + 0.759 g/L	y = 0.980x + 1.09 g/L
τ = 0.949	r = 0.998

The sample concentrations were between 19.7 and 107 g/L (1.97 and 10.7 g/dL).

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

COBAS INTEGRA systems

TP2

Total Protein Gen. 2

cobas®

System information

Serum/plasma

Test TP2: Test ID 0-027

*Serum/plasma-Primary tube**

Test TP2M: Test ID 0-227

*The application is intended for customers facing non-valid results due to a contamination of the plasma supernatant in primary tubes with cell aggregates.

Reagents - working solutions

R1 Sodium hydroxide: 400 mmol/L; sodium potassium tartrate: 89 mmol/L

SR Sodium hydroxide: 400 mmol/L; sodium potassium tartrate: 89 mmol/L; potassium iodide: 61 mmol/L; copper sulfate: 24.3 mmol/L

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

Storage and stability

Shelf life at 15-25 °C	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	4 weeks

Application for serum and plasma

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A/B	552/659 nm
Calc. first/last	33/52
Unit	g/L

Pipetting parameters

		Diluent (H_2O)
R1	90 µL	0 µL
Sample	2 µL	28 µL
SR	32 µL	0 µL
Total volume	152 µL	

Application for serum and plasma-Primary tube

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A	552 nm
Calc. first/last	33/52
Unit	g/L

Pipetting parameters

		Diluent (H_2O)
R1	90 µL	0 µL
Sample	2 µL	28 µL
SR	32 µL	0 µL
Total volume	152 µL	

Calibration

Calibrator	Calibrator f.a.s. Use deionized water as zero calibrator.
Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	Each lot and 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

Reference range	Precinorm U plus, Precinorm Protein or PreciControl ClinChem Multi 1
Pathological range	Precipath U plus, Precipath Protein or PreciControl ClinChem Multi 2
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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.

Limitations - interference

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

Serum/plasma

Icterus:[11] 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:[11] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

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

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.[12,13]

Low recovery may be caused by the formation of cell aggregates in some heparin plasma samples. Not applicable to the primary tube application (TP2M, test ID 0-227).

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

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 INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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

Limits and ranges

Measuring range

2-120 g/L (0.2-12 g/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

Lower limits of measurement

Lower detection limit of the test:
2 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 a zero sample (zero sample + 3 SD, repeatability, n = 30).

Precision

Serum/plasma

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (1 aliquot per run, 1 run per day, 21 days). Results for repeatability and intermediate precision were obtained on the COBAS INTEGRA 700 analyzer.

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
Human serum 1	70.1	0.8	1.1
Human serum 2	84.2	0.4	0.5
Precinorm U	48.0	0.2	0.5
Precipath U	51.7	0.3	0.5

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
Human serum 1	65.4	1.4	2.2
Human serum 2	92.0	1.4	1.5
Precinorm U	52.6	0.5	1.0
Precipath U	51.2	0.9	1.7

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Serum/plasma-Primary tube

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (1 aliquot per run, 1 run per day, 10 days). Results for repeatability and intermediate precision were obtained on the COBAS INTEGRA 700 analyzer.

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
Human serum 1	55.6	0.4	0.7
Human serum 2	81.1	0.4	0.6
Precinorm U	65.2	0.3	0.5
Precipath U	48.4	0.5	0.7

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
Human serum 1	57.1	0.6	1.1
Human serum 2	81.9	0.6	0.7
Precinorm U	64.8	0.6	1.0
Precipath U	47.6	0.6	1.3

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Method comparison

Serum/plasma

Total protein values for human serum samples obtained on a COBAS INTEGRA 700 using the COBAS INTEGRA Total Protein Gen.2 reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and with those determined using the previous reagent (TP) on a COBAS INTEGRA 700 analyzer (x).

Roche/Hitachi 917 analyzer

Sample size (n) = 114

Passing/Bablok[15]	Linear regression
y = 0.979x + 0.249 g/L	y = 0.978x + 0.452 g/L
τ = 0.947	r = 0.998
SD (md 95) = 1.54	Sy.x = 0.732

The sample concentrations were between 32 and 100 g/L (3.2 and 10.0 g/dL).

COBAS INTEGRA 700 analyzer

Sample size (n) = 60

Passing/Bablok[15]	Linear regression
y = 1.033x - 0.541 g/L	y = 1.031x - 0.372 g/L
τ = 0.972	r = 0.999
SD (md 95) = 0.984	Sy.x = 0.467

The sample concentrations were between 24 and 113 g/L (2.4 and 11.3 g/dL).

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Serum/plasma-Primary tube

Total protein values for human serum samples obtained on a COBAS INTEGRA 700 using the COBAS INTEGRA Total Protein Gen.2 reagent and the monochromatic application TP2M (y) were compared with those determined using the corresponding reagent and instrument but the bichromatic application TP2 (x) and with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 65

COBAS INTEGRA 700 analyzer TP2 (bichromatic)

Passing/Bablok[15]	Linear regression
y = 0.970x - 0.450 g/L	y = 0.971x - 0.412 g/L
τ = 0.952	r = 0.999
SD (md 95) = 0.078	Sy.x = 0.038

The sample concentrations were between 11.8 and 113 g/L (1.18 to 11.31 g/dL).

Roche/Hitachi 917 analyzer

Passing/Bablok[15]	Linear regression
y = 0.964x + 0.107 g/L	y = 0.967x + 0.067 g/L
τ = 0.964	r = 0.999
SD (md 95) = 0.093	Sy.x = 0.039

The sample concentrations were between 11.8 and 113 g/L (1.18 to 11.31 g/dL).

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

References

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

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

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

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

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

CE 0123

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