AAT2

cobas®

Tina-quant α1-Antitrypsin ver.2

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03005771 322	Tina-quant α1-Antitrypsin ver.2, 100 tests	System-ID 07 9008 7	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
11355279 216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
11355279 160	Calibrator f.a.s. Proteins (5 x 1 mL, for USA)	Code 656	
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	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

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

AAT2: ACN 048

For **cobas c** 502 analyzer:

AAT2: ACN 8048

Intended use

In vitro test for the quantitative determination of α1-antitrypsin in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6]

α1-Antitrypsin is a glycoprotein consisting of a polypeptide chain to which 3 oligosaccharide chains are bonded (54000 daltons). It is synthesized in hepatocytes. α1-Antitrypsin is quantitatively the most important proteinase inhibitor (Pi) in serum and plasma. It specifically inactivates serine proteases (e.g. trypsin, chymotrypsin, collagenase, leukocyte elastase, plasmin and thrombin), with which it reversibly forms an enzyme-inhibitor complex. α1-Antitrypsin constitutes the major fraction of the electrophoretic α1-globulin fraction. Because it is a small molecule, α1-antitrypsin diffuses rapidly into other body fluids including bronchial secretions.

α1-Antitrypsin is an important, positive acute phase reactant found in elevated concentrations in inflammatory processes (e.g. infectious and rheumatoid diseases), tissue necrosis, malignancy and traumas. Inflammation of the liver parenchymal cells is often accompanied by elevated α1-antitrypsin levels, although levels of other acute phase reactants are not affected.

Acute hereditary α1-antitrypsin deficiency is suspected in cases of neonatal hepatitis accompanied by progressive liver cirrhosis in early childhood. It is also suspected when severe pulmonary emphysema occurs in adults due to the prevalence of leukocyte elastase, which can lead to unrestrained proteolytic degradation of the pulmonary parenchymal cells.

Various methods are available for assaying α1-antitrypsin, such as kinetic nephelometry or radial immunodiffusion. Roche's automated α1-antitrypsin assay is based upon the immunological agglutination test principle.

Test principle

Immunoturbidimetric assay.

Human α1-antitrypsin forms a precipitate with a specific antiserum which is determined turbidimetrically.

Reagents - working solutions

R1 Phosphate buffer: 12.7 mmol/L, pH 7.2; NaCl: 0.13 mol/L; PEG: 40 g/L; preservative

R2 Anti-human α1-antitrypsin antibody (rabbit): > 2 g/L; NaCl: 0.1 mol/L; preservative

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

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

Reagent handling

Ready for use

Storage and stability

AAT2

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

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation

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

Only the specimens listed below were tested and found acceptable.

Serum.

Plasma: Li-heparin 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.

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Tina-quant α1-Antitrypsin ver.2

cobas®

Stability:[7] 7 days at 15-25 °C
3 months at 2-8 °C
3 months at (-15)-(-25) °C

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 311 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 6-24		
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	45 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6 µL	9 µL	180 µL
Decreased	6 µL	4 µL	164 µL
Increased	6 µL	9 µL	180 µL

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 10-48		
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	45 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6 µL	9 µL	180 µL
Decreased	6 µL	4 µL	164 µL
Increased	6 µL	9 µL	180 µL

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 10-48		
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	45 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	6 µL	9 µL	180 µL
Decreased	6 µL	4 µL	164 µL
Increased	6 µL	18 µL	180 µL

Calibration

Calibrators S1: H_2O

S2: C.f.a.s. Proteins

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

S2: 0.233 S5: 1.56
S3: 0.467 S6: 2.28
S4: 0.952

Calibration mode RCM2

Calibration frequency Full calibration

- after reagent lot change
- as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against the certified reference material in human serum of the IRMM (Institute for Reference Materials 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.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Conversion factors:[8] g/L x 18.4 = µmol/L
g/L x 100 = mg/dL

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at an α1-antitrypsin concentration of 0.9 g/L (16.6 µmol/L, 90 mg/dL).

Icterus:[9] 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:[9] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: (1000 mg/dL or 621 µmol/L).

Lipemia (Intralipid):[9] No significant interference up to an L index of 350. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors up to 1200 IU/mL do not interfere.

High dose hook-effect: No false result occurs up to an α1-antitrypsin concentration of 12 g/L (221 µmol/L, 1200 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[10,11]

Elevated estrogen levels (oral contraceptives; third trimester of pregnancy) give rise to increased values. CRP and haptoglobin should therefore also be determined.[12]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[13]

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. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is not required.

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

Limits and ranges

Measuring range

0.2-6.0 g/L (3.68-110.4 µmol/L, 20-600 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Lower detection limit of the test

0.2 g/L (3.68 µmol/L, 20 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values[14]

0.9-2.0 g/L (16.6-36.8 µmol/L, 90-200 mg/dL)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

Repeatability	*Mean*	*SD*	*CV*
	g/L	*g/L*	*%*
	(µmol/L, mg/dL)	*(µmol/L, mg/dL)*	
Precinorm Protein	1.14 (21.0, 114)	0.01 (0.2, 1)	0.8
Precipath Protein	1.89 (34.8, 189)	0.02 (0.4, 2)	0.9
Human serum 1	1.04 (19.1, 104)	0.01 (0.2, 1)	0.8
Human serum 2	1.58 (29.1, 158)	0.01 (0.2, 1)	0.8
Intermediate precision	*Mean*	*SD*	*CV*
	g/L	*g/L*	*%*
	(µmol/L, mg/dL)	*(µmol/L, mg/dL)*	
Precinorm Protein	1.12 (20.6, 112)	0.01 (0.2, 1)	1.1
Precipath Protein	1.86 (34.2, 186)	0.02 (0.4, 2)	1.2
Human serum 3	1.05 (19.3, 105)	0.01 (0.2, 1)	1.4
Human serum 4	1.76 (32.4, 176)	0.03 (0.6, 3)	1.5

Method comparison

α1-Antitrypsin values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 119

Passing/Bablok[15]	Linear regression
y = 0.972x - 0.029 g/L	y = 0.979x - 0.043 g/L
τ = 0.976	r = 0.998

The sample concentrations were between 0.880 and 3.35 g/L (16.2 and 61.6 µmol/L, 88.0 and 335 mg/dL).

References

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4 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;66-67.

5 Johnson AM, Alper CA. Deficiency of α1-antitrypsin in childhood liver disease. Pediatrics 1970;46(6):921-925.

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

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11 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.

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

14 Consensus values of the "Deutsche Gesellschaft für Laboratoriumsmedizin", the "Deutsche Gesellschaft für Klinische Chemie" and the "Verband der Diagnostica-Industrie e.V." (VDGH). DG Klinische Chemie Mitteilungen 1995;26:119-122.

15 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

AAT2

Tina-quant α1-Antitrypsin ver.2

→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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