CRPLX

cobas®

C-Reactive Protein (Latex)

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
20764930 322	C-Reactive Protein (Latex) 300 tests	System-ID 07 6493 0	Roche/Hitachi **cobas c** 311, **cobas c** 501
11355279 216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
10557897 122	Precinorm Protein (3 x 1 mL)	Code 302	
11333127 122	Precipath Protein (3 x 1 mL)	Code 303	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

CRPLX: ACN 019

Intended use

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

Summary[1,2]

Most tissue-damaging processes such as infections, inflammatory diseases and malignant neoplasms are associated with a major acute phase response of the C-reactive protein (CRP) and other acute phase reactants (e.g. AAT, AAGP, C3C, C4, HAPT). The CRP response frequently precedes clinical symptoms, including fever. In normal healthy individuals CRP is a trace protein with a range up to 5 mg/L. After onset of an acute phase response the serum CRP concentration rises rapidly and extensively. Alterations are detectable within 6 to 8 hours and the peak value is reached within 24 to 48 hours. Levels of up to thousandfold the normal value are associated with severe stimuli such as myocardial infarction, major trauma, surgery, or malignant neoplasms.

CRP activates the classical complement pathway. CRP has a half-life of only a few hours, making it an ideal tool for clinical monitoring. Postoperative monitoring of CRP levels of patients indicates either the normal recovery process (decreasing levels to normal) or unexpected complications (persisting high levels). Measuring changes in the concentration of CRP provides useful diagnostic information about how acute and how serious a disease is. It also allows the assessment of complications during the disease and judgements about the disease genesis. Persistence of a high serum CRP concentration is usually a grave prognostic sign which generally indicates the presence of an uncontrolled infection. CRP determination may replace the classical determination of Erythrocytes Sedimentation Rate (ESR), due to its prompt response to changes in disease activity and its good correlation to ESR.

Test principle[3,4,5]

Particle enhanced immunoturbidimetric assay.

Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The precipitate is determined turbidimetrically.

Reagents - working solutions

R1 TRIS buffer with bovine serum albumin and immunoglobulins (mouse); preservative

R2 Latex particles coated with anti-CRP (mouse) in glycine buffer; preservative

R1 is in position B, and R2 is in position C.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

Reagent handling

Ready for use

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

Mix **cobas c** pack well before placing on the analyzer.

Storage and stability

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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

NaCl Diluent 9 %

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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 and K_2-EDTA plasma

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Stability:[6]	11 days at 15-25 °C
	2 months at 2-8 °C
	3 years 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	Rate A
Reaction time / Assay points	10 / 7-18
Wavelength (sub/main)	–/546 nm

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Reaction direction	Increase		
Units	mg/L (nmol/L, mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	82 µL	72 µL	
R2	28 µL	20 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	4 µL	15 µL	75 µL
Increased	2 µL	–	–

cobas c 501 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 12-28		
Wavelength (sub/main)	–/546 nm		
Reaction direction	Increase		
Units	mg/L (nmol/L, mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	82 µL	72 µL	
R2	28 µL	20 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	4 µL	15 µL	75 µL
Increased	2 µL	–	–

Calibration

Calibrators	S1: H_2O S2-S6: C.f.a.s. Proteins Multiply the lot-specific C.f.a.s. Proteins calibrator values by the factors below to determine the standard concentrations for the 6-point calibration curve: S2: 0.0500 S5: 1.90 S3: 0.303 S6: 2.50 S4: 0.907
Calibration mode	Line-graph
Calibration frequency	Full calibration • after reagent lot change • as required following quality control procedures

Traceability: This method has been standardized against the reference preparation of the IRMM (Institute for Reference Materials and Measurements) BCR470/CRM470 (RPPHS - Reference Preparation for Proteins in Human Serum).[7]

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

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

Limitations - interference

Criterion: Recovery within ± 10 % of initial values at a CRP concentration of 5.0 mg/L (47.6 nmol/L, 0.5 mg/dL).

Icterus:[8] 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:[8] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 311 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[8] No significant interference up to an L index of 400. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

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

High dose hook-effect: No false result occurs up to a CRP concentration of 1000 mg/L (9520 nmol/L, 100 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[9,10]

Therapeutic drugs: Significantly decreased CRP values may be obtained from samples taken from patients who have been treated with carboxypenicillins.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[11]

Although measures were taken to minimize interference caused by human anti-mouse antibodies, erroneous findings may be obtained from samples taken from patients who have been treated with monoclonal mouse antibodies or have received them for diagnostic purposes.

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

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/Multiclean/SCCS or the NaOHD/SMS/SmpCln1+2/SCCS Method Sheets. For further instructions refer to the operator's manual.

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

Limits and ranges

Measuring range

1.00-250 mg/L (9.52-2380 nmol/L, 0.1-25 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

Lower limits of measurement

Lower detection limit of the test

1.00 mg/L (9.52 nmol/L, 0.1 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying three standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values

Adults[12]	< 5 mg/L	(< 0.5 mg/dL)

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

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Specific performance data

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

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

Repeatability	*Mean*	*SD*	*CV*
	mg/L (nmol/L)	*mg/L (nmol/L)*	*%*
Precinorm Protein	22.4 (213, 2.24)	0.3 (3, 0.03)	1.2
Precipath Protein	49.4 (470, 4.94)	0.7 (7, 0.07)	1.3
Human serum 1	5.08 (48.4, 0.51)	0.08 (0.8, 0.01)	1.5
Human serum 2	40.3 (384, 4.03)	0.4 (4, 0.04)	0.9
Intermediate precision	*Mean*	*SD*	*CV*
	mg/L (nmol/L)	*mg/L (nmol/L)*	*%*
Precinorm Protein	22.5 (214, 2.25)	0.4 (4, 0.04)	1.6
Precipath Protein	51.2 (487, 5.12)	0.7 (7, 0.07)	1.4
Human serum 3	5.67 (54.0, 0.57)	0.14 (1.3, 0.01)	2.5
Human serum 4	39.9 (380, 3.99)	0.5 (5, 0.05)	1.3

Method comparison

CRP values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared to those determined with the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 324

Passing/Bablok[13]	Linear regression
y = 0.967x + 0.289 mg/L	y = 0.973x - 0.242 mg/L
τ = 0.963	r = 0.997

The sample concentrations were between 1.00 and 217 mg/L (9.52 and 2066 nmol/L).

CRP values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared to those determined with the corresponding reagent on a COBAS INTEGRA 800 analyzer (x).

Sample size (n) = 306

Passing/Bablok[13]	Linear regression
y = 1.022x + 0.246 mg/L	y = 1.007x + 0.400 mg/L
τ = 0.974	r = 0.999

The sample concentrations were between 1.02 and 178 mg/L (9.71 and 1695 nmol/L, 0.102 and 17.8 mg/dL).

References

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

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

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

CONTENT	Contents of kit
→	Volume after reconstitution or mixing

CE

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

Roche