Medical Devices Safety Notice

The National Health Regulatory Authority would like to alert all governmental and private healthcare facilities, local agents and distributors that the below medical device:

Device Details	
Device Name	Tina-Quant Ferritin Gen.4
Manufacturer	Roche Diagnostics
Country of Origin	Germany
Model No.	04885317190 & 08057648190
Reference	Refer to the attachment below.
Reason of Alert	NHRA initiates this FSN due to on cobas c instruments, claims in the Instructions for Use (IFU) and settings in the applications are updated. The claim for lipemia interference (L index) is updated based on recent investigation results showing that interference is observed above 700. The adaptation of LOQ and further editorial changes are implemented for harmonization purposes within the Roche instrument family approach (pro-active improvement, no non- compliance).
Action should be taken	For more information about the New IFU please contact the authorized representative General Medical W.L.L at registration.medics@intercol.com.

Your cooperation is highly appreciated in improving health services in the Kingdom of Bahrain.

For more information please contact Medical_Devices@nhra.bh

Quality Notification

30 May 2023

Subject: Tina-quant Ferritin Gen.4 for cobas c: Updated Claims for Interference by Lipemia and for Limit of Quantitation

Dear Valued Customer,

Product	**GMMI**
Tina-quant Ferritin Gen.4	04885317190
	05172390190
	08057648190
Instrument/System	**cobas**® c 303 analytical unit
	cobas® c 311 analyzer
	cobas® c 501 module
	cobas® c 502 module
	cobas® c 503 analytical unit
	cobas® c 701 module
	cobas® c 702 module
Component	Reagent
Target Group	Application

روش دياجنوستيكس ميدل ايست ش م ح
شركة ذات مسؤولية محدودة تأسست بموجب القانون رقم ٢ سنة ١٩٨٦
ووفقا للائحة التنفيذية رقم ١ لسنة ١٩٩٩
رقم السجل التجاري: ١٥٠٤١٦ –رقم الرخصة: ١٣٠٢٩٤
Roche Diagnostics Middle East FZCO
Formed Pursuant to Law No. 2 of 1986
& Implementing Regulation No. 1 of 1999 with Limited Liability
Registration No.: 150416 – License No.: 130294

ص. ب. ٢٦١٠٠١ – المنطقة الحرة لجبل علي
دبي – الإمارات العربية المتحدة
PO Box 261001- Jebel Ali Free Zone
Dubai, United Arab Emirates

هاتف: ٠٠٠ ٨١٦ ٩٠٠٠ ٤ (٠) ٩٧١+
فاكس: ٠٠١ ٨١٦ ٩٠٠١ ٤ (٠) ٩٧١+
Tel. +971 (0) 4 816 9000
Fax +971 (0) 4 816 9001

Subject

For the Tina-quant ® Ferritin Gen.4 (FERR4) assay on cobas c instruments, claims in the Instructions for Use (IFU) and settings in the applications are updated as described:

1.) **Interference by Lipemia** (Limitations section in IFUs):
Based on internal investigations in the context of the recently announced master instrument switch from cobas c 501 to cobas c 503 aimed at checking FERR4 performance on cobas c., the L index specification is adapted from 1000 to 700 as it was demonstrated that interference by lipemia may cause reduced ferritin recoveries and with L sample indices exceeding 700, recoveries may be reduced by more than -10%.

For all countries the FERR4 application settings are updated in ACN 692 for cobas c 311/501, ACN 8692 for cobas c 502/701/702 and ACN 20570 for cobas c 503/303.

Updated wording in IFU:
Section "Limitations - interference":
Lipemia (Intralipid): No significant interference up to an L index of 700 (approximate intralipid concentration: 700 mg/dL)

2.) **Limit of Quantitation (LOQ)**:
Adaptation from 5 µg/L to 8 µg/L in the IFUs for cobas c 311/501/502/701/702.
The low end of measuring range is not changed (as defined by LOD=5 µg/L).

Note that LOQ was already adapted to 8 µg/L for cobas c 503/303 based on performance data. Therefore, the updated LOQ communicated in this QN is part of the harmonization approach across instrument types and across countries.

Updated wording in IFU:
Section "Lower limits of measurement":
Limit of Quantitation = 8 µg/L (18.0 pmol/L)

3.) **Editorial changes to the IFU**:
Additional IFU updates are implemented for harmonization purposes as described into detail below.

Updated wording in IFU:
Section "Reagent handling": Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

Section "Calibration": Calibration mode: Changed from "Spline" to "Non-linear" (Note that the alternative characterization of calibration mode as "Non-linear" is a change in wording only, the calibration algorithm does not change.)
Calibrator set point factors are removed from the cobas c 311/501/502 IFU as set point values are provided in calibrator value sheets (see also SN-RDS-CoreLab-2021-001).

Note that the Ferritin Gen.2 test for COBAS INTEGRA 400 plus instruments (test ID 0-27) is not affected due to different reagent composition and application settings.

Root Cause

The claim for lipemia interference (L index) is updated based on recent investigation results showing that interference is observed above 700. The adaptation of LOQ and further editorial changes are implemented for harmonization purposes within the Roche instrument family approach (pro-active improvement, no non-compliance).

Risk Assessment

Severity

Concerning LOQ adaptation: No patient or diagnostic test results are affected and a medical risk to patients and users can be excluded. Therefore, an HHE is not required.

Concerning L index adaptation: The chain of events potentially leading to discrepant results was analyzed. Based upon the investigation results, the probability of occurrence of harm was assessed to be unlikely. Therefore, an HHE is not required.

Important Information

In general, the serum index check field on all cobas c systems (except cobas c 503/303) belongs to a group of settings that can be changed by the customer.
Nevertheless, this is the only 'user-editable' field that will be overwritten by an updated e-barcode on all cobas c systems (on cobas c 701/702/502/503/303 with partial and full overwrite).

LOQ is updated to 8 µg/L for all countries and further editorial changes are implemented in the IFU.

Updated IFUs and the Important Notes for all affected systems are attached to this Quality Notification.

Updated e-library packages will be published to e-Content Portal with reference to this Quality Notification.

Customer Details:

Facility Name: Contact Name: Position: Phone: Date: Signature and Stamp:

If you have any questions, please do not hesitate to contact our Application Support Team or your local Account Manager.

Yours sincerely,

For on behalf of
Roche Diagnostics Middle East FZCO

Venkatesan Veeraraghavan
Regional Quality Manager

Hassan Kassem
Regional Quality & Product Safety Lead, Middle East

FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04885317190	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[1,2,3,4,5,6,7,8,9]

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon 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 acidic 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 extent - 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 for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

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

Test principle[9]

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.

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

FERR4

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, 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.

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[10]

Stability:[11]	7 days at 15-25 °C
	7 days at 2-8 °C

FERR4

Tina-quant Ferritin Gen.4

cobas®

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	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).

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:[12]	µg/L = ng/mL
	µg/L × 2.247 = pmol/L
	µmol/L × 445000 = 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:[13] 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:[13] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[13] 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.[14,15]

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.[16]

FERR4

Tina-quant Ferritin Gen.4

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[17]

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 a **cobas c** 501 analyzer). The following results were obtained:

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[18]	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[18]	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 dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number

CE 0123

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

Roche

FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
05172390190	Tina-quant Ferritin Gen.4 650 tests	System-ID 05 6966 5	**cobas c** 701/702

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	
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3	

English

System information

FERR4: ACN 8692

Intended use

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

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

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon 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 acidic 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 extent - 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 for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

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

Test principle[9]

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.

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

FERR4

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

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:	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: Separate immediately from the clot and analyze promptly.
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.

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[10]

Stability:[11]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-25) °C

FERR4

Tina-quant Ferritin Gen.4

cobas®

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 / 20-38		
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	–	–

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).

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:[12]	µg/L = ng/mL
	µg/L x 2.247 = pmol/L
	µmol/L x 445000 = 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:[13] 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:[13] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[13] 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.[14,15]

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.[16]

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, 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

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 by 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[17]

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

Repeatability	*Mean*	*SD*	*CV*
	µg/L (pmol/L, ng/mL)	*µg/L (pmol/L, ng/mL)*	*%*
Precinorm Protein	125 (281, 125)	1 (2, 1)	0.9
Precipath Protein	295 (663, 295)	3 (7, 3)	1.2
Human serum A	194 (436, 194)	1 (2, 1)	0.5
Human serum B	825 (1854, 825)	15 (34, 15)	1.9
Human serum C	22.6 (50.8, 22.6)	1.0 (2.3, 1.0)	4.3
Human serum D	14.4 (32.4, 14.4)	0.7 (1.6, 0.7)	4.6
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

Method comparison

Ferritin 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) = 70

Passing/Bablok[18]	Linear regression
y = 0.996x - 1.44 µg/L	y = 0.973x + 3.78 µg/L
τ = 0.978	r = 0.998

The sample concentrations were between 10.6 and 949 µg/L (23.8 and 2132 pmol/L, 10.6 and 949 ng/mL).

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

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number

FERR4

Tina-quant Ferritin Gen.4

cobas®

CE 0123

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

Roche

FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057648190	Tina-quant Ferritin Gen.4 (400 tests)	System-ID 2057 001	**cobas c** 303, **cobas c** 503

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 20656	
10557897122	Precinorm Protein (3 x 1 mL)	Code 20302	
11333127122	Precipath Protein (3 x 1 mL)	Code 20303	
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

FERR4: ACN 20570

Intended use

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

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

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon 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 acidic 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 extent - 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 for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

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

Test principle[9]

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.

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:	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, 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:[10]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at (–15)-(–25) °C

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

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

See "Order information" section

General laboratory equipment

FERR4

Tina-quant Ferritin Gen.4

cobas®

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)	800/570 nm		
Reagent pipetting		Diluent (H_2O)	
R1	60 µL	–	
R3	60 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	7.5 µL	–	–
Decreased	7.5 µL	10 µL	70 µL
Increased	7.5 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
	S2-6: 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 Elecsys Ferritin assay (immunological method) which is traceable to NIBSC (WHO).

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. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks. 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 µg/L (pmol/L, ng/mL).

Conversion factors:[12]	µg/L × 2.247 = pmol/L
	µg/L = ng/mL

Limitations - interference

Criterion: Recovery within ± 4 µg/L of initial values for samples ≤ 40 µg/L and within ± 10 % for samples > 40 µg/L.

Icterus:[13] 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:[13] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[13] 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.[14,15]

High-dose hook effect: Using prozone check automatically performed by the analyzer, 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.[16]

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 information. For further instructions refer to the operator's manual.

Limits and ranges

Measuring range

5-1000 µg/L (11.2-2247 pmol/L)

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)
Limit of Detection	= 5 µg/L (11.2 pmol/L)
Limit of Quantitation	= 8 µg/L (18.0 pmol/L)

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 ferritin samples.

Expected values[17]

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.

µg/L

Men (20-60 years)	30-400 µg/L

Women (17-60 years)	15-150 µg/L

pmol/L

Men (20-60 years)	67-899 pmol/L
Women (17-60 years)	34-337 pmol/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. 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.

Repeatability	*Mean* µg/L	*SD* µg/L	*CV* %
PCCC1[a)]	108	0.906	0.8
PCCC2[b)]	202	1.37	0.7
Human serum 1	10.6	0.781	7.3
Human serum 2	29.8	1.18	4.0
Human serum 3	207	1.14	0.6
Human serum 4	479	2.71	0.6
Human serum 5	827	4.68	0.6

Intermediate precision	*Mean* µg/L	*SD* µg/L	*CV* %
PCCC1[a)]	108	1.26	1.2
PCCC2[b)]	202	2.10	1.0
Human serum 1	10.6	0.816	7.7
Human serum 2	29.8	1.30	4.4
Human serum 3	206	1.62	0.8
Human serum 4	479	3.96	0.8
Human serum 5	827	7.50	0.9

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).

Method comparison

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

Sample size (n) = 73

Passing/Bablok[18]	Linear regression
y = 1.007x + 0.488 µg/L	y = 0.980x + 2.67 µg/L
τ = 0.960	r = 0.999

The sample concentrations were between 6.70 and 800 µg/L.

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

Sample size (n) = 89

Passing/Bablok[18]	Linear regression
y = 1.030x - 0.666 µg/L	y = 1.029x - 0.379 µg/L
τ = 0.966	r = 1.000

The sample concentrations were between 6.00 and 979 µg/L.

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10 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.

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17 Lotz J, Hafner G, Prellwitz W. Reference Study for Ferritin Assays. Kurzmitteilung Clin Lab 1997;43:993-994.

18 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.

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

FERR4

Tina-quant Ferritin Gen.4

CE 0123

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

FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

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

Materials required (but not provided):

11355279160	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
10557897160	Precinorm Protein (3 x 1 mL)	Code 302	
11333127160	Precipath Protein (3 x 1 mL)	Code 303	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

For use in the USA only

System information

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

FER4X: ACN 749

For **cobas c** 502 analyzer:

FER4X: ACN 8749

Intended use

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

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

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon 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 2 separate subunits, the acidic 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 extent - 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 for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

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

Test principle[9]

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.

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.

Storage and stability

FERR4

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, 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.

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.

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[10]

Stability:[11]	7 days at 20-25 °C

FERR4

Tina-quant Ferritin Gen.4

cobas®

7 days at 4-8 °C	
1 year at -20 °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	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).

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:[12]	µg/L = ng/mL
	µg/L × 2.247 = pmol/L
	µmol/L × 445000 = 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:[13] 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:[13] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[13] 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.[14,15]

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

FERR4

Tina-quant Ferritin Gen.4

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.[16]

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

8-1000 µg/L (18.0-2247 pmol/L, 8-1000 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 (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ)

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[17]

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, 1 lot of reagent, 21 days) on a **cobas c** 501 analyzer. The following results were obtained:

Repeatability	*Mean µg/L (pmol/L, ng/mL)*	*SD µg/L (pmol/L, ng/mL)*	*CV %*
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 µg/L (pmol/L, ng/mL)*	*SD µg/L (pmol/L, ng/mL)*	*CV %*
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 using the Tina-quant Ferritin assay on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 87

Passing/Bablok[18]	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).

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 using the Tina-quant Ferritin Gen.3 assay on the same analyzer (x).

Sample size (n) = 88

Passing/Bablok[18]	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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7 Franco RS. Ferritin. In: Pesce AJ, Kaplan LA, eds. Methods in clinical chemistry. St. Louis/Washington/Toronto: CV Mosby Company 1987:1240-1242.

8 Dati F, Sauder U. Immunchemische Methoden im klinischen Labor. GIT Labor-Medizin 1990;7-8:357-372.

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10 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests, 4th edition. St. Louis (MO): Saunders Elsevier 2006;441-451.

11 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev.2 2002.

12 Young DS, Huth EJ. SI Units For Clinical Measurement. American College of Physicians 1998.

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

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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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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

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.

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
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Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

FERR4

cobas®

Tina-quant Ferritin Gen.4

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
05172390190	Tina-quant Ferritin Gen.4, 650 tests	System-ID 05 6966 5	**cobas c** 701/702

Materials required (but not provided):

11355279160	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
10557897160	Precinorm Protein (3 x 1 mL)	Code 302	
11333127160	Precipath Protein (3 x 1 mL)	Code 303	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3	

English

For use in the USA only

System information

FER4X: ACN 8749

Intended use

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

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

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon the iron content, and consists of a protein shell (apoferritin) of 24 subunits and an iron core containing an average of approximately 2500 Fe^{3+} ions (in the basic isoforms). Common to all isoforms is their construction from 2 separate subunits, the acidic 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 extent - 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 for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

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

Test principle[9]

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.

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.

Storage and stability

FERR4

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

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:	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: 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.

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.

Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.[10]

Stability:[11] 7 days at 20-25 °C

FERR4

Tina-quant Ferritin Gen.4

cobas®

7 days at 4-8 °C	
1 year at -20 °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 701/702 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 20-38		
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	–	–

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).[12]

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:[13] µg/L = ng/mL

µg/L x 2.247 = pmol/L

µmol/L x 445000 = 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:[14] 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:[14] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[14] 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.[15,16]

High dose hook-effect: Using the prozone check automatically performed by the analyzer, 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.[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 **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

8-1000 µg/L (18.0-2247 pmol/L, 8-1000 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 %).

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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[18]

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 = 21) and intermediate precision (4 aliquots per run, 1 run per day, 1 lot of reagent, 21 days, on a **cobas c** 501 analyzer). The following results were obtained:

Repeatability	*Mean µg/L (pmol/L, ng/mL)*	*SD µg/L (pmol/L, ng/mL)*	*CV %*
Precinorm Protein	125 (281, 125)	1 (2, 1)	0.9
Precipath Protein	295 (663, 295)	3 (7, 3)	1.2
Human serum A	194 (436, 194)	1 (2, 1)	0.5
Human serum B	825 (1854, 825)	15 (34, 15)	1.9
Human serum C	22.6 (50.8, 22.6)	1.0 (2.3, 1.0)	4.3
Human serum D	14.4 (32.4, 14.4)	0.7 (1.6, 0.7)	4.6

Intermediate precision	*Mean µg/L (pmol/L, ng/mL)*	*SD µg/L (pmol/L, ng/mL)*	*CV %*
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

Method comparison

Ferritin 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) = 70

Passing/Bablok[19]	Linear regression
y = 0.996x - 1.44 µg/L	y = 0.973x + 3.78 µg/L
τ = 0.978	r = 0.998

The sample concentrations were between 10.6 and 949 µg/L (23.8 and 2132 pmol/L, 10.6 and 949 ng/mL).

References

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2 Kaltwasser IP, Werner E, eds. Serumferritin: Methodische und klinische Aspekte. Berlin/Heidelberg/New York: Springer-Verlag 1980.

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4 Albertini A, Arosio P, Chiancone E, et al. eds. Ferritins and isoferritins as biochemical markers. Amsterdam/New York/Oxford: Elsevier 1984.

5 San Diego Declaration, Erythropoietin use and response in end-stage renal disease. The American Society of Nephrology, Annual meeting, San Diego. J Am Soc Nephrol 1995;3:35.

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7 Franco RS. Ferritin. In: Pesce AJ, Kaplan LA, eds. Methods in clinical chemistry. St. Louis/Washington/Toronto: CV Mosby Company 1987:1240-1242.

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

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

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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

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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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Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336

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Tina-quant Ferritin Gen.4

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057648190	Tina-quant Ferritin Gen.4 (400 tests)	System-ID 2057 001	**cobas c** 303, **cobas c** 503

Materials required (but not provided):

11355279160	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 20656	
10557897160	Precinorm Protein (3 x 1 mL)	Code 20302	
11333127160	Precipath Protein (3 x 1 mL)	Code 20303	
05947626160	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391	
05947774160	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

English

For use in the USA only

System information

FER4X: ACN 20571

Intended use

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

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

Ferritin is the iron storage protein. It has a molecular weight of ≥ 440000 daltons, depending upon 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 2 separate subunits, the acidic 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 extent - 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 for the level of the iron stores.

A variety of routine methods are available for determining ferritin, e.g. enzyme-linked immunosorbent assays (ELISA), fluorescence immunoassays (FIA), luminescence immunoassays (LIA), nephelometric and turbidimetric immunoassays.

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

Test principle[9]

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.

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.

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, 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:[10]	7 days at 20-25 °C
	7 days at 4-8 °C
	1 year at –20 °C

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

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.

Materials provided

See "Reagents – working solutions" section for reagents.

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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)	800/570 nm		
Reagent pipetting		Diluent (H_2O)	
R1	60 µL	–	
R3	60 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	7.5 µL	–	–
Decreased	7.5 µL	10 µL	70 µL
Increased	7.5 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
	S2-6: 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 Elecsys Ferritin assay (immunological method) which is traceable to NIBSC (WHO).

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. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks. 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 µg/L (pmol/L, ng/mL).

Conversion factors:[12]	µg/L x 2.247 = pmol/L
	µg/L = ng/mL

Limitations - interference

Criterion: Recovery within ± 4 µg/L of initial values for samples ≤ 40 µg/L and within ± 10 % for samples > 40 µg/L.

Icterus:[13] 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:[13] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 310 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[13] 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.[14,15]

High-dose hook effect: Using prozone check automatically performed by the analyzer, no false result without a flag was observed up to a ferritin concentration of 80000 µg/L.

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.[16]

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

8-1000 µg/L (18.0-2247 pmol/L, 8-1000 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, 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 ferritin samples.

Expected values[17]

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.

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µg/L

Men (20-60 years)	30-400 µg/L
Women (17-60 years)	15-150 µg/L

pmol/L

Men (20-60 years)	67-899 pmol/L
Women (17-60 years)	34-337 pmol/L

ng/mL

Men (20-60 years)	30-400 ng/mL
Women (17-60 years)	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. 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.

Repeatability	*Mean*	*SD*	*CV*
	µg/L (ng/mL)	*µg/L (ng/mL)*	*%*
PCCC1[a)]	108	0.906	0.8
PCCC2[b)]	202	1.37	0.7
Human serum 1	10.6	0.781	7.3
Human serum 2	29.8	1.18	4.0
Human serum 3	207	1.14	0.6
Human serum 4	479	2.71	0.6
Human serum 5	827	4.68	0.6

Intermediate precision	*Mean*	*SD*	*CV*
	µg/L (ng/mL)	*µg/L (ng/mL)*	*%*
PCCC1[a)]	108	1.26	1.2
PCCC2[b)]	202	2.10	1.0
Human serum 1	10.6	0.816	7.7
Human serum 2	29.8	1.30	4.4
Human serum 3	206	1.62	0.8
Human serum 4	479	3.96	0.8
Human serum 5	827	7.50	0.9

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).

Method comparison

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

Sample size (n) = 67

Passing/Bablok[18]	Linear regression
y = 1.004x + 0.746 µg/L	y = 0.979x + 3.28 µg/L
τ = 0.972	r = 0.999

The sample concentrations were between 8.30 and 800 µg/L (8.30 and 800 ng/mL).

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

Sample size (n) = 87

Passing/Bablok[18]	Linear regression
y = 1.030x - 0.666 µg/L	y = 1.029x - 0.377 µg/L
τ = 0.965	r = 1.000

The sample concentrations were between 9.70 and 979 µg/L (9.70 and 979 ng/mL).

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10 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.

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18 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.

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 (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
	Volume for reconstitution
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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Tina-quant Ferritin Gen.4

REF **08057648** 190

cobas c 303

Reason for change

ACN 20570 / FERR4	Old	**New**
Version	0202	**0203**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
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FERR4

Tina-quant Ferritin Gen.4

REF **04885317** 190

cobas c 311

Reason for change

ACN 692 / FERR4	Old	**New**
Version	0603	**0604**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **04885317** 190

cobas c 501

Reason for change

ACN 692 / FERR4	Old	**New**
Version	0803	**0804**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **04885317** 190

cobas c 502

Reason for change

ACN 8692 / FERR4	Old	**New**
Version	0102	**0103**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **08057648** 190

cobas c 503

Reason for change

ACN 20570 / FERR4	Old	**New**
Version	0204	**0205**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **05172390** 190

cobas c 701

Reason for change

ACN 8692 / FERR4	Old	**New**
Version	0203	**0204**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **05172390** 190

cobas c 702

Reason for change

ACN 8692 / FERR4	Old	**New**
Version	0404	**0405**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **08057648** 190

cobas c 303

Reason for change

ACN 20571 / FER4X	Old	**New**
Version	0202	**0203**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

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FERR4

Tina-quant Ferritin Gen.4

REF **04885317** 190

cobas c 311

Reason for change

ACN 749 / FER4X	Old	**New**
Version	0101	**0102**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
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FERR4

Tina-quant Ferritin Gen.4

REF **04885317** 190

cobas c 501

Reason for change

ACN 749 / FER4X	Old	**New**
Version	0101	**0102**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **04885317** 190

cobas c 502

Reason for change

ACN 8749 / FER4X	Old	**New**
Version	0101	**0102**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **08057648** 190

cobas c 503

Reason for change

ACN 20571 / FER4X	Old	**New**
Version	0201	**0202**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

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www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **05172390** 190

cobas c 701

Reason for change

ACN 8749 / FER4X	Old	**New**
Version	0101	**0102**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

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www.roche.com

FERR4

Tina-quant Ferritin Gen.4

REF **05172390** 190

cobas c 702

Reason for change

ACN 8749 / FER4X	Old	**New**
Version	0101	**0102**
Sample Index Limits L/H/I	1000/500/60	**700**/500/60

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