**Intended Use**
System reagent for the quantitative determination of D-Dimer in human plasma on Beckman Coulter AU analyzers.

**Summary**
Plasmin degradation of cross-linked fibrin results in the formation of specific degradation products including D-Dimer. As D-Dimer is released into the circulation during the fibrinolytic process, the measurement of D-Dimer and higher molecular weight oligomers containing D-Dimer epitopes is considered to reflect the overall activity of clot formation and lysis. Elevated levels of D-Dimer can occur in a variety of clinical conditions associated with fibrin breakdown, including Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE) and Disseminated Intravascular Coagulation (DIC).

**Methodology**
Immune complexes formed in solution scatter light in proportion to their size, shape and concentration. Turbidimeters measure the reduction of incident light due to reflection, absorption or scatter.

In this procedure, the decrease in light intensity transmitted (increase in absorbance) through particles suspended in solution is as a result of complexes formed during the immunological reaction between the D-Dimer in the patient plasma and the anti-human D-Dimer antibodies coated on the latex particles.

**System Information**
AU400/4000/4800, AU600/640/640/680, AU2700/5400 Analyzers.

**Reagents**
Reagent Composition:
- Tris/HCl
- NaCl
- Bovine Serum Albumin
- Latex coated monoclonal anti human D-Dimer antibodies (mouse)
- 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.
4. Dispose of all waste material in accordance with local guidelines.

**Preparation of Reagents**
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.

**Storage and Stability**
1. The unopened reagent is stable until the expiration date printed on the label when stored at 2 - 8°C.
2. Opened bottles of reagent are stable for 30 days when stored in the refrigerated compartment of the analyzer.

**Indications of Deterioration**
Visible signs of microbial growth, gross turbidity, precipitate or change in color in the D-Dimer reagent may indicate degradation and warrant discontinuation of use.

**Specimen Collection and Preparation**
Citrated plasma is the recommended specimen type.
Lithium Heparin plasma may also be used. Unlike when using citrated plasma, there is no sample dilution with heparin tubes. Therefore the D-Dimer values in heparin plasma are on average 16% higher over the entire measuring range.
Use samples undiluted.

**Sample Storage and Stability**
D-Dimer is stable in citrated or lithium heparinized plasma for 4 days when stored at 2 - 8°C and 6 months when stored at -20°C.

**Interfering Substances**
Results of studies’ show that the following substances may interfere with this D-Dimer 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
- **Hemolysis:** No significant interference up to 500 mg/dL Hemolysate
- **Lipemia:** No significant interference up to 700 mg/dL Intralipid®
- **Rheumatoid Factor:** No significant interference up to 100 IU/mL
- **Heparin:** No significant interference up to 1.5 IU/mL

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

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

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

Materials provided
D-Dimer Reagent.

Materials required but not provided
D-Dimer Calibrator (Cat. No. ODR3033)
D-Dimer Control (Cat. No. ODC0029)

Stability of Final Reaction Mixture
The Beckman Coulter AU analyzers automatically compute every determination at the same time interval.

Calibration
The frequency of calibration for the D-Dimer procedure is every 30 days. This D-Dimer assay has been aligned with another commercially available immuno-turbidimetric assay which reports results in µg FEU/mL (FEU = Fibrinogen Equivalent Units) and is traceable to an in-house Master Calibrator.

Recalibration of this test is required when any of these conditions exist:
1. A reagent lot 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 appropriate control material, such as D-Dimer Control ODC0029, should be tested a minimum of once a day. In addition, these controls should be tested 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
Results are automatically printed out for each sample in µg FEU/mL.

Dynamic Range
The D-Dimer procedure is linear from 0.25 – 8.00 µg FEU/mL. Samples exceeding the upper limit of linearity should not be diluted, but instead should be reported as > 8 µg FEU/mL.

Samples with very elevated D-Dimer concentrations (> 200 µg FEU/mL) can generate false low results without appropriate “Z” flags due to excess antigen in the sample, such as can occur during lysis therapy.
Samples containing heterophilic antibodies may cause falsely elevated results.
Samples with extremely abnormal optical characteristics, especially turbidity, may produce atypical results.

Expected Values
< 0.50 µg FEU/mL

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 were obtained using the D-Dimer 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 10% CV and total precision is less than 10% CV. Assays of plasma pools and control sera were performed and the data reduced following CLSI guidelines above.

<table>
<thead>
<tr>
<th>N= 80</th>
<th>Mean, µg FEU/mL</th>
<th>SD</th>
<th>CV%</th>
<th>Total</th>
<th>SD</th>
<th>CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.28</td>
<td>0.01</td>
<td>4.60</td>
<td>9.14</td>
<td>0.03</td>
<td>7.95</td>
<td></td>
</tr>
<tr>
<td>0.55</td>
<td>0.02</td>
<td>4.22</td>
<td>7.95</td>
<td>0.04</td>
<td>7.95</td>
<td></td>
</tr>
<tr>
<td>5.66</td>
<td>0.04</td>
<td>0.69</td>
<td>3.02</td>
<td>0.17</td>
<td>3.02</td>
<td></td>
</tr>
</tbody>
</table>

Functional Sensitivity
Precision results (40-fold determination) for a level below 0.15 µg FEU/mL have a CV of ≤ 20% for each application.

<table>
<thead>
<tr>
<th>Mean Concentration (µg FEU/mL)</th>
<th>Delete tableSD</th>
<th>CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>AU400/400</td>
<td>0.136</td>
<td>0.017</td>
</tr>
<tr>
<td>AU600/AU640/640</td>
<td>0.134</td>
<td>0.020</td>
</tr>
<tr>
<td>AU2700/5400</td>
<td>0.124</td>
<td>0.025</td>
</tr>
</tbody>
</table>

OSR Special Chemistry

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D-Dimer

Method Comparison

Plasma samples were used to compare this D-Dimer Reagent. The table below demonstrates representative performance on AU analyzers.

<table>
<thead>
<tr>
<th>Y Method</th>
<th>AU640/AU640°</th>
</tr>
</thead>
<tbody>
<tr>
<td>X Method</td>
<td>Method 2</td>
</tr>
<tr>
<td>Slope</td>
<td>1.010</td>
</tr>
<tr>
<td>Intercept (µg FEU/mL)</td>
<td>0.079</td>
</tr>
<tr>
<td>Correlation Coeff. (r)</td>
<td>0.996</td>
</tr>
<tr>
<td>No. of Samples (n)</td>
<td>104</td>
</tr>
<tr>
<td>Range (µg FEU/mL)</td>
<td>0.28-7.53</td>
</tr>
</tbody>
</table>

Lower Limit of Detection

The LLD is calculated as mean recovery +3 SD of a 20-fold determination of an analyte-free sample. LLD: ≤ 0.08 µg FEU/mL.

References

7. CLSI/NCCLS. Interference testing in clinical chemistry. CLSI/NCCLS document EP7-A2; 2004
12. Data is on file for specific AU analyzers.

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