ALBT2

Tina-quant Albumin Gen.2

cobas®

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04469658190	04469658500	Tina-quant Albumin Gen.2 (100 tests)	System-ID 07 6743 3	**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
03121305122	C.f.a.s. PUC (5 x 1 mL)	Code 489	System-ID 07 6755 7
03121313122	Precinorm PUC (4 x 3 mL)	Code 240	System-ID 07 6756 5
03121291122	Precipath PUC (4 x 3 mL)	Code 241	System-ID 07 6757 3
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.
20756350322	NaCl Diluent 9 % (6 x 22 mL)	n.a.	System-ID 07 5635 0

English

Intended use

In vitro test for the quantitative determination of albumin in human serum, plasma, urine and CSF (albumin CSF/serum ratio) on **cobas c** and COBAS INTEGRA systems.

Intended use of the specific applications for Reiber diagnostic*

*not available in all countries

In vitro test for the quantitative determination of albumin in human cerebrospinal fluid and corresponding human serum/plasma on **cobas c** systems.

Summary

Albumin measurement in human serum and plasma with this device can be used to aid in the assessment of hyperalbuminemia (seen only in case of dehydration) or hypoalbuminemia (seen in a multitude of clinical conditions such as inflammation, liver diseases, Inflammatory disease of the intestinal tract, tissue damage like burns, nephrotic disease or neoplastic disease).

Albumin measurements in urine can be used to aid in the assessment of glomerular, tubular, glomerulotubular and postrenal proteinuria. Microalbuminuria (slightly elevated albumin excretion in urine) is of particular importance in the early diagnosis of diabetic nephropathy.

Albumin measurement in human cerebrospinal fluid (CSF) can be used to aid in the assessment of increased permeability of the blood-brain barrier, indicative of a blood brain barrier disorder. Albumin measurements in CSF aid in the determination of intrathecal IgG production associated with demyelinating disorders.

Albumin is a carbohydrate-free protein, which constitutes 55-65 % of total plasma protein. It maintains plasma oncotic pressure, is involved in the transport and storage of a wide variety of ligands and is a source of endogenous amino acids.[1]

In serum and plasma, hyperalbuminemia is of little diagnostic significance except in dehydration. Hypoalbuminemia instead is very common in many diseases and is caused by several factors: impaired synthesis, either primary as a result of a liver disease or secondary due to diminished protein intake; increased catabolism because of tissue damage (severe burns) or inflammation; malabsorption of amino acids or increased gastrointestinal loss (inflammatory bowel disease such as Crohn's disease and ulcerative colitis); proteinuria due to nephrotic syndrome; negative protein and energy balance due to neoplastic disease(s).[2,3,4]

In severe cases of hypoalbuminemia, plasma albumin levels are below 25 g/L (380 µmol/L).[3] The low plasma oncotic pressure allows water to move out of the blood capillaries into the tissues (edema). Albumin measurements also allow monitoring of the patient's response to nutritional support and are a useful test of liver function.[1,5,6]

The kidney normally prevents loss of serum albumin into the urine. However, albumin is still found in normal urine in small amounts. Because size (69 kD), anionic charge, and tubular reabsorption all play a role in albumin's renal handling, excretion increases with altered glomerular size and charge selectivity as well as with tubular impairment.[1]

In glomerular disease far higher amounts of albumin may be secreted than in tubular disease. Urinary albumin is therefore considered the most important marker for glomerular dysfunction.[7] Nearly 40 % of insulin dependent diabetes patients develop diabetic nephropathy which presents in its earliest stage with microalbuminuria. Microalbuminuria is defined as excretion above normal but lower than the detection limit of traditional dipstick tests, i.e. between 20 and 200 µg/min.[8]

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.[1]

Impairment of the blood-brain barrier can be evaluated using the CSF/serum ratio (Q_{Alb}) which provides method independent values.[9]

$Q_{Alb} = Albumin_{CSF}/Albumin_{serum} \times 1000$

Normal Q_{Alb} values are < 6.5 for the population between 15 and 40 years old, < 8.0 for the population between 41 and 60 and < 9.0 for the population over 60 years old. Q_{Alb} values greater than or equal to the reported thresholds indicate impairment of blood brain barrier.[9,10]

The measurement of albumin in CSF is of further interest in the determination of intrathecal IgG production which is associated with demyelinating disorders and inflammatory diseases of the central nervous system (CNS) (e.g. multiple sclerosis, neurosyphilis, acute inflammatory polyradiculoneuropathy, subacute sclerosing panencephalitis).[1]

An increased IgG concentration in CSF may be caused by increased permeability or increased intrathecal production. To determine the intrathecal IgG production, several formulae have been proposed and evaluated. The linear IgG index has been broadly used in the past because of its simplicity, but it has been replaced by non linear formulae, such as Reiber's hyperbolic formula that better reflects human neurophysiology.[11,12] Increase of the IgG index (Q_{IgG}) is a reflection of increased IgG intrathecal production. The most informative method indicating intrathecal synthesis of

IgG is the qualitative demonstration of two or more CSF-specific oligoclonal bands.[13,14]

Test principle

Immunoturbidimetric assay.
Anti-albumin antibodies react with the antigen in the sample to form antigen/antibody complexes which, following agglutination, are measured turbidimetrically.[15]

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.[16,17]

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
Urine
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.

Centrifuge samples containing precipitates before performing the assay.

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

Serum, plasma

Stability:[18]	10 weeks	at 15-25 °C
	5 months	at 2-8 °C
	4 months	at (-15)-(-25) °C

Freeze only once.

Urine

Spontaneous, 24-hour urine or 2nd morning urine.

Stability:[18]	7 days	at 15-25 °C
	1 month	at 2-8 °C
	6 months	at (-15)-(-25) °C

Freeze only once.

CSF

Stability:[19]	up to 3 days	at 2-8 °C
	6 months	at (-15)-(-25) °C
	indefinitely	at (-60)-(-80) °C

Freeze only once.

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 factors: g/L x 100 = mg/dL
g/L x 15.2 = µmol/L
mg/L x 0.1 = mg/dL
mg/L x 0.0152 = µmol/L

Customer using the specific application for calculation according to Reiber and Felgenhauer ALBT-C ACN 440 on **cobas c** 501 analyzer or ACN 8440 on **cobas c** 502 analyzer have the possibility to use the calculated test function.

To calculate serum/plasma samples in g/L a calculated test must be programmed under Utility > Calculated Test on the **cobas c** 501 analyzer. Please use the following settings.

cobas c 501

Sample Type	Ser/Pl
Unit of Measure	g/L
Report Name	ALBT Serum
Item	ALBTS
Formula	Alb-C/1000

The values for serum/plasma in g/L will be automatically calculated after result output. It is recommended to report the IgG values in serum/plasma to two decimal places, which can be entered in the editable field “Expected Values”.

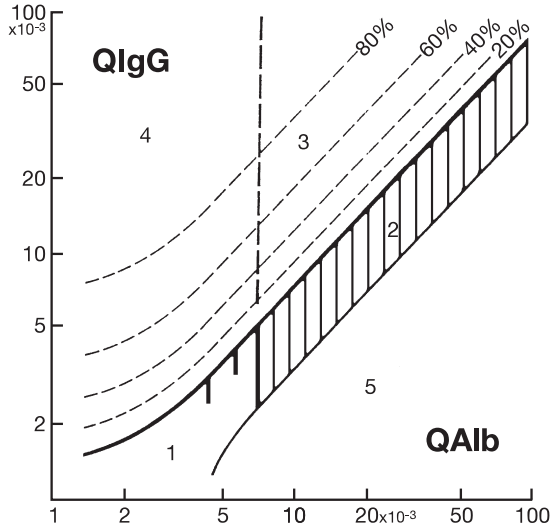
For the definition of the calculated test on the **cobas c** 502 analyzer, refer to the operator's manual of the cobas 8000 Data Manager.

Reiber Quotient Graph

The calculation employs a ratio diagram including hyperbolic functions as differential lines according to Reiber and Felgenhauer. Results from the determination of IgG and albumin in CSF and serum (IgG and albumin ratios)[20] are plotted. (Example for IgG, CSF/serum quotient diagrams for IgA and IgM are also possible.)

ALBT2

Tina-quant Albumin Gen.2



1. Reference range. 2. Blood brain barrier functional disorder without local IgG synthesis. 3. Blood brain barrier functional disorder with concomitant IgG-synthesis in the CNS. 4. IgG synthesis in the CNS without blood brain barrier functional disorder. 5. As confirmed empirically, there are no values in this region (i.e. values here are due to errors introduced by blood sampling or analytical errors). Generally speaking, cases not associated with local IgG synthesis in the CNS lie below the bold line (hyperbolic function). The percentage values indicate what percentage of the total IgG in CSF (minimum) originates in the CNS relative to the statistically-defined 0 % differential lines.

Expected values

Serum/plasma

Consensus values:[21]

Adults	3.5-5.2 g/dL (35-52 g/L; 532-790 µmol/L)

Reference intervals according to Tietz:[22]

Newborns 0-4 d:	2.8-4.4 g/dL (28-44 g/L; 426-669 µmol/L)
Children 4 d-14 yr:	3.8-5.4 g/dL (38-54 g/L; 578-821 µmol/L)

Urine

2nd morning urine:[23]

Adults:	< 20 mg albumin/g creatinine or
	< 2.26 g (34.35 µmol) albumin/mol creatinine
Children (3-5 years):[24]	< 20 mg/L (0.304 µmol/L, 2 mg/dL) albumin
	< 30 mg albumin/g creatinine
24-hour urine:[25]	< 20 mg/L (0.304 µmol/L, 2 mg/dL)
	< 30 mg/24 h (0.456 µmol/24 h)

CSF

Albumin CSF/serum ratio (Q_{ALB}x 10^3)

Adults:[9]	up to 15 years	5.0
	up to 40 years	6.5
	up to 60 years	8.0

IgG_{CSF}/$albumin_{CSF}$ ratio[26]

Normal	< 0.27

An index > 0.27 indicates an increased intrathecal IgG synthesis.

IgG index[26]

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.

cobas c systems

System information

Serum/plasma/urine/CSF application

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

ALB2S: ACN 128 (serum, plasma)

ALBU2: ACN 253 (urine)

ALBC2: ACN 412 (CSF)

For **cobas c** 501 analyzers:

Specific application for Reiber diagnostic*

ALB-C: ACN 440 (serum, plasma, CSF)

* not available in all countries

For **cobas c** 502 analyzers:

ALB2S: ACN 8128 (serum, plasma)

ALBU2: ACN 8253 (urine)

ALBC2: ACN 8412 (CSF)

Specific application for Reiber diagnostic*

ALB-C: ACN 8440 (serum, plasma, CSF)

* not available in all countries

Reagents - working solutions

R1	TRIS buffer: 50 mmol/L, pH 8.0; PEG: ≥ 4.2 %; EDTA: 2.0 mmol/L; preservative
R2	Polyclonal anti-human albumin antibodies (sheep): dependent on titer; TRIS buffer: 100 mmol/L, pH 7.2; preservative
R3	Reagent for antigen excess check. Albumin in diluted serum (human); NaCl: 150 mmol/L; phosphate buffer: 50 mmol/L, pH 7.0; preservative

R1 is in position A, R2 is in position B and R3 is in position C.

Storage and stability

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

Application for serum and plasma

cobas c 311 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 6-18	
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	1.5 µL	1.5 µL	180 µL

Decreased	1.5 µL	1.5 µL	180 µL
Increased	1.5 µL	1.5 µL	180 µL

cobas c 501 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-34
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	2.0 µL	2.1 µL	175 µL
Decreased	2.0 µL	1.7 µL	180 µL
Increased	2.0 µL	2.1 µL	175 µL

cobas c 502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-34
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	2.0 µL	2.1 µL	175 µL
Decreased	2.0 µL	1.7 µL	180 µL
Increased	4.0 µL	2.1 µL	175 µL

Application for urine

cobas c 311 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 6-15
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	mg/L (µmol/L, mg/dL)

Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	–	–
Decreased	6.0 µL	15 µL	150 µL
Increased	6.0 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-34
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	mg/L (µmol/L, mg/dL)

Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	–	–
Decreased	6.0 µL	15 µL	150 µL
Increased	6.0 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-34
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	mg/L (µmol/L, mg/dL)

Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	–	–
Decreased	6.0 µL	15 µL	150 µL
Increased	12 µL	–	–

Application for CSF

cobas c 311 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 6-15

Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L (µmol/L, mg/dL)	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	10 µL	110 µL
Decreased	3 µL	5 µL	180 µL
Increased	6.0 µL	10 µL	110 µL

cobas c 501 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-34	
Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L (µmol/L, mg/dL)	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	10 µL	110 µL
Decreased	3 µL	5 µL	180 µL
Increased	6.0 µL	10 µL	110 µL

cobas c 502 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-34	
Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L (µmol/L, mg/dL)	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	10 µL	110 µL
Decreased	3 µL	5 µL	180 µL
Increased	12.0 µL	10 µL	110 µL

Specific applications for Reiber diagnostic*

*not available in all countries

Application for serum and plasma

cobas c 501 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-34	
Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.0 µL	2.1 µL	175 µL
Decreased	2.0 µL	1.7 µL	180 µL
Increased	2.0 µL	2.1 µL	175 µL

cobas c 502 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-34	
Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.0 µL	2.1 µL	175 µL
Decreased	2.0 µL	1.7 µL	180 µL
Increased	4.0 µL	2.1 µL	175 µL

Application for CSF

cobas c 501 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-34	
Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–

R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	10 µL	110 µL
Decreased	3 µL	5 µL	180 µL
Increased	6.0 µL	10 µL	110 µL

cobas c 502 **test definition**

Assay type	2-Point End	
Reaction time / Assay points	10 / 10-34	
Wavelength (sub/main)	700/340 nm	
Reaction direction	Increase	
Units	mg/L	
Reagent pipetting		Diluent (H_2O)
R1	100 µL	–
R2	20 µL	–
R3	6 µL	20 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6.0 µL	10 µL	110 µL
Decreased	3 µL	5 µL	180 µL
Increased	12.0 µL	10 µL	110 µL

Calibration

Calibrators S1: H_2O

S2-6: C.f.a.s. PUC

Multiply the lot-specific C.f.a.s. PUC calibrator value by the factors below to determine the standard concentrations for the 6-point calibration curve:

cobas c 501/502	S2:	0.0138	S5:	0.467
	S3:	0.0228	S6:	1.00
	S4:	0.0455		
cobas c 311	S2:	0.0276	S5:	0.467
	S3:	0.0456	S6:	1.00
	S4:	0.0909		

Calibration mode RCM

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 certified reference material in human serum of the IRMM (Institute for Reference Material and Measurements) ERM-DA470k/IFCC.

Quality control

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

In addition, other suitable control material can be used.

ALBS2:	Precinorm Protein, Precipath Protein, PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2
ALB-C: (Serum/plasma)	PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2
ALBU2: (Urine)	Precinorm PUC, Precipath PUC
ALBC2, ALB-C: (CSF)	undiluted Precipath PUC

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

Serum/plasma

Criterion: Recovery within ± 10 % of initial value at an albumin concentration of 35 g/L (532 µmol/L, 3500 mg/dL).

Icterus:[27] 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:[27] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[27] No significant interference up to an L index of 1500. 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.[28,29]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[30]

Urine

Criterion: Recovery within ± 10 % of initial value at an albumin concentration of 20 mg/L (0.304 µmol/L, 2.0 mg/dL).

Icterus: No significant interference up to a conjugated bilirubin concentration of 855 µmol/L or 50 mg/dL.

Hemolysis: No significant interference up to a hemoglobin concentration of 248 µmol/L or 400 mg/dL.

No significant interference from acetone ≤ 60 mmol/L, ammonia chloride ≤ 0.11 mol/L, calcium ≤ 40 mmol/L, creatinine ≤ 0.18 mol/L, γ-globulin ≤ 500 mg/L, glucose ≤ 0.19 mol/L, phosphate ≤ 70 mmol/L, urea ≤ 0.8 mol/L, uric acid ≤ 5.95 mmol/L and urobilinogen ≤ 378 µmol/L.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[29]

High dose hook-effect: Using the prozone check automatically performed by the analyzer, no false result without a flag was observed up to an albumin concentration of 40000 mg/L (608 µmol/L, 4000 mg/dL).

CSF

Criterion: Recovery within ± 10 % of initial value at an albumin concentration of 240 mg/L (3.65 µmol/L, 24 mg/dL).

Hemolysis: No significant interference up to a hemoglobin concentration of 620 µmol/L or 1000 mg/dL.

High dose hook-effect: Using the prozone check automatically performed by the analyzer, no false result without a flag was observed up to an albumin concentration of 30000 mg/L (456 µmol/L, 3000 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 **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

cobas c 501/502: 3-101 g/L (46-1540 µmol/L, 300-10100 mg/dL)

cobas c 311: 3-96 g/L (46-1459 µmol/L, 300-9600 mg/dL)

cobas c 501/502: Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:1.27 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 1.27.

cobas c 311: Determine samples having higher concentrations by a manual predilution of 1:2. Calculate the final results by multiplying the measured value with a factor of 2.

Urine

cobas c 501/502: 3-400 mg/L (0.05-6.08 µmol/L, 0.3-40 mg/dL)

cobas c 311: 3-200 mg/L (0.05-3.04 µmol/L, 0.3-20 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:11 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 11.

CSF

cobas c 501/502: 36-4800 mg/L (0.55-73.0 µmol/L, 3.6-480 mg/dL)

cobas c 311: 36-2400 mg/L (0.55-36.5 µmol/L, 3.6-240 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:6.2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 6.2.

Lower limits of measurement

Limit of Blank and Limit of Detection

Serum, plasma

Limit of Blank	= 1 g/L
Limit of Detection	= 3 g/L

Urine

Limit of Blank	= 2 mg/L
Limit of Detection	= 3 mg/L

CSF

Limit of Blank	= 20 mg/L
Limit of Detection	= 36 mg/L

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 (≤ 3 g/L (serum, plasma); ≤ 3 mg/L (urine); ≤ 36 mg/L (CSF)) will not be flagged by the instrument.

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:

Serum/plasma

Repeatability	*Mean*	*SD*	*CV*
	g/L (µmol/L, mg/dL)	*g/L (µmol/L, mg/dL)*	*%*
Precinorm Protein	39.9 (606, 3990)	0.5 (8, 50)	1.2
Precipath Protein	66.6 (1012, 6660)	1.4 (21, 140)	2.1
Human serum 1	27.6 (420, 2760)	0.3 (5, 40)	1.3
Human serum 2	62.5 (950, 6250)	0.9 (14, 90)	1.5
Intermediate precision	*Mean*	*SD*	*CV*
	g/L (µmol/L, mg/dL)	*g/L (µmol/L, mg/dL)*	*%*
Precinorm Protein	42.3 (643, 4230)	0.9 (14, 90)	2.0
Precipath Protein	70.5 (1072, 7050)	1.6 (24, 160)	2.2
Human serum 3	7.78 (118, 778)	0.74 (11, 74)	9.5
Human serum 4	36.2 (550, 3620)	0.7 (11, 70)	2.1

Urine

Repeatability	*Mean*	*SD*	*CV*
	mg/L (µmol/L, mg/dL)	*mg/L (µmol/L, mg/dL)*	*%*
Precinorm PUC	30.7 (0.467, 3.07)	0.2 (0.003, 0.02)	0.8
Precipath PUC	108 (1.64, 10.8)	1 (0.01, 0.1)	0.7
Human urine 1	14.3 (0.217, 1.43)	0.2 (0.003, 0.02)	1.6
Human urine 2	252 (3.83, 25.2)	4 (0.06, 0.4)	1.6
Intermediate precision	*Mean*	*SD*	*CV*
	mg/L (µmol/L, mg/dL)	*mg/L (µmol/L, mg/dL)*	*%*
Precinorm PUC	31.2 (0.474, 3.12)	0.5 (0.008, 0.05)	1.7
Precipath PUC	105 (1.60, 10.5)	1 (0.02, 0.1)	1.2
Human urine 3	13.6 (0.207, 1.36)	0.4 (0.006, 0.04)	2.8
Human urine 4	60.6 (0.921, 6.06)	1.4 (0.021, 0.14)	2.3

CSF

Repeatability	*Mean*	*SD*	*CV*
	mg/L (µmol/L, mg/dL)	*mg/L (µmol/L, mg/dL)*	*%*
Precipath PUC	99.2 (1.51, 9.92)	1.4 (0.02, 0.14)	1.4
Human CSF 1	174 (2.64, 17.4)	3 (0.05, 0.3)	1.7
Human CSF 2	383 (5.82, 38.3)	4 (0.06, 0.4)	1.0
C.f.a.s. PUC	454 (6.90, 45.4)	4 (0.06, 0.4)	0.8
Intermediate precision	*Mean*	*SD*	*CV*
	mg/L (µmol/L, mg/dL)	*mg/L (µmol/L, mg/dL)*	*%*
Precipath PUC	91.0 (1.38, 9.1)	2.9 (0.04, 0.29)	3.2
Control level 2	389 (5.91, 38.9)	7 (0.11, 0.7)	1.7
Human CSF 3	166 (2.53, 16.6)	4 (0.06, 0.4)	2.3
Human CSF 4	366 (5.56, 36.6)	5 (0.07, 0.5)	1.3

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

Method comparison

Serum/plasma

ALBT2

Tina-quant Albumin Gen.2

Albumin values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined with a nephelometric albumin test (x).

Sample size (n) = 80

Passing/Bablok[31]	Linear regression
y = 0.950x + 0.195 g/L	y = 0.941x + 0.581 g/L
τ = 0.923	r = 0.993

The sample concentrations were between 5.70 and 107 g/L (86.6 and 1626 µmol/L, 570 and 10700 mg/dL).

Urine

Albumin values for human urine 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) = 129

Passing/Bablok[31]	Linear regression
y = 1.021x - 2.91 mg/L	y = 1.026x - 3.66 mg/L
τ = 0.984	r = 0.999

The sample concentrations were between 4.60 and 386 mg/L (0.070 and 5.87 µmol/L, 0.460 and 38.6 mg/dL).

CSF

Albumin values for human CSF samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined with a nephelometric albumin test (x).

Sample size (n) = 85

Passing/Bablok[31]	Linear regression
y = 1.000x - 8.75 mg/L	y = 0.991x + 0.301 mg/L
τ = 0.936	r = 0.992

The sample concentrations were between 115 and 2640 mg/L (1.75 and 40.1 µmol/L, 11.5 and 264 mg/dL).

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

COBAS INTEGRA systems

System information

Serum/plasma/urine/CSF application

ALBS2: Test ID 0-172 (serum, plasma)

ALBU2: Test ID 0-171 (urine)

ALBC2: Test ID 0-170 (CSF)

Reagents - working solutions

R1 TRIS buffer: 50 mmol/L, pH 8.0; PEG: ≥ 4.2 %; EDTA: 2.0 mmol/L; preservative

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

SR Reagent for antigen excess check
Albumin in diluted serum (human); NaCl: 150 mmol/L; phosphate buffer: 50 mmol/L, pH 7.0; preservative

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

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

Application for serum and plasma

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
Antigen excess check	No
Predilution factor	250
Unit	g/L

Pipetting parameters

		Diluent (H_2O)
R1	100 µL	—
Sample	3 µL	10 µL
R2	20 µL	—
SR	6 µL	10 µL
Total volume	149 µL	

Application for urine

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	> 600 mg/L (> 60 mg/dL or > 9.12 µmol/L)
Antigen excess check	Yes (with SR)
Predilution factor	No
Postconcentration factor	No
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	

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	Undiluted and 1:2, 1:4, 1:8, 1:16, 1:32 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, 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 serum/plasma:	
Reference range	Precinorm Protein or PreciControl ClinChem Multi 1
Pathological range	Precipath Protein or PreciControl ClinChem Multi 2
Quality control urine:	
Reference range	Precinorm PUC
Pathological range	Precipath PUC
Quality control CSF:	
Reference range	Use commercially available CSF controls
Pathological range	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.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Serum/plasma

Icterus:[27] 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).[b)]

Hemolysis:[27] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).[b)]

Lipemia (Intralipid):[27]No significant interference up to an L index of 1500.[b)] 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.[28,29]

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

b) measured at analyte concentrations up to approximately 3.5 g/dL

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[30]

Urine

Icterus: No significant interference up to a conjugated bilirubin concentration of 855 µmol/L or 50 mg/dL.

Hemolysis: No significant interference up to a hemoglobin concentration of 248 µmol/L or 400 mg/dL.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[29]

No interference by acetone ≤ 60 mmol/L, ammonia chloride ≤ 0.11 mol/L, calcium ≤ 40 mmol/L, creatinine ≤ 0.18 mol/L, γ-globulin ≤ 500 mg/L, glucose ≤ 0.19 mol/L, phosphate ≤ 70 mmol/L, urea ≤ 0.8 mol/L, uric acid ≤ 5.95 mmol/L and urobilinogen ≤ 378 µmol/L.

Due to the antigen excess reagent (SR), no unflagged high-dose hook effect will occur up to an albumin concentration of 40000 mg/L (608 µmol/L).

CSF

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

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".

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

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

Serum/plasma

3-108 g/L (46-1642 µmol/L or 0.3-10.8 g/dL) (typical measuring range)

The upper and lower limits of the measuring range depend on the actual calibrator value.

Urine

3.0-200 mg/L (0.05-3.10 µmol/L or 0.3-20.0 mg/dL)

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.

CSF

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

Serum/plasma

Lower detection limit of the test:
3 g/L (46 µmol/L or 0.3 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 = 21).

Urine

Limit of Blank, Limit of Detection and Limit of Quantitation:

Limit of Blank = 2 mg/L (0.030 µmol/L or 0.200 mg/dL)

Limit of Detection = 3 mg/L (0.046 µmol/L or 0.300 mg/dL)

Limit of Quantitation = 12 mg/L (0.182 µmol/L or 1.20 mg/dL)

The Limit of Blank, the Limit of Detection and the Limit of Quantitation 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 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 30 %. It has been determined using low concentration albumin samples.

Values below the Limit of Quantitation (< 12 mg/L) will not be flagged by the instrument.

CSF

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).

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 on the COBAS INTEGRA 700 analyzer:

Serum/plasma

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
Serum low	25.5	0.5	1.8
Serum high	64.0	1.7	2.6
Precinorm Protein	40.2	1.0	2.5
Precipath Protein	61.4	1.8	2.9

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
Serum low	25.1	0.3	1.4
Serum high	62.2	1.5	2.4
Precinorm Protein	39.1	1.1	2.8
Precipath Protein	63.1	1.8	2.9

Urine

Repeatability	*Mean mg/L (µmol/L)*	*SD mg/L (µmol/L)*	*CV %*
Urine low	22.0 (0.334)	0.3 (0.004)	1.2
Urine high	115 (1.75)	2 (0.03)	1.9
Control (normal)	23.4 (0.356)	0.2 (0.003)	0.9
Control (pathological)	88.8 (1.35)	1.0 (0.02)	1.1

Intermediate precision	*Mean mg/L (µmol/L)*	*SD mg/L (µmol/L)*	*CV %*
Urine low	22.5 (0.342)	0.4 (0.006)	1.9
Urine high	118 (1.79)	3 (0.04)	2.2
Control (normal)	23.6 (0.359)	0.3 (0.011)	1.1
Control (pathological)	90.3 (1.37)	1.1 (0.02)	1.2

CSF

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

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

Method comparison

Serum/plasma

Albumin values for human serum 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) = 80

Passing/Bablok[31] — Linear regression

y = 0.903x + 0.875 g/L — y = 0.875x + 2.336 g/L

τ = 0.945 — r = 0.995

The sample concentrations were between 6.9 and 97.7 g/L (105 and 1485 µmol/L or 0.69 and 9.77 g/dL).

Urine

Albumin values for human urine 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) = 75

Passing/Bablok[31] — Linear regression

y = 1.057x - 5.48 mg/L — y = 1.047x - 5.35 mg/L

τ = 0.951 — r = 0.994

The sample concentrations were between 6.50 and 181 mg/L (0.650 and 18.1 mg/dL or 0.099 and 2.75 µmol/L).

CSF

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[31]	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).

The data obtained on COBAS INTEGRA 800 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

References

1 Rifai N, Horvath AR, Wittwer CT. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 6th Edition. Elsevier Missouri, Saunders. 2017.1888 p.

2 Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med 2016 Jul 15;9:229-255. doi: 10.2147/IJGM.S102819.

3 Gatta A, Verardo A, Bolognesi M. Hypoalbuminemia. Intern Emerg Med 2012 Oct;7 Suppl 3:S193-199.doi: 10-1007/s11739-012-0802-0.

4 Furfaro F, Bezzio C, Maconi G. Protein-losing enteropathy in inflammatory bowel diseases. Minerva Gastroenterol Dietol 2015 Dec;61(4):261-265. Epub 2015 Oct 7.

5 Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017 Feb;36(1):49-64. doi: 10.1016/j.clnu.2016.09.004.

6 Johnson PJ, Berhane S, Kagebayashi C, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol 2015 Feb 20;33(6):550-558. doi: 10.1200/JCO.2014.57.9151.

7 Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021.

8 Macisaac RJ, Ekinci EI, Jerums G. Markers of and risk factors for the development and progression of diabetic kidney disease. Am J Kidney Dis 2014 Feb;63(2 Suppl 2):S39-62. doi: 10.1053/j.ajkd.2013.10.048

9 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(2):256-263.

10 Reiber H, Otto M, Trendelenburg C, et al. Reporting cerebrospinal fluid data: knowledge base and interpretation software. Clin Chem Lab Med 2001 Apr;39(4):324-332. doi: 10.1515/CCLM.2001.051.

11 Freedman MS, Thompson EJ, Deisenheimer F, et al. Recommended standard of cerebrospinal fluid analysis in the diagnosis of multiple sclerosis: a consensus statement. Arch Neurol 2005 Jun;62(6):865-870. doi: 10.1001/archneur.62.6.865.

12 Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018 Feb;17(2):162-173. doi: 10.1016/S1474-4422(17)30470-2.

13 Gastaldi M, Zardini E, Leante R, et al. Cerebrospinal fluid analysis and the determination of oncoclonal bands. Neurol Sci 2017 Oct;38(Suppl 2):217-224. doi: 10.1007/s10072-017-3034-2.

14 Boufidou F, Vakrakou AG, Anagnostouli M, et al. An Updated Evaluation of Intrathecal IgG Synthesis Markers in Relation to Oligoclonal Bands. Diagnostics (Basel) 2023 Jan 20;13(3):389. doi: 10.3390/diagnostics13030389.

15 Multicenter study of Tina-quant Albumin in urine and β-N-acetyl-glucosaminidase (β-NAG) in urine. Workshop Munich, November 29-30, 1990 Wien Klin Wschr 1991;103 Suppl.189:1-64.

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

17 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.

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

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

20 Reiber H. The hyperbolic function: a mathematical solution of the protein flux/CSF flow model for blood-CSF barrier function. J Neurol Sci 1994;126:243-245.

21 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.

22 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests, 4th ed. WB Saunders Company, 2006:66.

23 Hofmann W, Guder WG. A diagnostic program for quantitative analysis of proteinurea. J Clin Chem Clin Biochem 1989;27:589-600.

24 Hubbuch A. Results of multicenter determination of preliminary reference values for albumin in urine of children and adults. Wien Klin Wochenschr Suppl. 1991;189:48-49.

25 Hasslacher C. Diagnostische Überwachung und Therapie in den Stadien der diabetischen Nierenerkrankung. Akt Endokr Stoffw 1989;10:60-63.

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

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

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

29 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.

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

31 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 for reconstitution
GTIN	Global Trade Item Number

ALBT2

Tina-quant Albumin Gen.2

CE 0123

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