ALBT2

cobas®

Tina-quant Albumin Gen.2 - CSF Application

Specific proteins

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04469658 190	Tina-quant Albumin Gen.2 (100 tests)	System-ID 07 6743 3	COBAS INTEGRA 400 plus

Materials required (but not provided):

03121305 122	C.f.a.s. PUC (5 × 1 mL)	System-ID 07 6755 7	
03121291 122	Precipath PUC (4 × 3 mL)	System-ID 07 6757 3	
20756350 322	NaCl Diluent 9 % (6 × 22 mL)	System-ID 07 5635 0	

English

System information

Test ALBC2, test ID 0-170

Intended use

In vitro test for the quantitative immunological determination of human albumin in serum, plasma, urine and cerebrospinal fluid.

The applications for urine and serum/plasma are described in the Tina-quant Albumin Gen.2 *Urine Application* and in the Tina-quant Albumin Gen.2 *Serum/Plasma Application* method sheets.

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

Albumin is a carbohydrate-free protein, representing 55-65 % of the total plasma proteins. It maintains the plasma colloidal osmotic pressure, transports and stores a wide variety of ligands, and serves as a source of endogenous amino acids.

About 80 % of the protein content in CSF originates from plasma as a result of ultrafiltration. Low molecular weight proteins predominate, albumin, prealbumin, and transferrin in particular. Albumin is neither synthesized nor metabolized within the central nervous system. Therefore, it is suitable to indicate increased permeability of the blood-brain barrier in case of pathological, traumatic, or inflammatory events.

Impairment of the blood-brain barrier can be evaluated using the CSF/serum albumin index.[5]

Abbreviated ratio name: ALB-I (0-178)

CSF/serum albumin index = $Albumin_{CSF}$ (mg/L)/$Albumin_{Ser}$ (g/L)

An index > 9 indicates impairment of blood-brain barrier.

The measurement of albumin in CSF is of further interest in the determination of intrathecal IgG production which is associated with demyelinating disorders like multiple sclerosis. An increased IgG concentration in CSF may be caused by increased permeability or increased intrathecal production. To accurately determine the intrathecal IgG production, the IgG fraction caused by increased permeability can be corrected by measuring albumin in CSF and making calculations as follows: [5]

Abbreviated ratio name: IGGR2 (0-179)

Ratio = IgG_{CSF} (mg/L)/$Albumin_{CSF}$ (mg/L)

An index > 0.27 indicates increased intrathecal IgG synthesis.

Abbreviated ratio name: IGGI2 (0-180)

IgG index = IgG_{CSF} (mg/L) × $Albumin_{Ser/Plasma}$ (g/L) / IgG_{Ser} (g/L) / $Albumin_{CSF}$ (mg/L)

Index values > 0.7 are considered indicative of increased IgG synthesis. In > 80 % of multiple sclerosis cases, the index exceeds 0.7.

Test principle[6,7]

Immunoturbidimetric assay

Human albumin forms a precipitate with a specific antiserum which is determined turbidimetrically at 340 nm.

Reagents - working solutions

R1 TRIS[a] buffer: 50 mmol/L, pH 8.0; PEG: ≥ 4.2 %; EDTA: 2 mmol/L; preservative

R2 Polyclonal anti-human albumin antibodies (sheep): dependent on titer; TRIS[a] buffer: 100 mmol/L, pH 7.2; preservative

SR Reagent for antigen excess check
Albumin in diluted serum (human); phosphate buffer: 50 mmol/L, pH 7.0; preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

R1 is in position A, R2 is in position B, and SR is in position C.

Precautions and warnings

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

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

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

Safety data sheet available for professional user on request.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[8,9]

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	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.
CSF

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.

Samples and controls are automatically prediluted 1:6 (1+5) with NaCl solution by the instrument.

Centrifuge samples containing precipitates before performing the assay.

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

Stability:[10]	up to 72 hours at 4 °C
	6 months at -20 °C
	indefinitely at -70 °C

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

NaCl Diluent 9 %, Cat. No. 20756350322, system-ID 07 5635 0 for automatic postdilution and standard serial dilutions. NaCl Diluent 9 % is placed in its predefined rack position and is stable for 4 weeks on-board the COBAS INTEGRA 400 plus analyzer.

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.

Application for CSF

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	R1-S-R2-SR
Reaction direction	Increase
Reaction start with	R2
Wavelength A/B	340/659 nm
Calc. first/last	33/49
Typical prozone effect	> 2400 mg/L (> 36.5 µmol/L or > 240 mg/dL)
Antigen excess check	Yes (with SR)
Predilution factor	6
Unit	mg/L

Pipetting parameters

		Diluent (H_2O)
R1	100 µL	—
Sample	6 µL	15 µL
R2	20 µL	—
SR	6 µL	10 µL
Total volume	157 µL	

Calibration

Calibrator	C.f.a.s. PUC
Calibration dilution ratio	1:2, 1:4, 1:8, 1:16, 1:32, 1:64 performed automatically by the instrument
Calibration mode	Logit/log 4
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.

Enter the assigned lot-specific albumin value of the undiluted calibrator (mg/L), indicated in the package insert of C.f.a.s. PUC.

Traceability: This method has been standardized against an internal method traceable to the certified reference material in human serum of the IRMM (Institute for Reference Materials and Measurements) ERM-DA470k/IFCC.

Quality control

Quality control	Use commercially available CSF controls or Precipath PUC.
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.

Calculation

The COBAS INTEGRA 400 plus analyzer automatically calculates the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help.

Conversion factors:	mg/L x 0.0152 = µmol/L
	mg/L x 0.1 = mg/dL

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

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

High-dose hook effect does not occur at albumin concentrations below 36.5 µmol/L or 2400 mg/L . Samples with concentrations > 2400 mg/L are flagged either ">TEST RNG" or "AG EXCESS".

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

b) measured at analyte concentrations up to approximately 175 mg/L

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

18-1260 mg/L (0.274-19.2 µmol/L or 1.8-126 mg/dL) (typical measuring range)

The upper limit of the measuring range depends on the actual calibrator value.

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

Lower limits of measurement

Lower detection limit of the test:
18 mg/L (0.274 µmol/L or 1.8 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 a zero sample (zero sample + 3 SD, repeatability, n = 21).

Expected values

Albumin CSF/serum index ($Q_{ALB} \times 10^3$)

Adults:[11]	up to 15 years	5.0
	up to 40 years	6.5
	up to 60 years	8.0

IgG_{CSF}/$albumin_{CSF}$ ratio[5]

Normal	< 0.27

An index > 0.27 indicates an increased intrathecal IgG synthesis.

IgG index[5]

Normal	0.30-0.70

An index > 0.70 indicates an increased intrathecal IgG synthesis.

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 COBAS INTEGRA 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 (1 aliquot per run, 1 run per day, 10 days). The following results were obtained:

Repeatability	*Mean mg/L*	*SD mg/L*	*CV %*
CSF low	111	1	1.0
CSF high	340	3	0.9
Control low	88.1	1.7	1.9
Control high	448	4	1.0

Intermediate precision	*Mean mg/L*	*SD mg/L*	*CV %*
CSF low	104	1	1.2
CSF high	336	6	1.7
Control low	87.2	1.8	2.1
Control high	446	3	0.7

Method comparison

Albumin values for human CSF samples obtained on a COBAS INTEGRA 800 analyzer using the COBAS INTEGRA Tina-quant Albumin Gen.2 reagent (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

cobas c 501 analyzer	Sample size (n) = 66
Passing/Bablok[12]	Linear regression
y = 1.050x + 2.452 mg/L	y = 1.096x - 14.754 mg/L
τ = 0.967	r = 0.998

The sample concentrations were between 36.7 and 1168 mg/L (0.558 and 17.8 µmol/L or 3.67 and 117 mg/dL).

References

1 Grant GH, Silverman LM, Christenson RH. Amino acids and proteins. In: Tietz NW, ed. Fundamentals of Clinical Chemistry, 3rd edition Philadelphia, PA: WB Saunders 1987:291-345.

2 Marshall WJ, ed. Illustrated Textbook of Clinical Chemistry, 3rd ed. London: Gower Medical Publishing 1989;207-218.

3 Dati F, Lammers M. Immunochemical methods for determination of urinary proteins (albumin and α1-microglobulin) in kidney disease. J Int Fed Clin Chem 1989;1:68-77.

4 Watts NB. Albuminuria and diabetic nephropathy: an evolving story. Clin Chem 1991;37:2027-2028.

5 Silverman LM, Christenson RH. Amino acids and proteins. In Tietz NW, ed. Fundamentals of Clinical Chemistry. 4th ed. Philadelphia: WB Saunders 1996;240-282.

6 Gerbaut L.Immunoturbidimetry of albumin in serum, cerebrospinal fluid, and urine with a unique calibration curve. Clin Chem 1987;33:1260-1261.

7 Croci D, Nespolo A, Bosoni MA, et al. A simple immunoturbidimetric method for IgG and albumin quantitation in cerebrospinal fluid and serum. J Clin Chem Clin Biochem 1989;27:863-868.

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

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

10 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;24.

11 Reiber H. External Quality Assessment in Clinical Neurochemistry: Survey of Analysis for Cerebrospinal Fluid (CSF) Proteins based on CSF/Serum Quotients. Clin Chem 1995;41:256-263.

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.

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 after reconstitution or mixing
GTIN	Global Trade Item Number

CE 0123

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

Roche