BECKMAN COULTER CE

AU

Instructions For Use

CRP
CRP Latex

REF OSR6199 4 x 30 mL R1, 4 x 30 mL R2
OSR6299 4 x 50 mL R1, 4 x 50 mL R2

For *in vitro* diagnostic use only.

PRINCIPLE

INTENDED USE

Immuno-turbidimetric test for the quantitative determination of C-reactive protein (CRP) in human serum and plasma on Beckman Coulter AU analysers. The normal application is to be used for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. The Highly Sensitive application is not a general screening test for infection/inflammation.

SUMMARY AND EXPLANATION

C-reactive protein (CRP) is one of the most sensitive acute-phase reactants. With the Beckman Coulter System CRP Latex reagent, CRP can be measured down to very low concentrations, however due to the non specificity of CRP and the wide inter-individual variation, interpretation of CRP levels must be undertaken with care, usually in comparison with previous CRP values or other markers.

Depending on the application used (different instrument settings) two measuring ranges are available:

1. Normal Application (0.2-480 mg/L):[1,2,3,4] C-reactive protein levels in serum can rise dramatically after myocardial infarction, trauma, infection, inflammation, surgery, or neoplastic proliferation. The increase occurs within 24 to 48 hours, and the level may be 2000 times normal.

   Studies have shown that the detection of much lower CRP levels can indicate an increased risk for coronary heart disease in asymptomatic patients. CRP concentrations above 3 mg/L at the time of hospital admission can predict subsequent cardiac events.

2. Highly Sensitive Application (0.08 – 80 mg/L):[5,6] Cord blood normally has very low CRP concentrations (median 0.12 mg/L). In the diagnostic evaluation of neonates with suspected infection, measurements of serial CRP levels are useful. Two low CRP levels obtained 24 hours apart, 8-48 hours after presentation, indicate that bacterial infection is unlikely. Thus CRP Latex reagent is providing a valuable tool for the early diagnosis of infection in preterm infants and neonates. It assesses both the need for and the effectiveness of antibiotic treatment however CRP values alone cannot be used as a basis for early discontinuance of antibiotic therapy.

METHODOLOGY

When a sample is mixed with R1 buffer and R2 latex suspension, CRP reacts specifically with anti-human CRP antibodies coated on the latex particles to yield insoluble aggregates. The absorbance of these aggregates is proportional to the CRP concentration in the sample.

SPECIMEN

TYPE OF SPECIMEN

Serum, EDTA and lithium heparinised plasma: Stable in serum and plasma for 2 months when stored at 2…8°C and 11 days when stored at 15…25°C.[7]

SPECIMEN STORAGE AND STABILITY

Specimen storage and stability information provides guidance to the laboratory. Based on specific needs, each laboratory may establish alternative storage and stability information according to good laboratory practice or from alternative reference documentation.

REAGENTS

WARNING AND PRECAUTIONS

Exercise the normal precautions required for handling all laboratory reagents.

Dispose of all waste material in accordance with local guidelines.

Antisera was produced in healthy animals in facilities free from rinderpest, foot and mouth disease, peste des petits ruminants, Rift Valley fever, bovine spongiform encephalopathy and blue tongue disease.

This product contains material of animal origin. The product should be considered as potentially capable of transmitting infectious diseases.

REACTIVE INGREDIENTS

Final concentration of reactive ingredients:

Glycine buffer	100 mmol/L
Latex, coated with anti-CRP antibodies	< 0.5% w/v
Preservative	< 0.1% w/v

The concentrations of the reactive components of the reagents shown on the kit label are the actual concentrations in the individual R1/R2 vials. The reagent composition which is shown in the Instructions For Use is the final concentration of these components in the reaction cuvette after addition of R1, Sample, and R2.

⚠ CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).
To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.

GHS HAZARD CLASSIFICATION

Not classified as hazardous

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

REAGENT PREPARATION

R1 is ready for use and can be placed directly on board the instrument. R2 should be mixed by inversion 5 - 10 times before placing on board the instrument and at weekly intervals thereafter.

REAGENT STORAGE AND STABILITY

The reagents are stable, unopened, up to the stated expiry date when stored at 2…8°C. Once open, reagents stored on board the instrument are stable for 90 days.

CALIBRATION

CALIBRATION INFORMATION

Application	Calibrator	Cat. No.
Normal	CRPLatex Calibrator Normal Set	ODC0026
Highly sensitive	CRP Latex Calibrator Highly Sensitive Set	ODC0027

The calibrator CRP values are traceable to IFCC (International Federation of Clinical Chemistry) standard CRM 470.

Recalibrate the assay every 90 days or when the following occur:

Change in reagent bottle or significant shift in control values;

Major preventative maintenance was performed on the analyser or a critical part was replaced.

Following calibration, the resulting curve should be visually reviewed, on the Beckman Coulter analyser, for acceptability using the software options - Routine, Calibration Monitor, Calibration Curve. Quality control procedures should be undertaken immediately following calibration in accordance with good laboratory practice.

QUALITY CONTROL

ITA Control Sera ODC0014, ODC0015 and ODC0016 should be used for the Normal and Highly Sensitive applications, and CRP (Latex) Control Sera ODC0013 (two levels) should be used for the Highly Sensitive application only. Other control materials with values determined by this Beckman Coulter system may also be used.

Each laboratory should establish its own control frequency however good laboratory practice suggests that controls be tested each day patient samples are tested and each time calibration/blanking is performed.

The results obtained by any individual laboratory may vary from the given mean value. It is therefore recommended that each laboratory generates analyte specific control target values and intervals based on multiple runs according to their requirements. These target values should fall within the corresponding acceptable ranges given in the relevant product literature.

If any trends or sudden shifts in values are detected, review all operating parameters.

Each laboratory should establish guidelines for corrective action to be taken if controls do not recover within the specified limits.

Please note that the recovery of non-Beckman Coulter controls may vary with reagent lots of immunoassay products, due to the use of non-human materials in the controls.

TESTING PROCEDURE(S)

Refer to the appropriate Beckman Coulter AU analyser User Guide/Instructions For Use (IFU) for analyser-specific assay instructions for the sample type as listed in the Intended Use statement.

Data check parameters must be applied when using Highly Sensitive application on AU2700/AU5400, see setting sheets for specific instrument details.

CALCULATIONS

The Beckman Coulter analyzers automatically compute the CRP concentration of each sample.

REPORTING RESULTS

REFERENCE INTERVALS

Normal application[8]	< 5 mg/L
Highly sensitive application[9]	< 1 mg/L

Expected values may vary with age, sex, sample type, diet and geographical location. Each laboratory should verify the transferability of the expected values to its own population, and if necessary determine its own reference interval according to good laboratory practice. For diagnostic purposes, results should always be assessed in conjunction with the patient's medical history, clinical examinations and other findings.

PROCEDURAL NOTES

LIMITATIONS

Sample contamination avoidance parameters should be programmed on the AU5800/480/680 and DxC 700 AU instruments and are available on the Beckman Coulter website.

Samples containing heterophilic antibodies can cause falsely elevated results.

Samples with extremely abnormal optical characteristics, especially turbidity, may produce atypical results.

Samples with very high CRP concentrations (> 750 mg/L) can generate false low results without appropriate "Z" flags due to excess antigen in the sample.

INTERFERENCES

Results of studies conducted to evaluate the susceptibility of CRP Latex normal,and highly sensitive assays to interference were as follows:

Normal Application	
Icterus:	Interference less than 5% up to 40 mg/dL or 684 µmol/L bilirubin
Haemolysis:	Interference less than 5% up to 5 g/L haemoglobin
Lipemia:	Interference less than 10% up to 1,000 mg/dL Intralipid
Highly Sensitive Application	
Icterus:	Interference less than 5% up to 40 mg/dL or 684 µmol/L bilirubin
Haemolysis:	Interference less than 5% up to 5 g/L haemoglobin
Lipemia:	Interference less than 10% up to 1,000 mg/dL Intralipid

In very rare cases Gammopathy, especially monoclonal IgM (Waldenström’s macroglobinemia), may cause unreliable results

Refer to Young[10] for further information on interfering substances.

PERFORMANCE CHARACTERISTICS

PERFORMANCE CHARACTERISTICS

Data contained within this section is representative of performance on Beckman Coulter systems. Data obtained in your laboratory may differ from these values.

LINEARITY

The test is linear within a concentration range of 0.2 - 480mg/L for the Normal Application, 0.08 - 80 mg/L for the Highly Sensitive Application.

SENSITIVITY

The lowest detectable level was estimated as follows:

Application	Lowest Detectable Level (mg/L)
	DxC 700 AU
Normal	0.20
Highly Sensitive	0.05

The lowest detectable level represents the lowest measurable level of CRP that can be distinguished from zero. It is calculated as the absolute mean plus three standard deviations of 20 replicates of an analyte free sample.

METHODS COMPARISON

Patient serum samples were used to compare the normal and highly sensitive CRP Latex OSR6199 assays on the AU640 against another commercially available CRP assay (Method 2). Results of linear regression analysis were as follows:

	Normal	Highly sensitive
Y Method	AU640	AU640
X Method	Method 2	Method 2
Slope	1.024	0.993
Intercept	0.546	-0.825
Correlation Coefficient (r)	0.998	0.997
No. of samples	119	118
Range (mg/L)	0.20 – 167.38	0.20 – 155.86

PRECISION

The following data was obtained for CRP (Latex) normal and highly sensitive assays on an AU5800 and DxC 700 AU using 3 serum pools analysed over 20 days.

AU5800

	n=80	Within-run		Total	
Application	Mean mg/L	SD	CV%	SD	CV%
Normal	6.03	0.08	1.30	0.18	3.00
	65.88	0.57	0.90	0.83	1.30
	137.33	1.13	0.80	1.36	1.00

DxC 700 AU

	n=80	Within-run		Total	
Application	Mean mg/L	SD	CV%	SD	CV%
Highly Sensitive	0.49	0.02	3.84	0.02	3.48
	10.28	0.12	1.17	0.13	1.22
	50.08	0.31	0.63	0.39	0.78

ADDITIONAL INFORMATION

DxC 700 AU requires that each reagent application has a standard format of abbreviated Closed Test Name. This Closed Test Name is required to allow automated loading of the calibrator information for each application as part of the DxC 700 AU Closed System. Refer to the table below for the Closed Test Name assigned to each application for this assay.

Test Name	Description
CRP1N	CRP Latex (Serum)
CRP2N	CRP Latex (Serum)

Setting Sheet Footnotes
User defined
† Beckman Coulter CRP Latex Calibrator Normal Set Cat No.: ODC0026

† Beckman Coulter CRP Latex Calibrator Highly Sensitive Set Cat No.: ODC0027

* Values set for working in mg/L.

§ Saline should be used for the Level 1 calibrator.

REVISION HISTORY

Added new languages

Preceding version revision history

Remove reference to obsolete analyzer

REFERENCES

1. Grant GH, Silverman LM, Christenson RH. Amino acids and proteins. In: Tietz NW, ed. Fundamentals of clinical chemistry. Philadelphia:WB Saunders Company, 1987:334pp.

2. Morrow DA, Ridker PM. C-reactive protein, inflammation, and coronary risk. Med Clin North Am 2000;84:149-161.

3. Ridker PM. Novel risk factors and markers for coronary disease. Adv Intern Med 2000;45:391-419.

4. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB, Maseri A. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med 1994;331:417-424.

5. Wasunna A, Whitelaw A, Gallimore R, Hawkins PN, Pepys MB. C-reactive protein and bacterial infection in preterm infants. EurJ Pediatr 1990;149:424-427.

6. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics 1998;102: 4:E41.

7. Ehret W, Heil W, Schmitt Y, Töpfer G, Wisser H, Zawta B, et al. Use of anticoagulants in diagnostic laboratory investigations and stability of blood, plasma and serum samples. WHO/DIL/LAB/99.1 Rev.2:28pp.

8. Baudner S, Dati F. Standardization of the measurement of 14 proteins in human serum based on the new IFCC/BCR/CAP international reference material CRM 470. J Lab Med 1996;20:145-152.

9. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, Criqui M et al. Markers of inflammation and cardiovascular disease. Application to clinical and public health practice. A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003;107:499-511.

10. Young DS. Effects of drugs on clinical laboratory tests, 5th ed. AACC Press, 2000.

EC REP Beckman Coulter Ireland Inc., Lismeehan, O'Callaghan's Mills, Co. Clare, Ireland +(353) (0) 65 683 1100

Beckman Coulter, Inc., 250 S. Kraemer Blvd., Brea, CA 92821 U.S.A.
www.beckmancoulter.com