FERR3

cobas®

Tina-quant Ferritin Gen.3

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04745515 190	Tina-quant Ferritin Gen.3 250 tests	System-ID 07 6965 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:

FERR3: ACN 165

For **cobas c** 502 analyzer:

FERR3: ACN 8165

Intended use

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

Summary[1,2,3,4,5,6,7,8,9,10]

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending on the iron content, and consists of a protein shell (apoferritin) of 24 subunits and an iron core containing an average of approx. 2500 Fe^{3+} ions (in the basic isoforms). Common to all isoforms is their construction from two separate subunits, the acid H (heavy)-type subunit and the weakly basic L (light)-type subunit. The basic isoferritins are responsible for the long-term iron storage function and are mainly detectable in the liver, spleen and bone marrow. Acid isoferritins are found mainly in the myocardium, placenta, tumor tissue and - to a lesser content - in the depot organs.

The determination of ferritin is necessary above all in iron metabolism diagnosis, monitoring iron therapy, ascertaining the iron reserves in groups at risk and in the differential diagnosis of anemias. It encompasses prelatent and latent iron deficiency as well as iron overloading. It is also used to distinguish between hypoferric anemia and hypochromic anemia (chronic infection and tumor anemias, sideroblastic anemia or thalassemia).

Ferritin determinations are particularly suitable for monitoring renal anemia when iron utilization and distribution disorders are present during therapy with erythropoietin. The ferritin detectable in blood is in equilibrium with the body's depot iron and hence acts as an indicator of the level of iron stores.

A variety of methods are available for determining ferritin, e.g. radio-immunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), fluorescence immunoassay (FIA), luminescence immunoassay (LIA) and nephelometric immunoassay.

The automated Roche ferritin assay is based on the immunological agglutination principle with enhancement of the reaction by latex.

Test principle[10]

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 Buffer, pH 8.0; rabbit gamma globulin; stabilizers and preservative

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

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.

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

FERR3

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: Separate immediately from the clot and analyze promptly.
Plasma: Li-heparin or 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; with K_2-EDTA tubes pay particular attention that the tubes are adequately filled.

Centrifuge samples containing precipitates before performing the assay.

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[11]

Stability:[12]	7 days at 15-25 °C
	7 days at 2-8 °C

1 year 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 / 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	5 µL	–	–
Decreased	8 µL	10 µL	118 µL
Increased	15 µL	–	–

cobas c 501/502 **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	5 µL	–	–
Decreased	8 µL	10 µL	118 µL
Increased	15 µL	–	–

Calibration

Calibrators S1: H_2O

S2-6: 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: 0.0234	S5: 0.4000
S3: 0.0938	S6: 1.0000
S4: 0.1875	

Calibration mode RCM

Calibration frequency Full calibration
- after reagent lot change
- as required following quality control procedures

Traceability: This method has been standardized against a selected manufacturer's measurement procedure (immunological method).[13]

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: µg/L = ng/mL

µg/L x 2.247 = pmol/L

µmol/L x 445000 = ng/mL

Limitations - interference

Criterion: Recovery within ± 10 % of initial values at ferritin levels of 40 µg/L (89.9 pmol/L, 40 ng/mL).

Icterus:[14] No significant interference up to an I index of 60 (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[14] No significant interference up to an H index of 400 (approximate hemoglobin concentration: 248 µmol/L or 400 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.
Lipemia (triglycerides): No significant interference up to 750 mg/dL (8.48 mmol/L).

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

Drugs: No interference was found at therapeutic concentrations using common drug panels.[15,16]

High dose hook-effect: Using the prozone check, no false result without a flag was observed up to a ferritin concentration of 50000 µg/L (112350 pmol/L, 50000 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.[17]

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/Multiclean/SCCS or 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

15-800 µg/L (34-1800 pmol/L, 15-800 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 by the rerun function are automatically multiplied by a factor of 8.

Determine samples having lower concentrations via the rerun function. For samples with lower concentrations, the rerun function increases the sample volume by a factor of 3. The results are automatically divided by this factor.

Lower limits of measurement

Lower detection limit of the test

Normal pipetting volume: 10 µg/L (22.5 pmol/L, 10 ng/mL)

Increased pipetting volume: 3.3 µg/L (7.4 pmol/L, 3.3 ng/mL) (for automatic rerun)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from 0. 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[18]

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

Men	30-400 µg/L (67-899 pmol/L, 30-400 ng/mL)
Women (< 50 years)	15-150 µg/L (34-337 pmol/L, 15-150 ng/mL)
Women (> 50 years)	Approximation to reference interval for men

Children: For detailed information about reference intervals in children refer to the publication: Heiduk M, Päge I, Kliem C et al. Pediatric reference intervals determined in ambulatory and hospitalized children and juveniles. Clin Chim Acta 2009;406:156–161.

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*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	70.9 (159, 70.9)	1.0 (2, 1.0)	1.4
Precipath Protein	272 (611, 272)	2 (4, 2)	0.6
Human serum 1	19.2 (43.1, 19.2)	1.4 (3.2, 1.4)	7.5
Human serum 2	71.6 (161, 71.6)	1.0 (2, 1.0)	1.4
Human serum 3	313 (703, 313)	2 (5, 2)	0.7
Intermediate precision	*Mean*	*SD*	*CV*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	72.5 (163, 72.5)	1.6 (4, 1.6)	2.2
Precipath Protein	274 (617, 274)	3 (7, 3)	1.1
Human serum 4	25.5 (57.3, 25.5)	1.7 (3.8, 1.7)	6.6
Human serum 5	150 (336, 150)	2 (5, 2)	1.5

Method comparison

Ferritin 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) = 260

Passing/Bablok[19]	Linear regression
y = 0.996x – 2.89 µg/L	y = 0.975x + 1.99 µg/L
τ = 0.930	r = 0.995

The sample concentrations were between 17.5 and 796 µg/L (39.3 and 1789 pmol/L, 17.5 and 796 ng/mL).

In addition a comparison of the Roche Tina-quant Ferritin Gen.3 assay on a Roche/Hitachi **cobas c** 501 analyzer (y) with the Elecsys Ferritin assay on the MODULAR ANALYTICS E170 analyzer (x) using human serum and plasma samples gave the following correlations.

Sample size (n) = 63

Passing/Bablok[19]	Linear regression
y = 0.963x + 1.67 µg/L	y = 0.957x + 2.33 µg/L
τ = 0.981	r = 1.000

The sample concentrations were between 13.7 and 720 µg/L (30.8 and 1618 pmol/L, 13.7 and 720 ng/mL).

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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.

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 after reconstitution or mixing

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