



07876726001V4.0

CRP4

Tina-quant C-Reactive Protein IV

Order information

REF	CONTENT	Analyzer(s) on which kit(s) can be used
07876432190	Tina-quant C-Reactive Protein IV (2 × 100 tests)	cobas c 111

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 × 1 mL)	Code 656	
20766321322	CRP T Control N (5 × 0.5 mL)	Code 235	
10557897122	Precinorm Protein (3 × 1 mL)	Code 302	
11333127122	Precipath Protein (3 × 1 mL)	Code 303	
05117003190	PreciControl ClinChem Multi 1 (20 × 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 × 5 mL)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 × 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 × 5 mL)	Code 392	
04774230190	NaCl Diluent 9 %	Code 951	
11930630001	Chimneys		

English

System information

CRP4: ACN 256

Intended use

Immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on the **cobas c 111** system.

Summary

CRP measurements, performed with this assay in human serum or plasma, are used as aid in diagnosis, monitoring, prognosis, and management of suspected inflammatory disorders and associated diseases, acute infections and tissue injury.

C-reactive protein is the classic acute phase protein in inflammatory reactions.¹ It is synthesized by the liver and consists of five identical polypeptide chains that form a five membered ring having a molecular weight of 105000 daltons.^{1,2,3,4} CRP is the most sensitive of the acute phase reactants and its concentration increases rapidly during inflammatory processes.^{2,3} Complexed CRP activates the classical complement pathway. The CRP response frequently precedes clinical symptoms, including fever.^{1,3} After onset of an acute phase response the serum CRP concentration rises rapidly and extensively.^{2,3,4} The increase begins within 6 to 12 hours and the peak value is reached within 24 to 48 hours.^{1,3,5} Levels above 100 mg/L are associated with severe stimuli such as major trauma and severe infection (sepsis).⁵ CRP response may be less pronounced in patients suffering from liver disease.⁶

CRP assays are used to detect systemic inflammatory processes (apart from certain types of inflammation such as systemic lupus erythematosus (SLE) and Colitis ulcerosa);^{1,3,4,6} to assess treatment of bacterial infections with antibiotics;^{1,4,6,7} to detect intrauterine infections with concomitant premature amniorrhexis;^{4,6} to differentiate between active and inactive forms of disease with concurrent infection, e.g. in patients suffering from SLE or Colitis ulcerosa;^{3,4,6} to therapeutically monitor rheumatic disease and assess anti-inflammatory therapy;^{1,4,6} to determine the presence of post-operative complications at an early stage, such as infected wounds, thrombosis and pneumonia, and to distinguish between infection and bone marrow transplant rejection.^{1,4,6}

Various assay methods are available for CRP determination, such as nephelometry and turbidimetry.^{8,9} The Roche CRP assay is based on the principle of particle-enhanced immunological agglutination.

Test principle^{10,8}

Particle enhanced immunoturbidimetric assay

Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The aggregates are determined turbidimetrically.

Reagents - working solutions

- R1** TRIS^{a)} buffer with bovine serum albumin; preservatives
- SR** Latex particles coated with anti-CRP (mouse) in glycine buffer; immunoglobulins (mouse); preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:

Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:

Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

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



Warning

- H317 May cause an allergic skin reaction.

Prevention:

- P261 Avoid breathing mist or vapours.
- P272 Contaminated work clothing should not be allowed out of the workplace.
- P280 Wear protective gloves.

Response:

- P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
- P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

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

Product safety labeling follows EU GHS guidance.

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

Reagent handling

- R1** Ready for use.
- SR** Ready for use.
Carefully invert reagent bottle several times prior to use to ensure that the reagent components are mixed. Avoid the formation of foam.



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Under conditions of extreme humidity, condensation may lead to a dilution of the reagent that affects the measurements. Hence under environmental conditions in which temperature and humidity are equal to, or in excess of 25 °C/80 %, 28 °C/70 %, 30 °C/60 % or 32 °C/55 % a chimney (Cat. No. 11930630001) should be used to reduce the condensation rate. Place a white chimney in R1 and a black chimney in SR. The chimneys can be reused for reagent bottles within the same kit. However, to avoid contamination of the reagent with detergent or dilution of the reagent with water it is not permitted to wash the chimneys before reuse.

Storage and stability

Shelf life at 2-8 °C:	See expiration date on reagent
On-board in use and refrigerated on the analyzer:	5 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, K₂-EDTA, K₃-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.

Centrifuge samples containing precipitates before performing the assay.

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

Stability in serum and Li-heparin plasma:	2 weeks at 15-25 °C
	3 weeks at 2-8 °C
	12 months at -20 °C (± 5 °C)
Stability in K ₂ - and K ₃ -EDTA plasma:	1 day at 15-25 °C
	3 weeks at 2-8 °C
	12 months at -20 °C (± 5 °C)

Freeze only once.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

See "Order information" section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

cobas c 111 test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction direction	Increase
Wavelength A	552 nm
Calc. first/last	16/24
Antigen excess check	No
Unit	mg/L
Reaction mode	R1-S-SR

Pipetting parameters

		Diluent (H ₂ O)
R1	150 µL	
Sample	2 µL	10 µL
SR	48 µL	14 µL
Total volume	224 µL	

Calibration

Calibrator	Calibrator f.a.s. Proteins Deionized water is used automatically by the instrument as the zero calibrator.
Calibration mode	Non-linear
Calibration replicate	Duplicate recommended
Calibration interval	Full calibration - after reagent lot change - every 6 months during shelf life - as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

This method has been standardized against the certified reference material in human serum of the IRMM (Institute for Reference Materials and Measurements) ERM-DA474/IFCC.¹¹

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

The **cobas c 111** analyzer automatically calculates the analyte concentration of each sample.

Conversion factors:	mg/L × 9.52 = nmol/L	mg/dL × 95.2 = nmol/L
	mg/L × 0.1 = mg/dL	mg/dL × 10 = mg/L
	mg/dL × 0.01 = g/L	g/L × 100 = mg/dL

Limitations - interference

Criterion: Recovery within ± 0.5 mg/L (4.76 nmol/L) of initial values of samples ≤ 5.0 mg/L (47.6 nmol/L) and within ± 10 % for samples > 5 mg/L.

Icterus:¹² No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 60 mg/dL or 1026 µmol/L).

Hemolysis:¹² No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 622 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):¹² No significant interference up to an L index of 1000. 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.

Immunoglobulins: No significant interference from immunoglobulins up to a concentration of 50 g/L (334 µmol/L) (simulated by human immunoglobulin G).

High-dose hook effect: No false result occurs up to a CRP concentration of 1200 mg/L (11424 nmol/L).

In vitro tests were performed on commonly used pharmaceuticals. In addition, special pharmaceuticals were tested. Among them, the following substance caused interference:

Substance	No significant interference up to
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Ticarcillin

225 mg/L

Drug interferences are measured based on recommendations given in CLSI guidelines EP07 and EP37 and other published literature. Effects of concentrations exceeding these recommendations have not been characterized.

As with any assay employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample which could cause falsely lowered results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.¹³

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 the **cobas c 111** analyzer. For information about test combinations requiring special wash steps, please refer to the latest version of the carry-over evasion list found with the CLEAN Method Sheet and the operator's manual for further instructions.

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

Limits and ranges

Measuring range

0.6-350 mg/L (5.7-3332 nmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 0.2 mg/L (1.9 nmol/L)

Limit of Detection = 0.3 mg/L (2.9 nmol/L)

Limit of Quantitation = 0.6 mg/L (5.7 nmol/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 $n \geq 60$ 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 C-reactive protein samples.

Expected values

Consensus reference interval for adults:¹⁴ < 5 mg/L (< 47.6 nmol/L)

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

Specific performance data

Representative performance data on the **cobas c 111** analyzer are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5-A3 requirements with repeatability ($n = 84$) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

Repeatability	Mean mg/L (nmol/L)	SD mg/L (nmol/L)	CV %
CRP T Control N	3.55 (33.8)	0.0338 (0.321)	1.0
Precinorm Protein	9.43 (89.8)	0.0750 (0.714)	0.8
Precipath Protein	53.8 (512)	0.471 (4.48)	0.9
Human serum 1	1.31 (12.5)	0.0269 (0.256)	2.1
Human serum 2	4.58 (43.6)	0.105 (1.00)	2.3
Human serum 3	83.9 (799)	1.21 (11.5)	1.4
Human serum 4	182 (1733)	3.20 (30.5)	1.8
Human serum 5	312 (2970)	4.25 (40.5)	1.4

Intermediate precision	Mean mg/L (nmol/L)	SD mg/L (nmol/L)	CV %
CRP T Control N	3.55 (33.8)	0.0426 (0.406)	1.2
Precinorm Protein	9.43 (89.8)	0.111 (1.06)	1.2
Precipath Protein	53.8 (512)	0.925 (8.81)	1.7
Human serum 1	1.31 (12.5)	0.0332 (0.316)	2.5
Human serum 2	4.58 (43.6)	0.111 (1.06)	2.4
Human serum 3	83.9 (799)	1.97 (18.8)	2.3
Human serum 4	182 (1733)	4.87 (46.4)	2.7
Human serum 5	312 (2970)	6.17 (58.7)	2.0

Method comparison

CRP values for human serum and plasma samples obtained on the **cobas c 111** analyzer (y) were compared with those determined using the corresponding reagent on a COBAS INTEGRA 400 plus analyzer (x).

Sample size (n) = 157

Passing/Bablok¹⁵ $y = 1.00x - 0.133$ mg/L $r = 0.990$

Linear regression

 $y = 1.02x - 0.801$ mg/L $r = 0.999$

The sample concentrations were between 0.689 and 314 mg/L (6.56 and 2989 nmol/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.

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):

	Contents of kit
	Reagent
	Volume for reconstitution
	Global Trade Item Number

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