**Cardiac C-Reactive Protein (Latex) High Sensitive**

**Order information**

<table>
<thead>
<tr>
<th>REF</th>
<th>CONTENT</th>
<th>Analyzer(s) on which kit(s) can be used</th>
</tr>
</thead>
<tbody>
<tr>
<td>05401607190</td>
<td>Cardiac C-Reactive Protein (Latex) High Sensitive (2 x 50 tests)</td>
<td>cobas c 111</td>
</tr>
</tbody>
</table>

Materials required (but not provided):

- 11355279160 Calibrator f.a.s. Proteins (5 x 1 mL)
- 20766321322 CRP T Control N (5 x 0.5 mL)
- 10557897160 Precinorm Protein (3 x 1 mL)
- 05947626160 PreciControl ClinChem Multi 1 (4 x 5 mL)
- 04774230190 NaCl Diluent 9 % (4 x 12 mL)

**Intended use**

In vitro test for the quantitative determination of C-reactive protein (CRP) in human serum and plasma on the cobas c 111 system. Measurement of CRP is of use for the detection and evaluation of inflammatory disorders and associated diseases, infection and tissue injury. Highly sensitive measurement of CRP may also be used as an aid in the assessment of the risk of future coronary heart disease. When used as an adjunct to other laboratory evaluation methods of acute coronary syndromes, it may also be an additional dependent indicator of recurrent event prognosis in patients with stable disease or acute coronary syndrome.

**Summary**

CRP 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-member ring having a molecular weight of 105,000 Daltons. CRP is the most sensitive of the acute phase reactants and its concentration increases rapidly during inflammatory processes. Complexed CRP activates the complement system beginning with C1q. CRP then initiates opsonization and phagocytosis of invading cells, but its main function is to bind to and detoxify endogenous toxic substances produced as a result of tissue damage.

**English**

**For use in the USA only**

**System information**

**CRPHS: AON 217**

**Reagents - working solutions**

- **R1** TRIS buffer with bovine serum albumin and immunoglobulins (mouse); preservative; stabilizers
- **SR** Latex particles coated with anti-CRP (mouse) in glycine buffer; preservative; stabilizers

**Precautions and warnings**

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

**Safety data sheet available for professional user on request.**

**Reagent handling**

- **R1** Ready for use.
- **SR** Ready for use.

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

**Storage and stability**

- **Shelf life at 2-8 °C:** See expiration date on reagent
- **On-board in use and refrigerated**
  - **4 weeks**
  - **the analyzer:**

**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.

**Plasma**

- **Li-heparin, K₂-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.

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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.

Stability:24
- 11 days at 15-25 °C
- 2 months at 2-8 °C
- 3 years at (-15)°(-25) °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**

<table>
<thead>
<tr>
<th>Measuring mode</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abs. calculation mode</td>
<td>Kinetic</td>
</tr>
<tr>
<td>Reaction direction</td>
<td>Increase</td>
</tr>
<tr>
<td>Wavelength A</td>
<td>552 nm</td>
</tr>
<tr>
<td>Calc. first/last</td>
<td>17/34</td>
</tr>
<tr>
<td>Unit</td>
<td>mg/L (nmol/L, mg/dL)</td>
</tr>
<tr>
<td>Reaction mode</td>
<td>R1-S-SR</td>
</tr>
</tbody>
</table>

**Pipetting parameters**

- Diluent (H2O)
  - R1: 82 µL
  - Sample: 6 µL
  - SR: 28 µL
  - Total volume: 178 µL

**Calibration**

- Calibrator: Calibrator f.a.s. Proteins
- Calibration dilution ratio: 1:5, 1:10, 1:20, 1:40, 1:80, performed automatically by the instrument, and Standard 6 = 0 mg/L
- Calibration mode: Linear interpolation
- Calibration interval: Each lot and as required following quality control procedures

Enter the assigned lot-specific CRPHS value of the undiluted calibrator (mg/L), indicated in the package insert of C.f.a.s. Proteins.

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

 Traceability: This method has been standardized against the reference preparation of the IRMM (Institute for Reference Materials and Measurements) BCR470/CRM470 (RPHS -Reference Preparation for Proteins in Human Serum).25

**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:**

\[
1 \text{mg/L} \times 9.52 = \text{nmol/L}
\]

\[
1 \text{mg/L} \times 0.1 = \text{mg/dL}
\]

**Limitations - interference**

Criterion: Recovery within ± 10 % of initial value at CRP levels of 3.0 mg/L.

Icterus:26 No significant interference up to an I index of 60 of conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:26 No significant interference up to an H index of 700 (approximate hemoglobin concentration: 435 µmol/L or 700 mg/dL).

Lipemia (Intralipid):26 No significant interference up to an L index of 500. 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: does not occur at CRP concentrations below 40 mg/L or 380 nmol/L. Samples with concentrations > 40 mg/L are flagged either “>TEST RNG” or “HIGH ACT”.

Drugs: No interference was found at therapeutic concentrations using common drug panels.7,28

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.29

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 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**

0.15-20.0 mg/L (1.43-190 nmol/L, 0.015-2.0 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:15 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 15.

**Lower limits of measurement**

Lower detection limit of the test:

0.15 mg/L (1.43 nmol/L, 0.015 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 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).
CRPHS
Cardiac C-Reactive Protein (Latex) High Sensitive

Functional sensitivity (Limit of Quantitation)
0.3 mg/L (2.86 nmol/L)
The functional sensitivity (Limit of Quantitation) is the lowest CRP concentration that can be reproducibly measured with an inter-assay coefficient of variation < 10%.

Expected values
Consensus reference interval for adults:30
IFCC/CRM 470
mg/L mg/L nmol/L
< 0.5 < 5.0 < 47.6

The CDC/AHA recommended the following hsCRP cut-off points (tertiles) for CVD risk assessment:20,31

hsCRP level (mg/L) hsCRP level (nmol/L) Relative risk
< 1.0 < 9.52 low
1.0-3.0 9.52-28.6 average
> 3.0 > 28.6 high

Patients with higher hsCRP concentrations are more likely to develop myocardial infarction and severe peripheral vascular disease.

5-95 % reference intervals of neonates and children:32
Neonates (0-3 weeks): 0.1-4.1 mg/L (0.95-39.0 nmol/L)
Children (2 months-15 years): 0.1-2.8 mg/L (0.95-26.7 nmol/L)

It is important to monitor the CRP concentration during the acute phase of the illness.

Roche has not evaluated reference ranges in a pediatric population. Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Increases in CRP values are non-specific and should not be interpreted without a complete clinical history. When using hsCRP to assess the risk of coronary heart disease, measurements should be made on metabolically stable patients and compared to previous values. Optimally, the average of hsCRP results repeated two weeks apart should be used for risk assessment.

Measurements should be compared to previous values. When the results are being used for risk assessment, patients with persistently unexplained hsCRP levels of above 10 mg/L (95.2 nmol/L) should be evaluated for non-cardiovascular origins. Testing for any risk assessment should not be performed while there is indication of infection, systemic inflammation or trauma.31

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 an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 10 days). The following results were obtained:

<table>
<thead>
<tr>
<th></th>
<th>Mean mg/L (nmol/L, mg/dL)</th>
<th>SD mg/L (nmol/L, mg/dL)</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinorm Protein</td>
<td>11.4 (109, 1.14)</td>
<td>0.0 (0, 0)</td>
<td>0.4</td>
</tr>
<tr>
<td>CRP T Control N</td>
<td>4.06 (38.7, 0.406)</td>
<td>0.01 (0.1, 0.01)</td>
<td>0.3</td>
</tr>
<tr>
<td>Human serum 1</td>
<td>0.49 (4.66, 0.049)</td>
<td>0.01 (0.07, 0.001)</td>
<td>1.5</td>
</tr>
<tr>
<td>Human serum 2</td>
<td>4.02 (38.3, 0.402)</td>
<td>0.02 (0.2, 0.002)</td>
<td>0.6</td>
</tr>
<tr>
<td>Human serum 3</td>
<td>16.9 (161, 1.69)</td>
<td>0.1 (0.01)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Intermediate precision

<table>
<thead>
<tr>
<th></th>
<th>Mean mg/L (nmol/L, mg/dL)</th>
<th>SD mg/L (nmol/L, mg/dL)</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preclinorm Protein</td>
<td>11.3 (108, 1.13)</td>
<td>0.1 (0.01)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Method comparison
CRP values for human serum and plasma samples obtained on a cobas c 111 analyzer using the Roche CRPHS reagent (y) were compared with those determined using the same reagent on a COBAS INTEGRA 400 analyzer (x).

Sample size (n) = 79

Passing/Bablok33

\[
y = 1.035x - 0.111 \\ m \quad y = 1.051x - 0.202 m \quad \tau = 0.962 \quad r = 0.999
\]

The sample concentrations of the reference system (x) were between 0.21 and 18.6 mg/L (2.0 and 177 nmol/L, 0.021 and 1.86 mg/dL).

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