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

Summary
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.

System Information
For AU400/400e/480, AU600/640/680 and AU2700/5400/AU5800 Beckman Coulter Analyzers.

Reagents
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.

Precautions
1. For in vitro diagnostic use.
2. Do not ingest. Harmful if swallowed.
3. Contains sodium azide as a preservative which may react with lead joints in copper plumbing to form explosive compounds. Even though the reagent contains minute quantities of sodium azide, drains should be well flushed with water when discarding the reagent.

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

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.

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.

Sample 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. However, please note that it has been reported that frozen specimens may give false-positive results.

Interfering Substances
Results of studies show that the following substances do not interfere with this C-reactive protein procedure.

The criteria for no significant interference is recovery within 10% of the initial value.

- Bilirubin: No significant interference up to 40 mg/dL Bilirubin. AU5800: No significant interference up to 28 mg/dL Bilirubin
- Hemolysis: No significant interference up to 500 mg/dL Hemolysate
- Lipemia: No significant interference up to 1000 mg/dL Intralipid*. AU5800: No significant interference up to 600 mg/dL Intralipid

* Intralipid, manufactured by KabiVitrum 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.

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. For further information on interfering substances, refer to Young for a compilation of reported interferences with this test.
C-Reactive Protein

Procedure
A complete list of test parameters and operational procedures can be found in the User’s Guide appropriate to the AU analyzer.

Materials Provided
C-Reactive Protein Reagent

Materials required but not provided
Serum Protein Multi-Calibrator (Cat # ODR3021)

Stability of Final Reaction Mixture
The Beckman Coulter AU analyzer automatically computes every determination at the same interval.

Calibration
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 analyzer, at least two levels of an appropriate Immunology 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 User’s Guide. Quality control testing should be performed in accordance with regulatory requirements and each laboratory’s standard procedure.

Results
Automatically printed out for each sample in mg/L at 37°C.

Dynamic 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/dL) 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.

Expected Values
Adults: < 5 mg/L

Expected values may vary with age, sex, diet and geographical location. Each laboratory should determine its own expected values as dictated by good laboratory practice.

Specific Performance Characteristics
The following data was obtained using the C-Reactive Protein turbidimetric reagent on Beckman Coulter AU analyzers according to established procedures. Results obtained in individual laboratories may differ.

Precision Estimates of precision, based on CLSI recommendations, 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.

<table>
<thead>
<tr>
<th>N= 100</th>
<th>Within run</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean, mg/L</td>
<td>SD</td>
<td>CV%</td>
</tr>
<tr>
<td>12.8</td>
<td>0.4</td>
<td>3.4</td>
</tr>
<tr>
<td>20.1</td>
<td>0.5</td>
<td>2.4</td>
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</tbody>
</table>

Method Comparison Patient samples were used to compare this C-Reactive Protein Reagent. The table below demonstrates representative performance on AU analyzers.

<table>
<thead>
<tr>
<th>Y Method</th>
<th>AU640</th>
</tr>
</thead>
<tbody>
<tr>
<td>X Method</td>
<td>AU600</td>
</tr>
<tr>
<td>Slope</td>
<td>1.017</td>
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<tr>
<td>Intercept</td>
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<tr>
<td>Correlation Coeff. (r)</td>
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<tr>
<td>No. of Samples (n)</td>
<td>101</td>
</tr>
<tr>
<td>Range (mg/L)</td>
<td>5-103</td>
</tr>
</tbody>
</table>
C-Reactive Protein

References
6. Beckman Coulter Inc., data on samples collected from 200 blood donors in North Texas.
7. Data is on file for specific AU analyzers.

Manufactured by: Beckman Coulter, Inc., 250 S. Kraemer Blvd. Brea, CA 92821, USA