# STFR2

cobas®

**Tina-quant Soluble Transferrin Receptor II**

**Order information**

| REF | | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|---|
| 07227892190 | 07227892500 | Tina-quant Soluble Transferrin Receptor II (150 tests) | System-ID 03 7473 1 | **cobas c** 701/702 |

Materials required (but not provided):

| | | | |
|---|---|---|---|
| 08753776190 | Calibrator sTfR II (3 x 1 mL) | Code 697 | |
| 08278202190 | ControlSet sTfR II<br>Level I (3 x 1 mL)<br>Level II (3 x 1 mL) | <br>Level I Code 153<br>Level II Code 154 | |
| 05172152190 | Diluent NaCl 9 % (119 mL) | System-ID 08 6869 3 | |

**English**

**System information**

**STFR2:** ACN 8439

**Intended use**

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

**Summary**

Soluble transferrin receptor measurements, performed with this assay, in human serum and plasma are used as an aid in diagnosis and monitoring of iron deficiency. Causes for iron deficiency can be broadly classified as: insufficient iron uptake, inadequate iron mobilization, excess iron loss, increased iron demand.

In healthy subjects, circulating iron binds to transferrin. The transferrin-iron complexes are recognized by the transferrin receptor (TfR) and enter the cells through endocytosis. Iron is then released in the cell cytosol and the remaining apotransferrin-TfR complex within the endocytic vesicle is transported back to the cell membrane.[1] The bone marrow takes up significant amounts of transferrin-bound iron to support maturation of erythrocytes, 80-95 % of the transferrin receptor molecules are localized on erythropoietic cells.[2] Cell surface TfR concentration reflects iron requirements of the cell. If the intracellular iron stores are exhausted - corresponding to a ferritin concentration of less than 12 µg/L - then more TfR is expressed.[3] Proteolysis of TfR leads to the soluble form of the transferrin receptor (sTfR). In plasma, sTfR is present in the form of a complex with transferrin-iron. The circulating sTfR level reflects total body TfR concentration, therefore is closely related to cellular iron demands and erythroid proliferation rate.[1,2,3]

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).[4]

In case of anemia, to ensure correct clinical intervention, it is important to distinguish between anemia of chronic disease / anemia of inflammation (ACD/AI) and iron deficiency anemia (IDA).[5,6] IDA is an anemia caused by low iron stores in the body, while ACD/AI is a functional anemia of iron-restricted erythropoiesis, characterized by insufficient erythropoietin (EPO) production and reduction of erythroid progenitor cell proliferation, together with disturbances in iron distribution. While in IDA sTfR levels increase and ferritin levels decrease, in case of ACD/AI, sTfR levels remain unaffected and ferritin levels increase.[2]

The following table summarizes the differences between IDA, ACD/AI and combined IDA plus ACD for tests of iron status including ferritin, total iron-binding capacity (TIBC) and serum iron:[2]

| Parameter | Change | IDA | ACD/-AI | IDA + ACD | | |
|---|---|---|---|---|---|---|
| Ferritin | Iron stores | ↓ | ↑ | — | or | ↑ |
| TIBC | Iron status | ↑ | ↓ | — | or | ↑ |
| Serum iron | Iron status | ↓ | ↓ | | ↓ | |
| sTfR | Functional iron status | ↑ | — | | ↑ | |

↓ decreased, ↑ increased, — unchanged

Elevated sTfR values are also found in conditions such as polycythemia, hemolytic anemia, thalassemia, hereditary spherocytosis, sickle cell anemia, megaloblastic anemia, myelodysplastic syndrome and vitamin B12 deficiency.

**Test principle**[7]

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** | TRIS buffer: with bovine serum albumin; preservatives |
| **R3** | Latex particles coated with monoclonal anti-human sTfR antibodies (mouse) in glycine buffer; 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.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

| | |
|---|---|
| H317 | May cause an allergic skin reaction. |
| **Prevention:** | |
| P261 | Avoid breathing mist or vapours. |
| P272 | Contaminated work clothing should not be allowed out of the workplace. |
| P280 | Wear protective gloves. |
| **Response:** | |
| P333 + P313 | If skin irritation or rash occurs: Get medical advice/attention. |
| P362 + P364 | Take off contaminated clothing and wash it before reuse. |
| **Disposal:** | |
| P501 | Dispose of contents/container to an approved waste disposal plant. |

Product safety labeling follows EU GHS guidance.

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Contact phone: all countries: +49-621-7590

**Reagent handling**

Ready for use

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

**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: | 4 weeks |
| On-board on the Reagent Manager: | 24 hours |

**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: Heparin (Li-, Na-, $NH_4^+$-) 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.

| | |
|---|---|
| Stability: | 6 days at 15-25 °C |
| | 15 days at 2-8 °C |
| | 13 weeks at -20 °C (± 5 °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** 701/702 **test definition**

| | | | |
|---|---|---|---|
| Assay type | 2-Point End | | |
| Reaction time/Assay points | 10 / 22-32 | | |
| Wavelength (sub/main) | 800/570 nm | | |
| Reaction direction | Increase | | |
| Unit | mg/L (nmol/L, mg/dL) | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 100 µL | - | |
| R3 | 40 µL | - | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 2 µL | - | - |
| Decreased | 2 µL | 25 µL | 75 µL |
| Increased | 2 µL | | |

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$ |
| | S2-S6: Calibrator sTfR II |
| Calibration mode | Non-linear |
| Calibration frequency | Full calibration<br>• after reagent lot change<br>• every 6 months during shelf life<br>• 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 in the unit mg/L (mg/dL, nmol/L)

| | |
|---|---|
| Conversion factors: | mg/L x 11.8 = nmol/L[8,a)] |
| | mg/L x 0.1 = mg/dL |

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

**Limitations – interference**

Criterion: Recovery within ± 0.2 mg/L (2.36 nmol/L) of initial values of samples ≤ 2 mg/L (23.6 nmol/L) and within ± 10 % for samples > 2 mg/L.

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: 622 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[9] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors: No signifcant interference from rheumatoid factors up to a concentration of 1200 IU/mL.

High dose hook-effect: No false result occurs up to an sTfR concentration of 80 mg/L (944 nmol/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.[10,11]

In very rare cases, gammopathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.[12]

In very rare cases, patient samples may contain particle agglutinating proteins (e.g. heterophilic antibodies or antibodies due to abnormal immunoglobulin synthesis, such as gammopathies like MGUS* or Waldenström‘s macroglobulinemia) which may lead to incorrect low or high results with this assay. Correct results cannot be obtained by sample dilution and these samples should be analyzed by an alternative method.
*Monoclonal Gammopathy of unknown significance

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

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**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, manual input is required in certain cases. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SmpCln1+2/SCCS Method Sheet and for further instructions refer to the operator's manual.

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

**Limits and ranges**

**Measuring range**

0.50-20.0 mg/L (5.9-236 nmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:4 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 4.

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

Limit of Blank = 0.25 mg/L (2.95 nmol/L)

Limit of Detection = 0.40 mg/L (4.72 nmol/L)

Limit of Quantitation = 0.50 mg/L (5.90 nmol/L)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95$^{th}$ 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 sTfR samples.

**Expected values**

The values shown below were performed on samples from an apparently healthy population, using the Tina-quant Soluble Transferrin Receptor II assay (STFR2). The calculation is based on 165 sera (101 men, 64 women). The age range was between 22 and 83 years. The analysis of the data with the 2.5 % and the 97.5 % percentile gave a soluble transferrin receptor (sTfR) range from 1.71 mg/L (20.2 nmol/L) to 4.13 mg/L (48.7 nmol/L).

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 accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days)

The following results were obtained on the **cobas c** 701 analyzer:

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mg/L* | *mg/L* | *%* |
| Control Set sTfR II L 1 | 2.37 | 0.0363 | 1.5 |
| Control Set sTfR II L 2 | 7.09 | 0.0509 | 0.7 |
| Human serum 1 | 1.23 | 0.0388 | 3.2 |
| Human serum 2 | 2.00 | 0.0437 | 2.2 |
| Human serum 3 | 5.33 | 0.0624 | 1.2 |
| Human serum 4 | 9.43 | 0.0929 | 1.0 |
| Human serum 5 | 17.7 | 0.131 | 0.7 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *mg/L* | *mg/L* | *%* |
| Control Set sTfR II L 1 | 2.37 | 0.0451 | 1.9 |
| Control Set sTfR II L 2 | 7.09 | 0.0783 | 1.1 |
| Human serum 1 | 1.23 | 0.0406 | 3.3 |
| Human serum 2 | 2.00 | 0.0444 | 2.2 |
| Human serum 3 | 5.33 | 0.0686 | 1.3 |
| Human serum 4 | 9.43 | 0.111 | 1.2 |
| Human serum 5 | 17.7 | 0.197 | 1.1 |

**Method comparison**

sTfR values for human serum and plasma samples obtained on a **cobas c** 701 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 66

| Passing/Bablok[13] | Linear regression |
|---|---|
| y = 1.000x + 0.090 mg/L | y = 1.000x + 0.0969 mg/L |
| τ = 0.981 | r = 0.999 |

The sample concentrations were between 0.560 and 18.6 mg/L.

**References**


1 Skikne BS. Serum transferrin receptor. Am J Hematol 2008 Nov;83(11):872-5. doi: 10.1002/ajh.21279.

2 Beguin Y. Soluble transferrin receptor for the evaluation of erythropoiesis and iron status. Clin Chim Acta 2003 Mar;329(1-2):9-22. doi: 10.1016/s0009-8981(03)00005-6.

3 Speeckaert MM, Speeckaert R, Delanghe JR. Biological and clinical aspects of soluble transferrin receptor. Crit Rev Clin Lab Sci 2010 Dec;47(5-6):213-28. doi: 10.3109/10408363.2010.550461.

4 Cook JD, Flowers CH, Skikne BS. The quantitative assessment of body iron. Blood 2003 May 1;101(9):3359-64. doi: 10.1182/blood-2022-10-3071.

5 Lopez A, Cacoub P, Macdougall IC, et al. Iron deficiency anaemia. Lancet 2016 Feb 27;387(10021):907-16. doi: 10.1016/S0140-6736(15)60865-0.

6 Peng YY, Uprichard J. Ferritin and iron studies in anaemia and chronic disease. Ann Clin Biochem 2017 Jan;54(1):43-48. doi: 10.1177/0004563216675185.

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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.

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

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.

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

13 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 for reconstitution |
| GTIN | Global Trade Item Number |



CE 0123

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