STFR

Tina-quant Soluble Transferrin Receptor

cobas®

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
20763454 122	Tina-quant Soluble Transferrin Receptor (80 tests)	System-ID 07 6345 4	**cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

12148331 122	Preciset sTfR (5 x 1 mL)	Codes 750-754	
12148340 122	sTfR Control Set		
	Level I (2 x 3 mL)	Level I Code 211	
	Level II (2 x 3 mL)	Level II Code 212	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

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

STFR: ACN 665

For **cobas c** 502 analyzer:

STFR: ACN 8665

Intended use

In vitro test for the quantitative determination of soluble transferrin receptor (sTfR) in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6,7]

The transferrin receptor is an integral membrane glycoprotein having a molecular weight of 190 kilodalton (kDa). It consists of two identical subunits linked by disulfide bridges. Each of the monomers has an 85 kDa C-terminal component which can bind an iron-laden transferrin molecule. Proteolysis leads to the soluble form of the transferrin receptor (sTfR). In plasma, the soluble transferrin receptor is present in the form of a complex with transferrin having a molecular weight of approximately 320 kD. The serum concentration of sTfR is directly proportional to the concentration of the receptor on the membrane.

The uptake of iron by the body's cells is controlled by expression of the transferrin receptor (TfR). If the intracellular iron stores are exhausted - corresponding to a ferritin concentration of less than 12 µg/L - then more TfR is expressed. The affinity of the transferrin receptor to transferrin depends on the latter's loading state. As 80-95 % of the transferrin receptor molecules are localized on erythropoietic cells, the TfR concentration (and hence also the sTfR concentration) reflects the iron requirement of these cells. When iron deficiency exists, the sTfR concentration in serum rises even before the hemoglobin concentration is significantly depressed. The sTfR concentration can therefore describe the functional iron status while ferritin reflects the iron storage status. A precise assessment of the iron status can be obtained by determining the sTfR index (= sTfR concentration/log ferritin concentration).

As - in contrast to ferritin - the concentration of sTfR is not affected by acute-phase reactions, acute liver function disorders or malignant tumors, it is possible to differentiate between anemia of chronic disease (ACD) and iron deficiency anemia (IDA). Elevated sTfR values are also found in polycythemia, hemolytic anemia, thalassemia, hereditary spherocytosis, sickle cell anemia, megaloblastic anemia, myelodysplastic syndrome and vitamin B_{12} deficiency. Elevated sTfR concentrations occur during pregnancy when there is a deficiency of functional iron.

Parameter	Change	IDA	ACD		IDA + ACD	
Ferritin	iron stores	↓	↑	—	or	↑
TIBC/TRSF	iron status	↑	↓	↑	or	—
Serum iron	iron status	↓	↓		↓	
sTfR	functional iron deficiency	↑	—		↑	

↓ decreased, ↑ increased, — unchanged

Test principle[8]

Particle enhanced immunoturbidimetric assay.

Human soluble transferrin receptor agglutinates with latex particles coated with anti-soluble transferrin receptor antibodies. The precipitate is determined photometrically.

Reagents - working solutions

R1 TES/HCl buffer: 20 mmol/L, pH 7.7; NaCl: 500 mmol/L; preservative

R2 Latex particles coated with monoclonal anti-human sTfR antibodies (mouse); TRIS/HCl buffer: 20 mmol/L, pH 8.0; preservative

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

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.

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

Reagent handling

Ready for use

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

Mix **cobas c** pack well before placing on the analyzer.

Storage and stability

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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 plasma

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

Centrifuge samples containing precipitates before performing the assay.

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

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Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability:	3 days at 15-25 °C
	7 days at 2-8 °C
	4 weeks at (-15)-(-25) °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.

Application for serum and plasma

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time/Assay points	10 / 8-17		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	mg/L (mg/dL, nmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	110 µL	-	
R2	110 µL	-	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	-	-
Decreased	10 µL	10 µL	90 µL
Increased	2 µL		

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time/Assay points	10 / 13-25		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	mg/L (mg/dL, nmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	110 µL	-	
R2	110 µL	-	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	-	-
Decreased	10 µL	10 µL	90 µL
Increased	2 µL		

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time/Assay points	10 / 13-25		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	mg/L (mg/dL, nmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	110 µL	-	
R2	110 µL	-	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	-	-
Decreased	10 µL	10 µL	90 µL
Increased	4 µL		

Calibration

Calibrators	S1: H_2O
	S2-S6: Preciset sTfR
Calibration mode	RCM2
Calibration frequency	Full calibration • daily and 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 an in-house reference preparation.

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

cobas c systems automatically calculate the analyte concentration of each sample.

Conversion factors:	mg/L x 11.8 = nmol/L[9,a)]
	nmol/L x 0.085 = mg/L
	mg/L x 0.1 = mg/dL
	mg/dL x 10 = mg/L

a) Based on a molecular mass of 85 kDa for circulating transferrin receptor.

Limitations – interference

Criterion: Recovery within ± 10 % of initial value at a sTfR concentration of 2.00 mg/L (0.20 mg/dL).

Icterus:[10] 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:[10] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 497 µmol/L or 800 mg/dL).

Lipemia (Intralipid):[10] No significant interference up to an L index of 1000. 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 150 IU/mL.

Besides rheumatoid factors patient samples may contain other heterophilic antibodies of different nature which could react in immunoassays to give falsely elevated or decreased results.

High dose hook-effect: No false result occurs up to an sTfR concentration of 80 mg/L.

The antibodies are specific for sTfR. There is no cross-reactivity with diferrotransferrin, apotransferrin or ferritin under the assay conditions.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[11,12]

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

As for any assay employing mouse antibodies, erroneous findings may be obtained from samples taken from patients who have been treated with monoclonal mouse antibodies or have received them for diagnostic purposes.

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

0.50-40.0 mg/L (5.9-472 nmol/L, 0.05-4.00 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

0.50 mg/L (5.9 nmol/L, 0.05 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

Men (n = 202)	1.80-4.70 mg/L	21.2-55.5 nmol/L	0.180-0.470 mg/dL
(aged 20-76 years)			
Women (n = 194)	1.78-4.59 mg/L	21.0-54.2 nmol/L	0.178-0.459 mg/dL
(aged 20-71 years)			

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*
	mg/L	*mg/L*	*%*
	(nmol/L, mg/dL)	*(nmol/L, mg/dL)*	
sTfR Control Set Level 1	2.16 (25.5, 0.216)	0.03 (0.35, 0.002)	1.5
sTfR Control Set Level 2	6.82 (80.5, 0.682)	0.06 (0.71, 0.006)	0.9
Human serum 1	1.93 (22.8, 0.193)	0.04 (0.47, 0.004)	2.1
Human serum 2	3.38 (39.9, 0.338)	0.04 (0.47, 0.004)	1.3

Intermediate precision	*Mean*	*SD*	*CV*
	mg/L	*mg/L*	*%*
	(nmol/L, mg/dL)	*(nmol/L, mg/dL)*	
sTfR Control Set Level 1	2.05 (24.2, 0.205)	0.08 (0.94, 0.008)	4.0
sTfR Control Set Level 2	6.67 (78.7, 0.667)	0.11 (1.30, 0.011)	1.6
Human serum 3	1.37 (16.2, 0.137)	0.05 (0.59, 0.005)	3.8
Human serum 4	12.1 (143, 1.21)	0.2 (2.36, 0.02)	1.4

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

Method comparison

sTfR values for human serum and plasma 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) = 119

Passing/Bablok[14]	Linear regression
y = 0.976x + 0.260 mg/L	y = 0.979x + 0.244 mg/L
τ = 0.957	r = 1.000

The sample concentration were between 1.41 and 39.9 mg/L (16.6 to 471 nmol/L, 0.141 to 3.99 mg/dL).

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

References

1 Wick M, Pinggera W, Lehmann P, eds. Iron Metabolism, Diagnosis and Therapy of Anemias. 4th ed. Vienna/New York: Springer Verlag 1999.

2 Ferguson BJ, Skikne BS, Simpson KM, et al. Serum transferrin receptor distinguishes the anemia of chronic diseases from iron deficiency anemia. J Lab Clin Med 1992;19:385-390.

3 Baynes RD, Skikne BS, Cook JD. Circulating transferrin receptors and assessment of iron status. J Nutr Biochem 1994;5:322-330.

4 Kuiper-Kramer EPA, Huisman CMS, van Raan J, et al. Analytical and clinical implications of soluble transferrin receptors. Eur J Clin Chem Clin Biochem 1996;34:645-649.

5 Baynes RD. Assessment of iron status. Clin Biochem 1996;29:209-215.

6 Punnonen K, Irjala K, Rajamäki A. Serum transferrin receptor and its ratio to serum ferritin in the diagnosis of iron deficiency. Blood 1997;89:1052-1057.

7 Suominen P, Punnonen K, Rajamäki A, et al. Serum transferrin receptor and transferrin receptor-ferritin index identify healthy subjects with subclinical iron deficits. Blood 1998;92:2934-2939.

8 Haeckel R, ed. Evaluation methods in laboratory medicine. VCH Verlagsgesellschaft, Weinheim 1993.

9 Cook JD, Skikne BS, Baynes RD. Serum transferrin receptor. Annu Rev Med 1993;44:63-74.

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

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

12 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.

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 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.

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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 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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