TRSF2

cobas®

Tina-quant Transferrin ver.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08058733190	08058733500	Tina-quant Transferrin ver.2 (500 tests)	System-ID 2115 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 20656	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 20391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 20392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

English

System information

TRSF2: ACN 21150

TRSF2U: ACN 21151

Intended use

In vitro test for the quantitative determination of transferrin in human serum, plasma and urine on **cobas c** systems.

Summary

Transferrin measurements, performed with this assay in human serum, plasma or urine, are used as an aid in the diagnosis of iron deficiency or iron overload. Transferrin measurements performed in urine are also used as an aid in the diagnosis of glomerular diseases.

Transferrin is a protein that plays a crucial role in transporting iron throughout the body. Its primary function is to bind and transport iron, facilitating its delivery to cells that require it for essential processes like oxygen transport and energy production.[1] It is a glycoprotein with a molecular weight of 79570 daltons.[2] It consists of a polypeptide strand with two N-glycosidically linked oligosaccharide chains and exists in numerous isoforms.[3,4] Transferrin is synthesized in the liver and released into the bloodstream. The rate of synthesis in the liver can be altered in accordance with the body's iron requirements and iron reserves.[3,5] Transferrin binds to iron in a reversible manner, allowing it to pick up iron from areas of high concentration such as the intestines (where iron is absorbed from the diet), and deliver it to cells that require iron for their metabolic processes. Excess iron that is not immediately needed for cellular processes is stored in the form of ferritin within cells, particularly in the liver, spleen, and bone marrow.[6] This iron can be released from ferritin when needed to maintain iron homeostasis. The total iron content of the body is about 3 to 3.5 g, where the majority (> 95 %) is contained in hemoglobin of erythrocytes (or their precursors in the bone marrow), and also intracellular storages (e.g. ferritin).[1,7] Only a small amount (~ 3 mg) of Fe is bound to the circulating serum protein transferrin, a complex of ferric iron Fe(III) bound to the plasma protein apotransferrin.[1,3] Normally, about one third of the iron-binding sites of transferrin are occupied by Fe(III). The additional amount of iron that can be bound is the unsaturated (or latent) iron-binding capacity UIBC. The sum of the serum iron and UIBC represents total iron-binding capacity TIBC. TIBC is a measurement for the maximum iron concentration that transferrin can bind. It is used to calculate the transferrin saturation TSAT, which is the percentage of transferrin occupied by iron, and can be calculated by a ratio of serum iron and TIBC.[8]

In cases of iron deficiency (which can be the result of prior blood loss, altered iron uptake, or increased iron demand)[9], cells produce more transferrin receptors on their surface to increase iron uptake.[1] The degree of transferrin saturation appears to be an extremely sensitive indicator of functional iron depletion.[10] Iron deficiency anemia (when hemoglobin production is decreased because of iron deficiency) can be diagnosed by abnormally low serum ferritin levels, and increased transferrin levels.[10,11,12] In conditions of iron overload (such as hereditary hemochromatosis), transferrin levels may be decreased as the body tries to limit iron absorption. Determination of TSAT is a central step for the diagnosis of hereditary hemochromatosis, either before or in parallel with the establishment of hyperferritinemia.[13,14] Very high TSAT values (> 80 %) indicate a significant presence of highly toxic non-transferrin-bound serum iron.[14] Apart from hereditary hemochromatosis, other causes of iron overload include alcoholic liver disease, nonalcoholic fatty liver disease, and hepatitis C infection.[15] Chronic liver diseases are also associated with iron overload and elevated TSAT, but the degree of TSAT elevation tends to be higher in alcoholic liver disease compared to nonalcoholic fatty liver disease and hepatitis C.[15,16]

Transferrin excreted in urine indicates increased glomerular permeability to plasma proteins that are normally not freely filtered through the glomerulus. Transferrin has a similar small size as albumin (established protein marker to assess glomerular protein filtration), but because it is less anionic, it can pass through the glomeruli more easily than albumin. Hence, urinary transferrin can be used as a biomarker for detection of glomerular damage and renal abnormalities.[17,18,19]

A variety of methods are available for determining transferrin including radial immunodiffusion, nephelometry and turbidimetry. The Roche transferrin assay is based on the immunological agglutination principle.[20]

Test principle

Immunoturbidimetric assay.[21,22,23]

Human transferrin forms a precipitate with a specific antiserum which is determined turbidimetrically.

Reagents - working solutions

R1 Phosphate buffer: 55 mmol/L, pH 7.2; NaCl: 25 mmol/L; polyethylene glycol: 5 %; preservative

R3 Anti-human transferrin antibodies (rabbit): dependent on titer; NaCl: 100 mmol/L; preservative

R1 is in position B and R3 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.

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 and refrigerated on the analyzer:	26 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. Do not use EDTA or citrate plasma.

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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.

Urine

Each urine sample must be centrifuged (10 minutes at approximately 3000 x g) prior to testing.[24] Random and timed urine collections are suitable specimens for testing transferrin in urine.
The pH of the urine should be adjusted to pH 7.0.[25]

Stability in serum and Li-heparin plasma: [26]	8 days at 15-25 °C
	8 days at 2-8 °C
	6 months at -20 °C (± 5 °C)
Freeze only once.	
Stability in urine:	4 days at 15-25 °C
	7 days at 2-8 °C
	Freezing and thawing is not allowed.

Centrifuge samples containing precipitates before performing the assay.

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

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

Test definition

Reporting time	10 min	
Wavelength (sub/main)	700/505 nm	
Reagent pipetting		Diluent (H_2O)
R1	84 µL	–
R3	18 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	7.5 µL	5.0 µL	100 µL
Decreased	7.5 µL	4.0 µL	122 µL
Increased	7.5 µL	5.0 µL	100 µL

For further information about the assay test definitions refer to the application parameters screen of the corresponding analyzer and assay.

Application for urine

Test definition

Reporting time	10 min	
Wavelength (sub/main)	700/340 nm	
Reagent pipetting		Diluent (H_2O)
R1	84 µL	–
R3	18 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	9 µL	-	-
Decreased	9 µL	25 µL	50 µL
Increased	9 µL	-	-

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration

Calibrators	S1: H_2O
	S2-S6: C.f.a.s. Proteins
Calibration mode	Non-linear
Calibration frequency	Automatic full calibration - after reagent lot change
	Full calibration - 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 reference preparation of the IFCC (International Federation of Clinical Chemistry and Laboratory Medicine) ERM-DA470k/IFCC (RPPHS - Reference Preparation for Proteins in Human Serum).[27] ERM-DA470k/IFCC is a new batch of the originally certified reference material BCR470/CRM470.

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.

ACTION REQUIRED

Urine: Roche controls must be diluted 1:201 manually with 0.9 % NaCl solution (e.g. mix vigorously 2000 µL of NaCl solution with 10 µL of control material).

Calculation

cobas c systems automatically calculate the analyte concentration of each sample in the unit g/L or mg/L (µmol/L, mg/dL).

Conversion factors:	g/L x 12.6 = µmol/L
	g/L x 100 = mg/dL
	mg/L x 0.1 = mg/dL

Limitations - interference

Serum/plasma

Criterion: Recovery within ± 0.2 g/L of initial values of samples ≤ 2.0 g/L and within ± 10 % for samples > 2.0 g/L.

Icterus:[28] 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:[28] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[28] No significant interference up to an L index of 500. 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.

High-dose hook effect: No false result occurs up to a transferrin concentration of 17 g/L.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[29,30]

Urine

Criterion: Recovery within ± 0.5 mg/L of initial values of samples ≤ 5.0 mg/L and within ± 10 % for samples > 5.0 mg/L

Hemolysis: No significant interference up to an H index of 20 (approximate hemoglobin concentration: 20 mg/dL).[28] Urine specimen, colored due to presence of erythrocytes or hemoglobin, should not be used.

No significant interference from h-albumin ≤ 5000 mg/L, calcium ≤ 8 mmol/L, citrate ≤ 10 mmol/L, creatinine ≤ 44 mmol/L, glucose ≤ 111 mmol/L, h-immunoglobulin G ≤ 500 mg/L, magnesium ≤ 75 mmol/L, oxalate ≤ 2.2 mmol/L, phosphate ≤ 40 mmol/L, urea ≤ 1000 mmol/L, uric acid ≤ 6 mmol/L and urobilinogen ≤ 15 mg/dL.

High-dose hook effect: No false result occurs up to a transferrin concentration of 650 mg/L (65 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels. Exception: Ofloxacine causes artificially high transferrin results.[30]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[31]

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. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges

Measuring range

Serum/plasma

0.1-5.2 g/L (1.26-65.5 µmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:1.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 1.5.

Urine

2.2-35.0 mg/L (0.22-3.5 mg/dL)

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

Lower limits of measurement

Serum/plasma

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 0.1 g/L (1.26 µmol/L)
Limit of Detection	= 0.1 g/L (1.26 µmol/L)
Limit of Quantitation	= 0.1 g/L (1.26 µmol/L)

Urine

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 1.0 mg/L (0.10 mg/dL)
Limit of Detection	= 1.5 mg/L (0.15 mg/dL)
Limit of Quantitation	= 2.2 mg/L (0.22 mg/dL)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 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 20 %. It has been determined using low concentration transferrin samples.

Expected values

Serum/plasma[32]

2.0-3.6 g/L (25.2-45.4 µmol/L)*

* calculated by unit conversion factor

Urine

Normally, transferrin is not freely filtered through the glomerulus.[17]

≤ 1.9 mg/L* (0.19 mg/dL**)[33]

* The concentration of transferrin in urine of healthy individuals is below the detection limit of this method.
**calculated by unit conversion factor

Because of daily variation in urine secretion, urinary concentrations are generally reported normalized such as mg/day, mg/g creatinine, mg/mmol creatinine, g per creatinine clearance.

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. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Serum/plasma

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
PCCC1[a)]	1.93	0.0118	0.6
PCCC2[b)]	3.09	0.0260	0.8
Human serum 1	0.255	0.00553	2.2
Human serum 2	1.84	0.0144	0.8
Human serum 3	2.46	0.0170	0.7
Human serum 4	3.19	0.0280	0.9
Human serum 5	4.10	0.0482	1.2

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
PCCC1[a)]	1.93	0.0198	1.0
PCCC2[b)]	3.09	0.0313	1.0
Human serum 1	0.255	0.00925	3.6
Human serum 2	1.84	0.0210	1.1
Human serum 3	2.46	0.0188	0.8
Human serum 4	3.19	0.0299	0.9
Human serum 5	4.04	0.0546	1.3

Urine

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Repeatability	*Mean mg/L*	*SD mg/L*	*CV %*
PCCC1[a)]	10.5	0.198	1.9
PCCC2[b)]	16.5	0.0945	0.6
Human urine 1	4.45	0.0879	2.0
Human urine 2	9.32	0.103	1.1
Human urine 3	16.7	0.110	0.7
Human urine 4	26.1	0.144	0.5
Human urine 5	31.6	0.221	0.7

Intermediate precision	*Mean mg/L*	*SD mg/L*	*CV %*
PCCC1[a)]	10.5	0.229	2.2
PCCC2[b)]	16.6	0.180	1.1
Human urine 1	4.41	0.156	3.5
Human urine 2	9.32	0.323	3.5
Human urine 3	16.7	0.185	1.1
Human urine 4	26.1	0.214	0.8
Human urine 5	31.6	0.301	1.0

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

Serum/plasma

Transferrin values for human serum and plasma samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 65

Passing/Bablok[34]	Linear regression
y = 1.000x + 0.0308 g/L	y = 0.999x + 0.0352 g/L
τ = 0.981	r = 0.999

The sample concentrations were between 0.120 and 5.08 g/L.

Transferrin values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 73

Passing/Bablok[34]	Linear regression
y = 0.987x + 0.0657 g/L	y = 0.963x + 0.109 g/L
τ = 0.963	r = 0.997

The sample concentrations were between 0.130 and 5.09 g/L.

Transferrin values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 74

Passing/Bablok[34]	Linear regression
y = 1.010x - 0.0466 g/L	y = 1.011x - 0.0418 g/L
τ = 0.947	r = 0.999

The sample concentrations were between 0.175 and 4.87 g/L.

Urine

Transferrin values for human urine samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 74

Passing/Bablok[34]	Linear regression
y = 1.028x - 0.170 mg/L	y = 1.020x - 0.144 mg/L
τ = 0.965	r = 0.998

The sample concentrations were between 2.20 and 33.1 mg/L.

Transferrin values for human urine samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 60

Passing/Bablok[34]	Linear regression
y = 1.065x - 0.0249 mg/L	y = 1.054x + 0.190 mg/L
τ = 0.942	r = 0.996

The sample concentrations were between 2.73 and 32.8 mg/L.

Transferrin values for human urine samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 62

Passing/Bablok[34]	Linear regression
y = 0.987x - 0.0967 mg/L	y = 0.992x - 0.167 mg/L
τ = 0.976	r = 0.999

The sample concentrations were between 2.30 and 34.1 mg/L.

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.

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Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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