C reactive protein

Order information

**REF** | **CONTENT** | **Analyzer(s) on which cobas c pack(s) can be used**
--- | --- | ---
07876033 190 | Tina-quant C-Reactive Protein IV (250 tests) | System-ID 07 7607 6
11355279 216 | Calibrator f.a.s. Proteins (5 x 1 mL) | Code 656
11355279 160 | Calibrator f.a.s. Proteins (5 x 1 mL, for USA) | Code 656
20766321 322 | CRP T Control N (5 x 0.5 mL) | Code 235
1057897 122 | Precinorm Protein (3 x 1 mL) | Code 302
1057897 160 | Precinorm Protein (3 x 1 mL, for USA) | Code 302
1133127 122 | Precipath Protein (3 x 1 mL) | Code 303
1133127 160 | Precipath Protein (3 x 1 mL, for USA) | Code 303
0517003 190 | PreciControl ClinChem Multi 1 (20 x 5 mL) | Code 391
05947626 190 | PreciControl ClinChem Multi 1 (4 x 5 mL) | Code 391
05947626 160 | PreciControl ClinChem Multi 1 (4 x 5 mL, for USA) | Code 391
0517216 190 | PreciControl ClinChem Multi 2 (20 x 5 mL) | Code 392
05947774 190 | PreciControl ClinChem Multi 2 (4 x 5 mL) | Code 392
05947774 160 | PreciControl ClinChem Multi 2 (4 x 5 mL, for USA) | Code 392
04489357 190 | Diluent NaCl 9 % (50 mL) | System-ID 07 6869 3

**English**

**System information**

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

**CRP4**: ACN 256

For **cobas c 502** analyzer:

**CRP4**: ACN 8256

**Intended use**

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

**Summary**

C-reactive protein is the classic acute phase protein in inflammatory reactions. 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. CRP is the most sensitive of the acute phase reactants and its concentration increases rapidly during inflammatory processes. Complexed CRP activates the classical complement pathway. 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. The increase begins within 6 to 12 hours and the peak value is reached within 24 to 48 hours. Levels above 100 mg/L are associated with severe stimuli such as major trauma and severe infection (sepsis). CRP response may be less pronounced in patients suffering from liver disease. CRP assays are used to detect systemic inflammatory processes; to assess treatment of bacterial infections with antibiotics; to detect intrauterine infections with concomitant premature amniorrhexis; to differentiate between active and inactive forms of disease with concurrent infection, e.g. in patients suffering from SLE or Collitis ulcerosa; to therapeutically monitor rheumatic disease and assess anti-inflammatory therapy; 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 rejection. Postoperative monitoring of CRP levels of patients can aid in the recognition of unexpected complications (persisting high or increasing levels). Measuring changes in the concentration of CRP provides useful diagnostic information about how acute and how serious a disease is. It also allows 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.

**Test principle**

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\(^{-}\) buffer with bovine serum albumin; preservatives

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

a) TRIS = Tris(hydroxymethyl)-aminomethane

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.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the European directive 1999/45/EC:

- 2-methyl-2H-isothiazol-3-one hydrochloride

EUH 208  May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

**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**

**CRP4**

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

On-board in use and refrigerated on the analyzer:

**Diluent NaCl 9 %**  See expiration date on **cobas c** pack label.

**On-board in use and refrigerated on the analyzer:**

See expiration date on **cobas c** pack label.

**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**
- 2 weeks at 15-25 °C
- 3 weeks at 2-8 °C
- 12 months at –20 ± 5 °C

**Stability in K2- and K3-EDTA plasma**
- 1 day at 15-25 °C
- 3 weeks at 2-8 °C
- 12 months at –20 ± 5 °C

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.

**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**

<table>
<thead>
<tr>
<th>Reaction direction</th>
<th>Units</th>
<th>Reagent pipetting</th>
<th>Sample volumes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase</td>
<td>mg/L</td>
<td>Diluent (H2O)</td>
<td>Sample</td>
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**Sample volumes**

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<td></td>
<td>2 µL</td>
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**cobas c 501 test definition**

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<td>75 µL</td>
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**Calculation**

cobas c systems automatically calculate the analyte concentration of each sample.
Conversion factors:  
- \( \text{mg/L} \times 9.52 = \text{nmol/L} \)  
- \( \text{mg/L} \times 0.1 = \text{mg/dL} \)  
- \( \text{mg/dL} \times 10 = \text{mg/L} \)  
- \( \text{mg/dL} \times 0.01 = \text{g/L} \)  
- \( \text{g/L} \times 100 = \text{mg/dL} \)

**Limitations - Interference**

- **Criterion:** Recovery within \( \pm 0.5 \text{ mg/L (4.76 nmol/L)} \) of initial values of samples \( \leq 5.0 \text{ mg/L (47.6 nmol/L)} \) and within \( \pm 10 \% \) for samples \( > 5 \text{ mg/L} \).

- **Icterus:** No significant interference up to \( \text{H index of 60 for conjugated and unconjugated bilirubin (approx. conjugated and unconjugated bilirubin concentration: 60 mg/dL or 1026 \mu \text{mol/L}}) \) (approximate hemoglobin concentration: 622 \mu \text{mol/L or 100 mg/dL}).

- **Hemolysis:** No significant interference up to \( \text{H index of 1000} \) (approximate hemoglobin concentration: 14424 \mu \text{mol/L}).

- **Lipemia (Intralipid):** No significant interference up to \( \text{L index of 1000} \). There is poor correlation between the \( \text{L index} \) (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 \mu \text{mol/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:** Ticarcillin  
  - **Concentration:** 225 mg/L

**Drug Interferences**

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, gammapathy, 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. The latest version of the carry-over evasion list can be found with the NaOH-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**

- 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 = 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)

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-A3 requirements with repeatability (\( n = 84 \)) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained:

<table>
<thead>
<tr>
<th></th>
<th>Mean (mg/L)</th>
<th>SD (mg/L)</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP T Control N</td>
<td>3.63 (3.46)</td>
<td>0.0608 (0.579)</td>
<td>1.7</td>
</tr>
<tr>
<td>Precinorm Protein</td>
<td>9.69 (92.2)</td>
<td>0.128 (1.22)</td>
<td>1.3</td>
</tr>
<tr>
<td>Precipath Protein</td>
<td>55.8 (531)</td>
<td>1.09 (10.4)</td>
<td>2.0</td>
</tr>
<tr>
<td>Human serum 1</td>
<td>1.27 (12.1)</td>
<td>0.0294 (0.280)</td>
<td>2.3</td>
</tr>
<tr>
<td>Human serum 2</td>
<td>4.56 (43.4)</td>
<td>0.0702 (0.668)</td>
<td>1.5</td>
</tr>
<tr>
<td>Human serum 3</td>
<td>88.4 (842)</td>
<td>2.06 (19.6)</td>
<td>2.3</td>
</tr>
<tr>
<td>Human serum 4</td>
<td>186 (1771)</td>
<td>3.76 (35.8)</td>
<td>2.0</td>
</tr>
<tr>
<td>Human serum 5</td>
<td>337 (3208)</td>
<td>5.79 (55.1)</td>
<td>1.7</td>
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<tr>
<td>Precinorm Protein</td>
<td>9.65 (91.9)</td>
<td>0.165 (1.57)</td>
<td>1.7</td>
</tr>
<tr>
<td>Precipath Protein</td>
<td>55.8 (531)</td>
<td>1.21 (11.5)</td>
<td>2.2</td>
</tr>
<tr>
<td>Human serum 1</td>
<td>1.27 (12.1)</td>
<td>0.0310 (0.295)</td>
<td>2.4</td>
</tr>
<tr>
<td>Human serum 2</td>
<td>4.56 (43.4)</td>
<td>0.0735 (0.700)</td>
<td>1.6</td>
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<td>Human serum 3</td>
<td>88.4 (842)</td>
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<td>186 (1771)</td>
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<tr>
<td>Human serum 5</td>
<td>337 (3208)</td>
<td>6.87 (65.4)</td>
<td>2.0</td>
</tr>
</tbody>
</table>

**Method comparison**

CRP values for human serum and plasma samples obtained on a cobas c 501 analyzer (\( y \)) were compared with those determined using the C-Reactive Protein Gen.3 assay on a cobas c 501 analyzer (\( x \)).

**Sample size (\( n \)) = 120**

<table>
<thead>
<tr>
<th>( y )</th>
<th>( x )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.988</td>
<td>0.999</td>
</tr>
</tbody>
</table>

The sample concentrations were between 0.670 and 347 mg/L (6.38 and 3303 nmol/L).

CRP values for human serum and plasma samples obtained on a cobas c 501 analyzer (\( y \)) were compared with those determined using the C-Reactive Protein Gen.2 assay on a cobas c 501 analyzer (\( x \)).

**2020-03, V 1.0 English**
Sample size (n) = 112

Passing/Bablok\textsuperscript{15}  Linear regression
\[ \begin{align*}
y &= 1.015x - 0.224 \text{ mg/L} \\
y &= 0.946x + 1.58 \text{ mg/L} \\
\tau &= 0.989 \\
r &= 0.997
\end{align*} \]

The sample concentrations were between 1.16 and 243 mg/L (11.0 and 2313 nmol/L).

References

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

- **CONTENT**
  - Contents of kit
- **STIN**
  - Volume after reconstitution or mixing
  - Global Trade Item Number

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