BECKMAN COULTER

AU/DxC AU US

Instructions For Use

CRP
C-Reactive Protein

REF OSR6147 4 x 14 mL R1, 4 x 6 mL R2

For *in vitro* diagnostic use only.

For Rx use only

PRINCIPLE

INTENDED USE

System reagent for the quantitative determination of C-Reactive Protein in human serum on Beckman Coulter AU/DxC AU Analyzers.

SUMMARY AND EXPLANATION

C-reactive protein (CRP) has long been recognized as one of the most, if not the most, sensitive of the acute-phase reactants. C-reactive protein levels in plasma can rise dramatically after myocardial infarction, stress, trauma, infection, inflammation, surgery, or neoplastic proliferation. The increase occurs within 24 to 48 hours, and the level may be 2000 times normal. Because the increase is nonspecific however, it cannot be interpreted without a complete clinical history, and even then only by comparison with previous values. Cord blood normally has low CRP concentrations (0.01 - 0.35 mg/L), but in intra-uterine infection, levels may be high as 260 mg/L.

For unknown reasons, the degree of C-reactive protein response varies in some diseases that are otherwise apparently similar. For example, the C-reactive protein response in systemic lupus and ulcerative colitis, even when there are obvious signs and symptoms of inflammation, is slight in contrast to its very large response in rheumatoid arthritis and Crohn's disease.

METHODOLOGY

Immune complexes formed in solution scatter light in proportion to their size, shape, and concentration. Turbidimeters measure the reduction of incidence light due to reflection, absorption, or scatter. In this procedure, the measurement of the rate of decrease in light intensity transmitted (increase in absorbance) through particles suspended in solution is the result of complexes formed during the antigen-antibody reaction.

SPECIMEN

SPECIMEN STORAGE AND STABILITY

C-reactive protein specimens are stable for 11 days at 20 - 25°C and 2 months at 4 - 8°C in serum and plasma. For longer storage, freeze serum to -20°C.[1] However, please note that it has been reported that frozen specimens may give false-positive results.[2]

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.

Additional handling conditions as designated by this laboratory:

SPECIMEN COLLECTION AND PREPARATION

Serum, free from hemolysis, is the recommended specimen. When used to evaluate patients with arthritis, serum is preferred specimen. Avoid highly lipemic samples which may produce excessively high scatter signals.

Additional instructions for patient sample preparation as designated by this laboratory:

Additional type conditions as designated by this laboratory:

REAGENTS

CONTENTS

C-Reactive Protein Reagent

Reagent storage location in this laboratory:

WARNING AND PRECAUTIONS

1. Exercise the normal precautions required for handling all laboratory reagents.
2. Dispose of all waste material in accordance with local guidelines.
3. 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:

Tris buffer (pH 7.5)	80 mmol/L
Sodium Chloride	125 mmol/L
Polyethylene glycol 6000	1.5%
Goat anti-CRP Antibodies	≈ 0.6 g/L
Also contains preservatives.	

⚠ 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

CRP R1

DANGER

H316	Causes mild skin irritation.
H318	Causes serious eye damage.
P280	Wear protective gloves, protective clothing and eye/face protection.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310	Immediately call a POISON CENTER or doctor/physician.
P332+P313	If skin irritation occurs: Get medical advice/attention.

Phenol < 0.1%

Tris(hydroxymethyl)– aminomethane 1 - 5%

Genapol X080 1 - 5%

Polyoxyethylene-10-tridecyl ether 1 - 5%

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

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

Serum Protein Multi-Calibrator (Cat # ODR3021)

Storage location of the Calibrator in this laboratory:

EQUIPMENT AND MATERIALS

For use on the AU480, AU680, AU5800, DxC 500 AU, DxC 500i and DxC 700 AU Beckman Coulter Analyzers.

Storage location of test tubes or sample cups in this laboratory:

REAGENT PREPARATION

The C-Reactive Protein reagents are ready for use. No preparation is required.

REAGENT STORAGE AND STABILITY

1. The unopened reagents are stable until the expiration date printed on the label when stored at 2 - 8°C.
2. Opened bottles of reagent are stable for 90 days when stored in the refrigerated compartment of the analyzer.

INDICATIONS OF DETERIORATION

Visible signs of microbial growth, turbidity, precipitate, or change in color in the C-Reactive Protein reagents may indicate degradation and warrant discontinuation of use.

Additional storage requirements as designated by this laboratory:

STABILITY OF FINAL REACTION MIXTURE

The Beckman Coulter AU/DxC AU analyzer automatically computes every determination at the same time interval.

CALIBRATION

CALIBRATION INFORMATION

The frequency of calibration for the C-reactive protein procedure is every 90 days. Calibration of this C-reactive protein procedure is accomplished by use of the Serum Protein Multi-Calibrator (Cat # ODR3021), which is traceable to IFCC (International Federation of Clinical Chemistry) standard CRM 470 (RPPHS).

The Serum Protein Multi-Calibrator is a 6 - level calibrator for serum proteins including CRP (Level 6 for use with CRP OSR6x47 only).

Recalibration of this test is required when any of these conditions exist:

1. A reagent lot number has changed or there is an observed shift in control values.
2. Major preventative maintenance was performed on the analyzer.
3. A critical part was replaced.

QUALITY CONTROL

During operation of the Beckman Coulter AU/DxC AU analyzer, at least two levels of an appropriate quality control material should be tested a minimum of once a day. In addition, controls should be performed after calibration with each new lot of reagent, and after specific maintenance or troubleshooting steps described in the appropriate Beckman Coulter AU/DxC AU analyzer Instructions For Use (IFU) and Reference Manual. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

Location of controls used at this laboratory.

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

A complete list of test parameters and operational procedures are provided in the relevant AU/DxC AU analyzer IFU and Reference Manual.

RESULTS INTERPRETATION

The default unit of measure is mg/L, for conversion to mg/dL the result is divided by 10.

REPORTING RESULTS

EXPECTED RESULTS

Adults:[3] < 5 mg/L

Reference Intervals shown above were taken from the literature. 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.

Expected reference ranges in this laboratory:

INTERVALS	SAMPLE TYPE	UNITS

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

INTERFERENCES

Results of studies[4] show that the following substances do not interfere with this C-reactive protein procedure.

The criteria for no significant interference is recovery within 10% or 2.2 mg/L of the initial value.

Bilirubin:	No significant interference up to 40 mg/dL Bilirubin.
Hemolysis:	No significant interference up to 500 mg/dL Hemolysate
Lipemia:	No significant interference up to 1,000 mg/dL Intralipid.

* Intralipid, manufactured by KabiVitrium Inc., is a 20% IV fat emulsion used to emulate extremely turbid samples.

In very rare cases gammopathy, especially monoclonal IgM (Waldenström's macroglobulinemia), may cause unreliable results.

In addition, please note that oral contraceptives have been reported to affect results.[5]

The information presented is based on results from Beckman Coulter studies and is current at the date of publication. Beckman Coulter Inc., makes no representation about the completeness or accuracy of results generated by future studies. Further information on interfering substances is available.[6]

Laboratory specific procedure notes:

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.

DYNAMIC RANGE / ANALYTICAL MEASURING RANGE

1. The C-Reactive Protein reagent is linear from 5 - 300 mg/L using the Serum Protein Multi-Calibrator (Cat # ODR3021) 6pt calibration. Samples exceeding the upper limit of linearity should be diluted and repeated. The sample may be diluted, repeated and multiplied by the dilution factor automatically utilizing the AUTO REPEAT RUN.
2. This kit is not recommended for cardiovascular risk assessment or diagnostic evaluation of neonates. The CRP Latex reagent OSR6x99 is available for this purpose.
3. Results of this test should be interpreted with other clinical and laboratory findings.
4. 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.

Note: Samples from patients with abnormal lipoprotein metabolism such as those seen in cholecystitis or obstructive liver disease may give artificially elevated CRP results. These samples are characterised by having extremely elevated Cholesterol values (>387 mg/dL) and elevated Bilirubin. Such samples should be diluted 1 part sample to 4 parts deionized water prior to analysis and the result multiplied by 5.

METHODS COMPARISON

Reference[7]

Patient serum samples were evaluated in method comparison studies.

Results of Deming regression analysis were as follows:

Y Method	DxC 700 AU
X Method	AU5800
Slope	0.968
Intercept	0.1
Correlation Coeff. (r)	0.9999
No. of Samples (n)	119
Range (mg/L)	6-284

PRECISION

Reference[7]

Estimates of precision, based on CLSI recommendations[8], are consistent with typical performance. The within run precision is less than 5% CV or SD ≤ 1 and the total precision is less than 5% CV or SD ≤ 1. Assays of serum pools and control sera were performed and the data reduced following the CLSI guidelines above.

N=80	Within-run		Total	
Mean, mg/L	SD	CV%	SD	CV%
12.84	0.27	2.1	0.30	2.3
79.50	0.62	0.8	1.00	1.3
145.33	1.04	0.7	1.27	0.9

ADDITIONAL INFORMATION

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

Test Name	Description
CRP3G	CRP (Serum)

Refer to the Beckman Coulter Chemistry Systems Reagent Guide (BAGUIDE) for specific chemistry information for the AU/DxC AU clinical chemistry systems and guidance on symbols used on all AU/DxC AU product labelling.

Setting Sheet Footnotes

User defined

Lot or Lot + Bottle

† Beckman Coulter Serum Protein Multi-Calibrator Cat. No: ODR3021

* Values set for working in mg/L. To work in (mg/dL), divide by 10.

†† Reported dynamic range is 5-300 with B=1.0.

REVISION HISTORY

Updated REPORTING RESULTS section

Updated PROCEDURAL NOTES section

Updated Performance Characteristics section

Updated References section

Preceding version revision history

Add DxC 500i instrument to IFU

REFERENCES

1. WHO/DIL/LAB/99.1 Rev.2 World Health Organization. Use of Anticoagulants in Diagnostic Laboratory Investigations 2002.

2. Rose, N.R. et. al (ed) Manual of Clinical Laboratory Immunology, American Society of Microbiology, Washington, DC, 1986.

3. 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.

4. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition. CLSI document EP07-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2005.

5. Ashwood, E.R., Burtis, C.A., Tietz Textbook of Clinical Chemistry, 2nd Edition, W.B. Saunders, 1994.

6. AACC Effects on Clinical Laboratory Tests: Drugs, Disease, Herbs and Natural Products https://clinfx.wiley.com/aaccweb/aacc/

7. Data is on file for specific AU/DxC AU analyzers.

8. CLSI. Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

Beckman Coulter, Inc., 250 S. Kraemer Blvd., Brea, CA 92821 U.S.A.
+(1) 800-854-3633
www.beckmancoulter.com