

# FERR2

Ferritin Gen.2 - Application for C.f.a.s. Proteins

**cobas**<sup>®</sup>  
Specific proteins

## Order information

REF	CONTENT	Analyzer(s) on which <b>cobas c</b> pack(s) can be used
03528995 190	Ferritin Gen.2 (200 tests)	System-ID 07 6808 1 COBAS INTEGRA 400 plus COBAS INTEGRA 800
11355279 216	Calibrator f.a.s. Proteins (5 × 1 mL)	System-ID 07 6557 0
10557897 122	Precinorm Protein (3 × 1 mL)	System-ID 07 9105 9
11333127 122	Precipath Protein (3 × 1 mL)	System-ID 07 9106 7
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	System-ID 07 7469 3
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	System-ID 07 7469 3
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	System-ID 07 7470 7
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	System-ID 07 7470 7
20756350 322	NaCl Diluent 9 % (6 × 22 mL)	System-ID 07 5635 0

## English

### System information

Test FER2P, test ID 0-278

### Intended use

In vitro test for the quantitative immunological determination of human ferritin in serum and plasma on COBAS INTEGRA systems.

### Summary<sup>1,2,3,4,5,6,7,8,9,10</sup>

Ferritin is the iron storage protein. It has a molecular weight of  $\geq 440000$  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  $\text{Fe}^{3+}$  ions (in the basic isoforms). Common to all isoforms is their construction from two separate subunits, the acid H (heavy)-type subunit and the weakly basic L (light)-type subunit. The basic isoforms are responsible for the long-term iron storage function and are mainly detectable in the liver, spleen and bone marrow. Acid isoforms are found mainly in the myocardium, placenta, tumor tissue and - to a lesser content - in the depot organs.

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

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

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

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

### Test principle

Particle enhanced immunoturbidimetric assay.

Human ferritin agglutinates with latex particles coated with anti-ferritin antibodies. The precipitate is determined turbidimetrically at 552 nm.

### Reagents - working solutions

- R1** Glycine buffer: 0.17 mol/L, pH 8.3; rabbit globulin: 5 mg/mL; stabilizers and preservative.
- SR** Latex particles coated with anti-human ferritin (rabbit): 0.17 %; glycine buffer: 0.17 mol/L, pH 7.3; stabilizer and preservative.

R1 is in position B and SR is in position C.

### Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

### Reagent handling

Ready for use

### COBAS INTEGRA 400 plus analyzers

Mix all brand new (non-punctured) **cobas c** packs for 1 minute on a cassette mixer before loading on the analyzer.

### COBAS INTEGRA 800 analyzers

After **cobas c** packs puncture, the analyzer automatically mixes the reagent for 1 minute.

### Storage and stability

Shelf life at 2-8 °C See expiration date on **cobas c** pack label

#### COBAS INTEGRA 400 plus system

On-board in use at 10-15 °C 12 weeks

#### COBAS INTEGRA 800 system

On-board in use at 8 °C 12 weeks

### Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

The use of certain blood collection tubes containing separation gels and/or clotting accelerators may interfere with this test.

Only the specimens listed below were tested and found acceptable.

Serum

Plasma: Li-heparin plasma, K<sub>2</sub>- or K<sub>3</sub>-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.

When using K<sub>3</sub>-EDTA tubes pay particular attention that the tubes are adequately filled.

Blood collected in capillary blood collection tubes is unsuitable. Do not thaw frozen specimens in a 37 °C bath. Violent mixing may denature ferritin.<sup>11</sup>

Do not use turbid samples.

Centrifuge samples containing precipitates before performing the assay.

Stability:<sup>12</sup> 7 days at 15-25 °C  
7 days at 2-8 °C  
1 year at (-15)-(-25) °C

### Materials provided

See "Reagents – working solutions" section for reagents.

### Materials required (but not provided)

NaCl Diluent 9 %, Cat. No. 20756350 322, system-ID 07 5635 0 for automatic sample dilution and standard serial dilutions. NaCl Diluent 9 % is placed in its predefined rack position and is stable for 4 weeks on-board COBAS INTEGRA 400 plus/800 analyzers.

**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.

**Application for serum and plasma****COBAS INTEGRA 400 plus test definition**

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A	552 nm
Calc. first/last	35/42
Typical prozone effect	> 10000 µg/L (> 22470 pmol/L)
Antigen excess check	Yes*
Unit	µg/L

**Pipetting parameters**

		Diluent (H <sub>2</sub> O)
R1	50 µL	
Sample	20 µL	20 µL
SR	47 µL	10 µL
Total volume	147 µL	

**COBAS INTEGRA 800 test definition**

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A	552 nm
Calc. first/last	47/56
Typical prozone effect	> 10000 µg/L (> 22470 pmol/L)
Antigen excess check	Yes*
Unit	µg/L

**Pipetting parameters**

		Diluent (H <sub>2</sub> O)
R1	50 µL	
Sample	20 µL	20 µL
SR	47 µL	10 µL
Total volume	147 µL	

\*A "prozone effect" occurs with values of ferritin above 10000 µg/L. Such results are automatically flagged by the system up to a concentration of 75000 µg/L. In case of nonlinearity flagging, dilute the specimen manually with 0.9 % saline solution such that the concentration is less than the highest standard concentration. Multiply the result of the diluted specimen by the appropriate dilution factor.

**Calibration**

Calibrator	Calibrator f.a.s. Proteins
Calibration mode	Logit/log 5
Calibration dilution ratio	1:2, 1:3, 1:6, 1:9, 1:48, and 0 µg/L performed automatically by the instrument
Calibration replicate	Duplicate recommended

**Calibration interval**

Each lot, every 84 days and as required following quality control procedures.

Enter the assigned lot-specific ferritin value of the undiluted calibrator, indicated in the package insert of the Calibrator f.a.s. Proteins.

Traceability: This method has been standardized against the Elecsys Ferritin assay (immunological method) which is traceable to NIBSC (WHO).

**Quality control**

Reference range	Precinorm Protein or PreciControl ClinChem Multi 1
Pathological range	Precipath Protein or PreciControl ClinChem Multi 2
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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 INTEGRA analyzers automatically calculate the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help (COBAS INTEGRA 400 plus/800 analyzers).

Conversion factors:	µg/L = ng/mL
	µg/L × 2.247 = pmol/L
	pmol/L × 445000 = ng/mL

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial value.

Hemoglobin, bilirubin and Intralipid interferences were checked with a sample revealing a ferritin concentration of approximately 28 µg/L.

**Serum, plasma**

Icterus:<sup>13</sup> 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:<sup>13</sup> No significant interference up to an H index of 960 (approximate hemoglobin concentration: 596 µmol/L or 960 mg/dL).

Lipemia (Intralipid):<sup>13</sup> No significant interference up to an L index of 160. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors: No significant interference.

Therapeutic drug interference was tested according to the recommendations of the VDGH<sup>a)</sup>. No interferences were found.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.<sup>14</sup>

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

a) Verband der Diagnostica und Diagnostica Geräte Hersteller. Refer to section 1 / Introduction of this Method Manual for a list of drugs tested and their concentrations.

**ACTION REQUIRED**

**Special Wash Programming:** The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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

## Limits and ranges

### Measuring range

10-484 µg/L (22-1088 pmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted by the rerun function are automatically multiplied by a factor of 5.

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### Lower limits of measurement

Lower detection limit of the test:

10 µg/L (22 pmol/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of a zero sample (zero sample + 3 SD, repeatability, n = 21).

### Expected values<sup>1,15</sup>

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 pre-menopausal 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 or 30-400 ng/mL)
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Women (17-60 years)	15-150 µg/L (34-337 pmol/L or 15-150 ng/mL)
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Children: For detailed information about reference intervals in children refer to the publication: Heiduk M, Päge I, Kliem C, et al. Pediatric reference intervals determined in ambulatory and hospitalized children and juveniles. Clin Chim Acta 2009;406:156-161.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

### Specific performance data

Representative performance data on the COBAS INTEGRA analyzers are given below. Results obtained in individual laboratories may differ.

### Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (1 aliquot per run, 1 run per day, 10 days). The following results were obtained:

	Level 1	Level 2
Mean	19.8 ng/mL (44.5 pmol/L or 19.8 µg/L)	108 ng/mL (242 pmol/L or 108 µg/L)
CV repeatability	9.0 %	2.5 %

	Level 1	Level 2
Mean	20.3 ng/mL (45.6 pmol/L or 20.3 µg/L)	157 ng/mL (353 pmol/L or 157 µg/L)
CV intermediate precision	7.8 %	3.4 %

### Method comparison

Ferritin values for human serum samples obtained on a COBAS INTEGRA 700 analyzer with the COBAS INTEGRA Ferritin Gen.2 reagent (y) were compared with those determined using the COBAS INTEGRA Ferritin reagent on the same instrument (x) and with those determined using the Tina-quant Ferritin reagent on a Roche/Hitachi 917 analyzer (x).

### COBAS INTEGRA 700 analyzer

Sample size (n) = 49

### Passing/Bablok<sup>16</sup>

 $y = 1.298x + 13.0 \text{ ng/mL}$ 
 $r = 0.922$ 
 $SD \text{ (md 95)} = 17.8$ 

### Linear regression

 $y = 1.241x + 17.5 \text{ ng/mL}$ 
 $r = 0.994$ 
 $Sy.x = 9.09$ 

The sample concentrations were between 14.3 and 529 ng/mL (32.1 and 1189 pmol/L or 14.3 and 529 µg/L).

### Roche/Hitachi 917 analyzer

Sample size (n) = 57

### Passing/Bablok<sup>16</sup>

 $y = 1.031x - 6.07 \text{ ng/mL}$ 
 $r = 0.959$ 
 $SD \text{ (md 95)} = 56.3$ 

### Linear regression

 $y = 1.035x - 6.51 \text{ ng/mL}$ 
 $r = 0.997$ 
 $Sy.x = 21.6$ 

The sample concentrations were between 14.3 and 1840 ng/mL (32.1 and 4134 pmol/L or 14.3 and 1840 µg/L).

### 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.

# FERR2

Ferritin Gen.2 - Application for C.f.a.s. Proteins

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Specific proteins

## Symbols

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

CONTENT

Contents of kit



Volume after reconstitution or mixing

GTIN

Global Trade Item Number

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