Clearview Simplify D-dimer
Fingerprick blood
Kapillarblut aus der Fingerbeere
Fingerprikning
Colecta de Sangre por Punción Digital
Sang du bout du doigt
Fingerstick Blood
Sangue dal polpastrello
Vingerprikbloed
Blod fra fingertupp
Sangue por picada do dedo
Kapillärblod med fingerstick

Venous whole blood
Venöses Vollblut
Venøst helblod
Sangre Venosa Total
Sang veineux total
Φλεβικό ολόκληρο αίμα
Sangue intero venoso
Veneus vol bloed
Venøst fullblod
Sangue Venoso Total
Venöst helblod

Plasma
Πλάσμα
INTENDED USE
Rapid immunochromatography test for the qualitative detection of D-dimer in human whole blood and plasma; for use as an aid in the assessment and evaluation of patients with suspected disseminated intravascular coagulation (DIC), deep vein thrombosis (DVT), and pulmonary embolism (PE).

SUMMARY
During blood coagulation, fibrinogen is converted to fibrin by the activation of thrombin. The resulting fibrin monomers polymerise to form a soluble gel of non-cross-linked fibrin. This fibrin gel is then converted to cross-linked fibrin by thrombin activated Factor XIII to form an insoluble fibrin clot. Production of plasmin, the major clot-lysing enzyme, is triggered when a fibrin clot is formed. Although fibrinogen and fibrin are both cleaved by the fibrinolytic enzyme plasmin to yield degradation products, only degradation products from cross-linked fibrin contain D-dimer and are called cross-linked fibrin degradation products. Therefore, fibrin derivatives in human blood or plasma containing D-dimer are a specific marker of fibrinolysis.

TEST PRINCIPLE
The Clearview Simplify D-dimer test uses the D-dimer specific murine monoclonal antibody DD3B6/223 conjugated to colloidal gold particles to detect D-dimer containing molecules. The antibody-gold conjugate binds specifically to D-dimer containing molecules in the patient sample to form a complex. The antibody-gold-D-dimer complex migrates through a membrane in the aqueous phase until it is captured and concentrated on a zone to which a second, D-dimer specific murine monoclonal antibody has been bound. The capture of the complexes at this zone (test zone [T]) causes a pink/purple line to appear on the membrane. If D-dimer concentrations are below the clinically established cut-off, no visible line should be produced. Uncaptured gold conjugate continues to flow towards the end of the strip where it is bound on the procedural control (PC) zone by anti-murine antibody. Formation of a pink/purple PC line indicates the device is working as designed.

WARNINGS AND PRECAUTIONS
- Buffer contains sodium azide (0.05%). Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. If discarded into sink, flush with a large volume of water to prevent azide build-up.
- All human blood products should be handled as potentially infectious material. Wear disposable gloves while handling specimens.
- Testing materials (specimens, test devices and pipettes) should be disposed of in accordance with local, state and/or federal regulations.

COMPONENTS OF THE KIT
- Storage: Store at 2°C to 25°C. Do not freeze.
- Expiration: Refer to label for expiration date.
- Test Device x 10
- Buffer - 1 x 2.6mL
- Capillary Pipette x 10
- Venous Pipette x 10

MATERIALS REQUIRED BUT NOT PROVIDED
- Specimen collection tubes: Sodium citrate, EDTA or heparin (Venous Whole Blood or Plasma procedure).
- Sterile single use Safety Lancet (minimum depth 1.8mm), for example VI TREX SAFE® brand (Fingerprick Blood procedure).

SPECIMEN COLLECTION AND PREPARATION
Either Whole Blood (venous or fingerprick) or Plasma is suitable for use with this test.

Fingerprick Blood
1. Follow recommended fingerprick procedure.
2. Collect fingerprick blood with the capillary pipettes provided in the kit. Do not use the venous pipettes.
3. Hold a capillary pipette horizontally and touch the tip to the blood drop on the patient’s finger.
4. Do not squeeze the bulb of the pipette during sampling or obstruct the vent. Capillary action will automatically draw the blood into the pipette.
5. Allow the pipette to fill to the black line.
7. Immediately transfer the blood specimen to the round sample well of the test device.
8. Samples showing evidence of clotting are unsuitable for testing. If this is the case a further capillary sample must be taken from another finger. Use a new lancet and a new capillary pipette.
9. Samples with a haematocrit outside of the normal range may alter Clearview Simplify D-dimer sensitivity due to the differences in the plasma fraction.

**Venous Whole Blood**
1. Collect whole blood by venepuncture into sodium citrate (nine parts of venous blood drawn into one part 3.2% trisodium citrate), heparin or EDTA anticoagulant.
2. Store blood samples refrigerated and test within 24 hours of collection.
3. Samples showing evidence of clotting are unsuitable for testing.
4. Samples with a haematocrit outside of the normal range may alter Clearview Simplify D-dimer sensitivity due to differences in the plasma fraction.

**Plasma**
1. Collect whole blood by venepuncture into sodium citrate (nine parts of venous blood drawn into one part 3.2% trisodium citrate), heparin or EDTA anticoagulant.
2. Centrifuge the sample (1500g for 15 minutes at 4°C–10°C) and remove the plasma immediately from the blood cell interface.

**Plasma storage/stability:**
- +20°C to +25°C: 8 hours
- +2°C to +8°C: 4 days
- -20°C: 2 months

Frozen plasma samples should be thawed at 37°C or room temperature and mixed thoroughly before testing.

**Fingerprick Blood**
Tear open a foil pouch and place the test device on a flat horizontal surface.

NOTE: use the capillary pipettes provided in the kit for dispensing capillary fingerprick blood samples.
- Hold the capillary pipette containing the fingerprick blood specimen in a vertical position above the round sample well of the test device. Squeeze the bulb and dispense all the blood (35 µL) in the capillary pipette into the round sample well.
- Note: If the blood will not expel from the capillary pipette, place a finger over the vent hole and squeeze the bulb again. Discard used capillary pipette into biohazard waste receptacle.

- Allow the sample to completely penetrate the sample pad before adding buffer.
- Holding the bottle vertically apply 2 drops of buffer to the sample well.
- Leave the test device lying flat for the development period and read the result at 10 minutes.

**Venous Whole Blood**
Tear open a foil pouch and place the test device on a flat horizontal surface.

**Plasma**
Tear open a foil pouch and place the test device on a flat horizontal surface.

**Quality Control**
To confirm the proper functioning of the Clearview Simplify D-dimer test system it is recommended that both positive and negative controls be tested at regular intervals. Control
samples should also be run on receipt of each new consignment of Clearview Simplify D-dimer, and at any time that the validity of results is questioned. The samples selected as a positive control should produce a weak to moderate positive result on the test line (T) combined with a clearly visible PC line. The negative control should yield a negative result. Control samples should be tested by the same procedure as patient samples. Clearview Simplify D-dimer controls, product number 6101KCV, are available from Inverness Medical, or your local distributor.

RESULTS

Test Validity
- Valid Result: A pink/purple line must be present in the PC zone.
- Invalid Result: No line present in the PC zone. The device has failed to perform correctly and the test must be repeated.

Positive Result: Presence of a pink/purple line in the test zone (T).

Negative Result: Complete absence of a line in the test zone (T).

Notes
1. The PC line will appear before the 10 minute reading time has elapsed. This does not mean that a negative result can be read at this time.
2. A negative result must be read only at 10 minutes and not before or after.
3. A positive test band may develop before the 10 minute reading time and a result may be read as positive provided the PC line has also developed.
4. The PC line is intended as a test validity indicator only. It is not an internal reference for test line intensity and cannot be used for comparison with patient results.

LIMITATIONS OF PROCEDURE
Clinical diagnosis should not be based on the result of the Clearview Simplify D-dimer test alone. The full clinical context of the patient should be included when making a diagnostic decision taking into account the clinical signs and other relevant information such as the Wells pre-test probability score or equivalent.

Negative D-dimer results can occur very occasionally even in the presence of a DVT due to other factors including the age or position of a clot, heparin therapy and when the D-dimer concentration is below the sensitivity of the test.

EXPECTED VALUES
Elevated levels of D-dimer are an indication of active fibrinolysis and have been shown in patients with disseminated intravascular coagulation (DIC)\(^1\), deep vein thrombosis (DVT)\(^2\), and pulmonary embolism (PE)\(^3,4\).

Elevated levels of D-dimer have also been reported in surgery, trauma, sickle cell disease, liver disease, severe infection, sepsis, inflammation, malignancy, and in the elderly\(^5,6\). D-dimer levels also rise during normal pregnancy but very high levels are associated with complications\(^7\).

A positive result indicating active fibrinolysis should be obtained with Clearview Simplify D-dimer when D-dimer levels are greater than or equal to the cut off of approximately 80ng/ml as measured by an ELISA method (DIMERTEST\textsuperscript{®} GOLD EIA).

PERFORMANCE CHARACTERISTICS
Normal Blood Donor Samples (n = 99)
In-house study conducted at AGEN Biomedical Ltd, Brisbane, QLD, Australia.

<table>
<thead>
<tr>
<th>% Negative by Clearview Simplify D-dimer</th>
<th>Whole Blood</th>
<th>Plasma</th>
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<tbody>
<tr>
<td>86.8%</td>
<td>84.8%</td>
<td></td>
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DVT Study
Clinical performance of Clearview Simplify D-dimer was assessed in a prospective accuracy study\(^8\).

n = 120 consecutive outpatients referred for investigation for suspected DVT. Clearview Simplify D-dimer results were compared to bioMérieux VIDAS\textsuperscript{®} D-dimer New. DVT was confirmed by compression ultrasound (CUS).

<table>
<thead>
<tr>
<th>Assay</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearview Simplify D-dimer</td>
<td>100% (90.0-100%)</td>
<td>52.9% (41.8-63.8%)</td>
<td>100% (92.1-100%)</td>
</tr>
<tr>
<td>Vidas\textsuperscript{®} D-dimer New</td>
<td>100% (90.7-100%)</td>
<td>48.8% (37.6-60.1%)</td>
<td>100% (91.2-100%)</td>
</tr>
</tbody>
</table>

\(\text{*} = 95\% \text{ Confidence Intervals, NPV = Negative Predictive Value}\)

PE Study
Clinical performance of Clearview Simplify D-dimer was assessed in a retrospective accuracy study\(^9\).

n = 527 consecutive patients referred for investigation of suspected PE and chest pain. Clearview Simplify D-dimer results were compared to bioMérieux VIDAS\textsuperscript{®} D-dimer New and Diagnostica Stago STA\textsuperscript{®} Liatest D-DI (n=479). PE was confirmed by V/Q lung scan, CT scan or pulmonary angiography.

<table>
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<th>Assay</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearview Simplify D-dimer</td>
<td>100% (92.5-100%)</td>
<td>47.9% (43.3-52.6%)</td>
<td>100% (98.4-100%)</td>
</tr>
<tr>
<td>Vidas\textsuperscript{®} D-dimer New</td>
<td>100% (92.5-100%)</td>
<td>48.8% (44.1-53.4%)</td>
<td>100% (98.4-100%)</td>
</tr>
<tr>
<td>STA\textsuperscript{®} Liatest D-DI</td>
<td>100% (92.5-100%)</td>
<td>47.5% (42.7-52.3%)</td>
<td>100% (98.2-100%)</td>
</tr>
</tbody>
</table>

\(\text{*} = 95\% \text{ Confidence Intervals, NPV = Negative Predictive Value}\)
Precision
Intra-assay (within run) precision was determined for 10 replicates of 3 plasma samples containing D-dimer concentrations of 0ng/mL, 150ng/mL and 650ng/mL. The results were equivalent for all replicates of each sample.

5 plasma samples with D-dimer levels ranging from 0ng/mL to approximately 2000ng/mL were tested consecutively for 10 days with the same lot of Clearview Simplify D-dimer to assess inter-assay precision. Over the 10 day period, identical results were found for the 5 specimens assayed.

Interfering Substances
No assay interference was demonstrated with spiked specimens containing potential interferents at, or below, the following concentrations: bilirubin (0.2g/L), lipid (30g/L), protein (60g/L, gamma globulin) and haemoglobin (10g/L).

Rheumatoid Factor
In a study of 29 samples from patients with rheumatoid arthritis, 13 samples gave a positive result with Clearview Simplify D-dimer. With all 13 samples, the positive reaction could be blocked by the addition of a D-dimer specific monoclonal antibody. In comparison, the addition of a non-specific antibody of the same subgroup, IgG, had no effect on the results, with all results remaining positive. This suggests that Clearview Simplify D-dimer is insensitive to Rheumatoid Factor interference.

PRODUCT SUPPORT/ADVICE LINE
For further information please contact your distributor or call Inverness Medical Customer Service on:
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