3/ TEST PRINCIPLE

This assay is based on the change in turbidity of a microparticle suspension that is measured by photometry. A suspension of latex microspheres, coated with antibody specific for D-dimer, is mixed with the test plasma whose D-dimer level is to be assayed. An antigen-antibody reaction leading to an agglutination of the latex microspheres which increases in turbidity of the resulting mixture. This increase in turbidity is reflected by an increase in absorbance, the latter being measured photometrically. The increase in absorbance is a function of the D-dimer level present in the test sample.

4/ KIT REAGENTS

An Assay Value insert is provided in the box. This barcode contains the following information: lot number, kit code number, reagent code number, expiration date and calibration values.

Reagent 1: Tris buffer

Reagent 2: suspension of latex microspheres coated with two different mouse monoclonal anti-human D-dimer antibodies (BD and 2.1-16) that are then stabilized with bovine albumin.

5/ CAUTION

On the Florin clot plasmin degrades fibrin into various products. Antibody levels are measured and should not recognize fibrinogen, which are developed(13). The presence of these various fibrin degradation products, among which D-dimer is the terminal product, is greater than 0.010 µg/ml (i.e., less than or equal to 0.010 µg/ml). For example, a value of 0.50 µg/ml is approx. half of an FEU. For example, a value of 0.50 µg/ml is approx. half of an FEU. For example, a value of 0.50 µg/ml is approx. half of an FEU. For example, a value of 0.50 µg/ml is approx. half of an FEU. For example, a value of 0.50 µg/ml is approx. half of an FEU. For example, a value of 0.50 µg/ml is approx. half of an FEU.

6/ SPECIMEN COLLECTION AND TREATMENT

Sample collection must be in conformity with the recommendations for haemostasis tests.

Blood (9 ml) is collected in a 0.19 M (i.e., 3.2 %) trisodium citrate anticoagulant (1 vol) [in the USA follow CLSI guidelines GP4-A6 (16) and HT2-A5 (11)].

Concentration: 15 minutes at 2000-2500 g. Alternatively centrifugation conditions are as follows: 3 minutes at 2000 g (0.010 platelet/h). LIMITATIONS

Cloudy plasma may lead to an under-estimation of the D-dimer level. (Ensure that the absorbance value at 540 nm of the plasma diluted 1:6 is greater than 0.25 (actual D-dimer).

Ensure that the values obtained for the controls are within the ranges stated in the Assay Value insert provided in the box. If the control values do not fall within these ranges, check all components of the test system to ensure that all are functioning correctly, i.e., assay conditions, reagents, integrity of the plasmas being tested, etc. If necessary, repeat the test.

10/ RESULTS

The D-dimer level (µg/ml) of the plasmas being tested is displayed in the "Test Panel/Test Status" screen of the analyzer (see the Reference Manual). The result is to be interpreted according to the patient’s clinical and biological status. For D-dimer levels expressed in initial fibrinogen equivalent units (FEU), by definition, one FEU is the quantity of fibrinogen initially present that lead to a clotting time of 1 minute. The actual quantity of fibrinogen is approx. 1000 platelet/h.

11/ LIMITATIONS

Plasmin is the fibrinolytic enzyme derived from the inactive plasminogen by limited proteolytic degradation of fibrin by plasminogen activators. The main plasminogen activators are the tissue plasminogen activator (tPA) and the plasminogen activator inhibitor. Plasmin degrades fibrin, the main component of the fibrinolytic enzyme and activity of the clotting system in response to coagulation activation.

The calibration of these reagents and of patient samples. The disposal of waste materials must be carried out according to current local regulations.

In the US: wherever appropriate, observe CLIA-88 requirements. Caution: Federal law restricts this device to sale by or on the order of a physician.
Overall study population:

<table>
<thead>
<tr>
<th>D-dimer</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>86</td>
<td>3</td>
<td>89</td>
</tr>
<tr>
<td>Negative</td>
<td>3</td>
<td>777</td>
<td>780</td>
</tr>
<tr>
<td>Total</td>
<td>89</td>
<td>780</td>
<td>869</td>
</tr>
</tbody>
</table>

Sensitivity (95% CI) = 97.0% (91.8% - 99.4%)
Specificity (95% CI) = 75.6% (72.8% - 78.1%)
PPV (95% CI) = 99.7% (99.2% - 100.0%)
NPV (95% CI) = 97.7% (93.5% - 99.6%)

US prospective study population:

<table>
<thead>
<tr>
<th>D-dimer</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>22</td>
<td>492</td>
<td>514</td>
</tr>
<tr>
<td>Negative</td>
<td>6</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>518</td>
<td>546</td>
</tr>
</tbody>
</table>

Sensitivity (95% CI) = 100% (98.6% - 100.0%)
Specificity (95% CI) = 58.2% (52.8% - 63.5%)
PPV (95% CI) = 100% (99.2% - 100%)
NPV (95% CI) = 93.2% (84.4% - 91.3%)

European/Canadian prospective study population:

<table>
<thead>
<tr>
<th>D-dimer</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>16</td>
<td>24</td>
<td>40</td>
</tr>
<tr>
<td>Negative</td>
<td>17</td>
<td>50</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>74</td>
<td>107</td>
</tr>
</tbody>
</table>

Sensitivity (95% CI) = 100% (94.3% - 100.0%)
Specificity (95% CI) = 53.3% (49.0% - 57.5%)
PPV (95% CI) = 97.7% (87.8% - 99.6%)
NPV (95% CI) = 97.7% (93.4% - 99.7%)

US banked samples:

<table>
<thead>
<tr>
<th>D-dimer</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>53</td>
<td>335</td>
<td>388</td>
</tr>
<tr>
<td>Negative</td>
<td>64</td>
<td>1130</td>
<td>1194</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td>1465</td>
<td>1534</td>
</tr>
</tbody>
</table>

Sensitivity (95% CI) = 99.7% (99.2% - 100.0%)
Specificity (95% CI) = 97.7% (93.5% - 99.6%)
PPV (95% CI) = 99.7% (99.2% - 100.0%)
NPV (95% CI) = 97.7% (93.5% - 99.6%)

Banked samples:

<table>
<thead>
<tr>
<th>D-dimer</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>16</td>
<td>24</td>
<td>40</td>
</tr>
<tr>
<td>Negative</td>
<td>17</td>
<td>50</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>74</td>
<td>107</td>
</tr>
</tbody>
</table>

Sensitivity (95% CI) = 94.1% (71.3% - 99.9%)
Specificity (95% CI) = 85.3% (61.6% - 96.9%)

14.2 Deep Venous Thrombosis

16 sites were involved in this study. 980 samples of patients with a low or moderate PTP were used for the final analysis.

Patients with a low or moderate PTP score and a positive D-dimer result or a high PTP score were referred to imaging studies. Patients with a low or moderate PTP score and a negative D-dimer result were followed for a three-month period of time to evaluate a potential development of DVT.

The overall prevalence of DVT (low and moderate PTP patients with positive imaging) in the prospective study population was 8.3% with 6.0% in the US population and 9.8% in the European/Canadian population. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) with upper and lower limit of 95% confidence intervals (CI) were calculated in the overall study population and separately for the US population and the European/Canadian population with the STA®-Liatest®-D Clinical cut-off of 0.50 μg/ml (FEU) in the low (moderate) PTP group of patients.

Sensitivity (95% CI) = 95.8% (99.8% - 100%)
Specificity (95% CI) = 52.0% (51.9% - 58.5%)
PPV (95% CI) = 100% (99.3% - 100%)
NPV (95% CI) = 17.5% (14.2% - 21.2%)

REFERENCES