CRP4

cobas®

Tina-quant C-Reactive Protein IV

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057591190	08057591500	Tina-quant C-Reactive Protein IV (500 tests)	System-ID 2050 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 20656	
20766321322	CRP T Control N (5 x 0.5 mL)	Code 20235	
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

CRP4: ACN 20500

Intended use

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

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 5 identical polypeptide chains that form a 5 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

R3 Latex particles coated with anti-CRP (mouse) in glycine buffer; immunoglobulins (mouse); preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

R1 is in position B and R3 is in position C.

Precautions and warnings

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

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

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

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

Warning

H317 May cause an allergic skin reaction.

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

Ready for use

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

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Storage and stability

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation

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

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin, K_2-EDTA, 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.

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

Test definition

Reporting time	10 min	
Wavelength (sub/main)	800/570 nm	
Reagent pipetting		Diluent (H_2O)
R1	98 µL	
R3	31 µL	16 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	1.3 µL	–	–
Decreased	2.6 µL	20 µL	60 µL
Increased	1.3 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: Calibrator f.a.s. Proteins
Calibration mode	Non-linear
Calibration frequency	Full calibration - after reagent lot change - every 3 weeks on-board - 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. It is recommended to perform quality control always after lot calibration and subsequently at least every 12 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 mg/L (nmol/L, mg/dL).

Conversion factors:	mg/L × 9.52 = nmol/L
	mg/L × 0.1 = mg/dL

Limitations - interference

Criterion: Recovery within ± 0.5 mg/L of initial values of samples ≤ 5.0 mg/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.

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
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.

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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 **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

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 ≥ 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*)

*calculated by unit conversion factor

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) EP5-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 mg/L*	*SD mg/L*	*CV %*
CRP T Control N	3.33	0.0313	0.9
Precinorm Protein	9.72	0.0516	0.5
Precipath Protein	53.9	0.275	0.5
Human serum 1	1.11	0.0276	2.5
Human serum 2	4.09	0.0338	0.8
Human serum 3	82.9	0.474	0.6
Human serum 4	174	1.37	0.8
Human serum 5	305	2.10	0.7

Intermediate precision	*Mean mg/L*	*SD mg/L*	*CV %*
CRP T Control N	3.33	0.0375	1.1
Precinorm Protein	9.72	0.0708	0.7
Precipath Protein	53.9	0.854	1.6
Human serum 1	1.11	0.0296	2.7
Human serum 2	4.09	0.0397	1.0
Human serum 3	82.9	1.61	1.9
Human serum 4	174	3.94	2.3
Human serum 5	305	5.79	1.9

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

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

Sample size (n) = 157

Passing/Bablok[15]	Linear regression
y = 0.990x + 0.124 mg/L	y = 0.978x + 0.428 mg/L
τ = 0.995	r = 1.000

The sample concentrations were between 0.791 and 333 mg/L.

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

Sample size (n) = 79

Passing/Bablok[15]	Linear regression
y = 0.976x - 0.0226 mg/L	y = 0.973x + 0.340 mg/L
τ = 0.989	r = 1.000

The sample concentrations were between 0.920 and 348 mg/L.

CRP values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 101

Passing/Bablok[15]	Linear regression
y = 1.013x + 0.0240 mg/L	y = 1.018x - 0.501 mg/L
τ = 0.992	r = 1.000

The sample concentrations were between 0.620 and 335 mg/L.

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.

References

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

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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