FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04885317190	04885317500	Tina-quant Ferritin Gen.4 250 tests	System-ID 07 6966 5	**cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
10557897122	Precinorm Protein (3 x 1 mL)	Code 302	
11333127122	Precipath Protein (3 x 1 mL)	Code 303	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

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

FERR4: ACN 692

For **cobas c** 502 analyzer:

FERR4: ACN 8692

Intended use

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

Summary

Ferritin measurements, performed with this assay in human serum and plasma, are used as an aid in diagnosis of iron deficiencies and iron overload.

Ferritin is an iron-storage protein synthesized by many body cells and it is mainly found in the liver, spleen, muscle and bone marrow, with only a small fraction found in blood. The protein plays an important role in the cellular uptake, storage and release of iron.[1] The storage function is not only important for adequate amounts of bioavailable iron to be provided, but also to protect the cells from toxicity. Iron can indeed generate reactive species which can directly damage DNA and proteins.[2,3]

The iron-free protein, apoferritin, consists of 24 subunits and has a molecular weight of approximately 450 kDa. The iron core of ferritin can contain up to approximately 4500 iron atoms in the form of Fe^{3+} ions.[4,5] Several isoforms of ferritin exist which are composed of different subunits that are partially tissue specific.[1,4]

Under steady-state conditions, the serum ferritin concentration is proportional to the total body iron stores: 1 ng of serum ferritin per mL corresponds to 10 mg of total iron stores.[6,7,8] Therefore, in the literature, the measurement of serum ferritin levels is proposed as the best and most convenient laboratory test to estimate iron stores and diagnose iron deficiency or iron related disorders.[5,6,8,9] It has substituted the invasive and semiquantitative histochemical examination of bone marrow aspirate or biopsy as the gold standard for diagnosis of iron deficiency anemia.[2,9] Serum ferritin is a good indicator of storage iron in the body; however it does not provide information about the amount of iron actually available for erythropoiesis.[10]

Decreased serum ferritin concentrations of < 15 µg/L (ng/mL) always indicate iron deficiency and can be the result of prior blood loss, altered iron uptake, transferrin deficiency, reduced erythropoiesis (e.g. chronic kidney disease) or increased iron demand.[8,9,10,11,12,13,14]

Different aetiologies can cause increased serum ferritin levels, like iron overload, inflammation, liver or renal disease, malignancy or metabolic syndrome.[15,16] An elevated serum ferritin in the absence of infection or inflammation may suggest the presence of an iron overload state due to clinical conditions such as hereditary hemochromatosis, transfusional iron overload, ineffective erythropoiesis (e.g., thalassemia).[10,15,16]

Through release and leakage of damaged cells and tissue death, elevated serum ferritin is also recognized as an acute phase reactant. Patients with infections, acute or chronic inflammation, and malignancies have increased serum ferritin levels. Clinical conditions unrelated to iron stores, such as alcoholic or viral hepatitis and chronic renal failure, exhibit increased serum ferritin levels. The absolute ferritin level cannot be interpreted in isolation and should not be the sole basis for treatment decisions. Diagnosis should be made looking at the entire clinical situation of the individual patient.[2,10,15]

Test principle[17]

Particle enhanced immunoturbidimetric assay

Human ferritin agglutinates with latex particles coated with anti-ferritin antibodies. The precipitate is determined turbidimetrically at 570/800 nm.

Reagents - working solutions

R1 TRIS buffer, pH 7.5; immunoglobulins (rabbit); preservative, stabilizers

R3 Aqueous matrix containing latex particles coated with anti-human ferritin antibodies (rabbit); preservative, stabilizers

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.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing mist or vapours.
P273	Avoid release to the environment.
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.

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Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

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:	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, K_2- or K_3-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; with K_3-EDTA tubes pay particular attention that the tubes are adequately filled.

Centrifuge samples containing precipitates before performing the assay.

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

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

Freeze only once.

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[19]

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 / 24-57
Wavelength (sub/main)	800/570 nm
Reaction direction	Increase
Units	µg/L (pmol/L, ng/mL)

Reagent pipetting		Diluent (H_2O)
R1	80 µL	–
R3	80 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	140 µL
Increased	10 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 36-70
Wavelength (sub/main)	800/570 nm
Reaction direction	Increase
Units	µg/L (pmol/L, ng/mL)

Reagent pipetting		Diluent (H_2O)
R1	80 µL	–
R3	80 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	140 µL
Increased	10 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 36-70
Wavelength (sub/main)	800/570 nm
Reaction direction	Increase
Units	µg/L (pmol/L, ng/mL)

Reagent pipetting		Diluent (H_2O)
R1	80 µL	–
R3	80 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	140 µL
Increased	–	–	–

Calibration

Calibrators	S1: H_2O S2-6: C.f.a.s. Proteins
Calibration mode	Non-linear
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 Elecsys Ferritin assay (immunological method) which is traceable to NIBSC (WHO).

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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:[20] µg/L x 2.247 = pmol/L

µg/L = ng/mL

Limitations - interference

Criterion: Recovery within ± 4 µg/L (≤ 8.99 pmol/L, ≤ 4 ng/mL) of initial values for samples ≤ 40 µg/L (≤ 89.9 pmol/L, ≤ 40 ng/mL) and within ± 10 % for samples > 40 µg/L.

Icterus:[21] 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:[21] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[21] No significant interference up to an L index of 700 (approximate intralipid concentration: 700 mg/dL). 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.[22,23]

High-dose hook effect: Using prozone check, no false result without a flag was observed up to a ferritin concentration of 80000 µg/L (80000 ng/mL).

The polyclonal antibodies used in this assay are specific for ferritin from human liver and also recognize ferritin from human spleen. The antibodies show no cross reactivity to the human ferritin H subunit, which is the major component of human heart ferritin.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[24]

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

5-1000 µg/L (11.2-2247 pmol/L, 5-1000 ng/mL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:8 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 8.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 3 µg/L (6.7 pmol/L, 3 ng/mL)

Limit of Detection = 5 µg/L (11.2 pmol/L, 5 ng/mL)

Limit of Quantitation = 8 µg/L (18.0 pmol/L, 8 ng/mL)

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 (< 5 µg/L (11.2 pmol/L, 5 ng/mL)) will not be flagged by the instrument.

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a between-run coefficient of variation of ≤ 20 %. It has been determined using low concentration ferritin samples.

Expected values[25]

Adults: Expected values for ferritin concentrations in clinically healthy subjects are strongly dependent upon age and sex.

Results of a study with Tina-quant Ferritin on samples from 224 healthy test subjects (104 women, mainly premenopausal, and 120 men) are given below. These values correspond to the 5th and 95th percentiles.

Men (20-60 years) 30-400 µg/L (67-899 pmol/L, 30-400 ng/mL)

Women (17-60 years) 15-150 µg/L (34-337 pmol/L, 15-150 ng/mL)

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 requirements with repeatability (n = 84) and intermediate precision (4 aliquots per run, 1 run per day, one lot of reagent, 21 days, on the **cobas c** 501 analyzer). The following results were obtained on the **cobas c** 501 analyzer:

Repeatability	*Mean*	*SD*	*CV*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	125 (281, 125)	1 (2, 1)	0.8
Precipath Protein	306 (688, 306)	2 (4, 2)	0.6
Human serum 1	8.76 (19.7, 8.76)	0.83 (1.9, 0.83)	9.5
Human serum 2	26.1 (58.7, 26.1)	0.7 (1.6, 0.7)	2.8
Human serum 3	223 (501, 223)	1 (2, 1)	0.7
Human serum 4	568 (1276, 568)	5 (11, 5)	0.9
Human serum 5	781 (1755, 781)	7 (16, 7)	0.8

Intermediate precision	*Mean*	*SD*	*CV*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	125 (281, 125)	1 (2, 1)	1.1
Precipath Protein	306 (688, 306)	4 (9, 4)	1.3
Human serum 1	8.76 (19.7, 8.76)	1.14 (2.6, 1.14)	13.0
Human serum 2	26.1 (58.7, 26.1)	0.7 (1.6, 0.7)	2.8
Human serum 3	223 (501, 223)	3 (7, 3)	1.2
Human serum 4	568 (1276, 568)	10 (22, 10)	1.7

Human serum 5	781 (1755, 781)	14 (31, 14)	1.8

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

Method comparison

Ferritin values for human serum and plasma samples obtained on a **cobas c** 501 analyzer using the Tina-quant Ferritin Gen.4 assay (y) were compared with those determined on a Roche/Hitachi 917 analyzer using the Tina-quant Ferritin assay (x).

Sample size (n) = 87

Passing/Bablok[26]	Linear regression
y = 0.904x + 7.73 µg/L	y = 0.901x + 8.68 µg/L
τ = 0.983	r = 0.998

The sample concentrations were between 19.5 and 775 µg/L (43.8 and 1741 pmol/L, 19.5 and 775 ng/mL).

In addition a comparison of the Tina-quant Ferritin Gen.4 assay on a **cobas c** 501 analyzer (y) with the Tina-quant Ferritin Gen.3 assay on the same analyzer (x) using human serum and plasma samples gave the following correlations:

Sample size (n) = 88

Passing/Bablok[26]	Linear regression
y = 0.949x + 5.96 µg/L	y = 0.950x + 5.10 µg/L
τ = 0.989	r = 1.000

The sample concentrations were between 13.5 and 762 µg/L (30.3 and 1712 pmol/L, 13.5 and 762 ng/mL).

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

References

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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 navifyportal.roche.com for definition of symbols used):

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.

04885317500V8.0

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CE 0123

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