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Ksmart® D-DIMER + Controls

RAPID TEST FOR THE QUANTITATIVE DETECTION OF D-DIMERS IN HUMAN CAPILLARY AND VENOUS WHOLE BLOOD.

In vitro diagnostic medical device for professional use.

REF 1050003_C

1. INTENDED USE

Ksmart® D-DIMER + Controls is a rapid fluorescence immunoassay for the *in vitro* quantitative detection of D-dimer in human whole blood collected by fingertip or venipuncture. This test is intended for use only with the LabPad® Evolution. In the clinic, it is primarily used to exclude venous thrombosis, for the ancillary diagnosis of disseminated intravascular coagulation (DIC) and for the monitoring of thrombolytic therapy.

2. CLINICAL SUMMARY

D-dimers are a product of the degradation of fibrin by plasmin during the process of fibrinolysis. In clinical practice, the D-dimer blood test is often used for the exclusionary diagnosis of thrombotic diseases (DIC, deep vein thrombosis, pulmonary embolism, myocardial infarction, cerebral infarction, etc.) and as an indicator for monitoring the therapeutic dose of thrombolytic drugs and observing the curative effects[1,2,3].

3. TEST PRINCIPLE

Ksmart® D-DIMER + Controls is a rapid test that uses immunofluorescence for the quantification of D-dimers in capillary or venous whole blood. It should only be used with the LabPad® Evolution. The test consists of the following components: sample buffer, reagent buffer, reaction membrane and absorbent pad. The reagent pad contains fluorescently labelled monoclonal antibodies to D-dimer and the reaction membrane contains secondary monoclonal antibodies to D-dimer. The test strip is located inside a plastic cassette. When the sample is added to the sample well, the dry conjugates in the reaction buffer are dissolved and migrate with the sample. The D-dimers present in the sample form a reaction complex with the specific fluorescently labelled monoclonal antibodies. This complex migrates along the nitrocellulose membrane and moves towards the D-dimer detection line. The reaction complex is captured by the monoclonal antibodies bound at the detection line to form the final reaction. In the event of a positive reaction, a fluorescent band is detected by the LabPad® Evolution under the action of the excitation light. As a procedural control, a fluorescent band is detected by the LabPad® Evolution at the control line, indicating that the test is valid.
The Ksmart® D-DIMER + Controls assay result is only intended to be read by the LabPad® Evolution.

4. REQUIRED MATERIAL

Material provided:

- 25 Ksmart® D-DIMER cassettes in individual sachets with desiccant
- 25 tubes pre-filled with diluent
- 25 Minivette® POCT pipettes calibrated to 20 µL (for capillary whole blood sampling)
- 25 transfer pipettes calibrated to 80 µL (for sample delivery onto the Ksmart®)
- 4 lyophilized D-DIMER control beads in individual pouches with desiccant ("Control Bead Ksmart® D-DIMER")
- 2 pre-filled tubes with red caps for "Low" level D-DIMER control reconstitution ("Ksmart® D-DIMER Control Low")
- 2 pre-filled tubes with green caps for "High" level D-DIMER control reconstitution ("Ksmart® D-DIMER Control High")
- 1 card "Quality Control Card"
- 1 set of instructions for use

Material required but not provided:

- LabPad® Evolution (ref. 8001661)

BIOSYNEX SA- 22 Boulevard Sébastien Brant
67400 Illkirch-Graffenstaden, France

- Sterile lancets, gauge 21 recommended (for capillary whole blood sampling)
- Laboratory pipettes calibrated to 20 µL (for venous whole blood samples)
- Timer (for incubation on the bench)

Optional material not provided:

- Laboratory pipette calibrated to 80 µL (for control procedure)

5. PRECAUTIONS

- Do not use after the expiry date.
- The test should be stored in the sealed pouch until use. Do not use if pouch is damaged.
- Pipettes, tubes and test devices are for single use only.
- Read this instruction manual and the LabPad® Evolution user manual carefully before performing the test.
- Specimens and materials used should be considered potentially infectious and treated as such. Dispose of used components in accordance with local procedures for potentially infectious waste. Clean the surface and any spilled liquid with a suitable disinfectant.
- Follow good laboratory practice in collecting the sample and performing the test.
- Inadequate humidity and temperature conditions may affect the results. The following steps of the test and the interpretation of the result should be performed in a place without excessive humidity (< 85%) and at a temperature between 15°C and maximum 37°C.
- Do not interchange or mix components from different lots.
- Safety data sheet available on request.
- An incorrect test procedure or a damaged device can lead to incorrect results. Other factors such as operational errors or sample-related factors can also lead to incorrect results.
- The control beads should only be used with the Ksmart® D-DIMER cassettes from the same test kit. Each batch of control beads is manufactured specifically for a corresponding cassette batch.

6. KIT STORAGE

The kit can be stored at room temperature or in the refrigerator. The storage temperature of the kit should be between 2°C and 30°C. DO NOT FREEZE the kit components. Use Ksmart® D-DIMER cassettes within two hours of opening the sealed pouch.

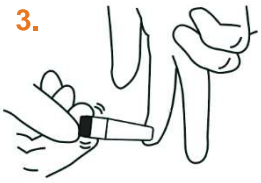
7. SAMPLE COLLECTION AND STORAGE

The Ksmart® D-DIMER + Controls assay can be performed on capillary whole blood or venous citrated blood samples.

Capillary whole blood sample collection:

1. Wash the patient's hand with soap and water or clean it with an alcohol wipe and let it dry.
2. Massage the hand without touching the puncture site, from the base to the tip of the ring or middle finger.
3. Prick the fingertip with a lancet (gauge 21 recommended).
4. Gently rub the hand from the palm to the finger to form a round drop of blood on the puncture site. Wipe off this first drop with a paper towel.
5. Repeat step 4 to form another round drop of blood at the puncture site.
6. Use the Minivette® POCT pipette provided: place the tip of the pipette horizontally in contact with the blood drop to draw up blood by capillary action. The pipette will fill with 20 µL of blood. Repeat steps 5 and 6 until the tip of the pipette is completely filled with blood.

3.



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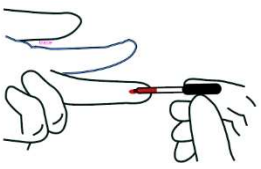


Venous whole blood sample collection:

Any anticoagulant other than sodium citrate should be avoided. Perform the test immediately after collection to avoid haemolysis. The venous whole blood sample can be stored for up to 24 hours at room temperature or between +4 and +8°C[4].

Control beads storage:

When stored in their aluminium pouch, the lyophilized control beads are stable at room temperature (2-30°C) until the expiry date printed on the pouch label. Keep the lyophilized control beads in their sealed pouch until use. When dissolved in the buffer solution, the controls must be used immediately.

8. TEST PROCEDURE

Allow the Ksmart® D-DIMER cassette, diluent tube and sample to reach room temperature (15-30°C) before testing.

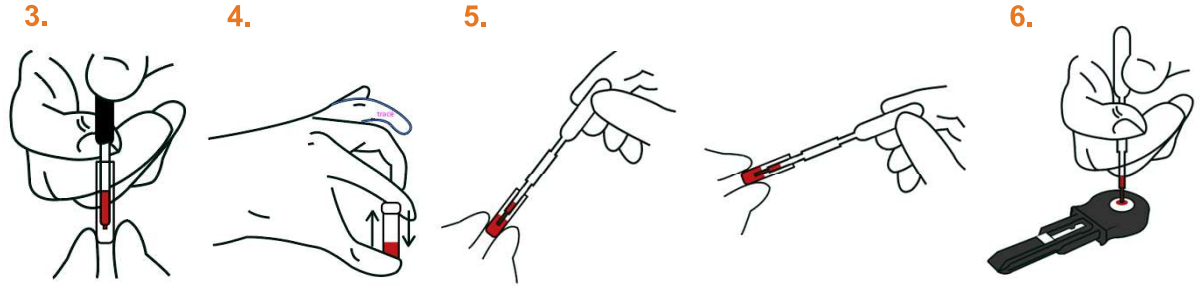
1. Prepare LabPad® Evolution: turn on LabPad® Evolution (please refer to LabPad® Evolution user manual for details)
2. Unpack the Ksmart® from its pouch and place it horizontally on a clean, dry surface.

Procedure for capillary whole blood samples:

3. Unscrew the cap of the diluent tube and discharge the entire capillary blood sample by gently squeezing the pipette plunger.
4. Close the diluent tube and homogenise by successive inversion (approximately 30 seconds). Tilt the tube with a rapid downward movement three times to recover the entire volume of diluted sample.
   ⚠ Do not vortex the diluent tube.
5. Unscrew the cap of the diluent tube and collect 80 µL of diluted sample using the transfer pipette provided: insert the tip of the pipette in contact with the liquid and gently tilt the diluent tube horizontally **without pressing the bulb**. The pipette fills automatically by capillary action to the black mark.
6. Dispense the entire contents of the transfer pipette into the sample well of the Ksmart®. Avoid the formation of air bubbles during transfer.
7. Start the timer and leave the Ksmart® on the bench for 1 minute (until the migration front reaches the bottom of the cassette) and then insert it into the LabPad® Evolution. The reader will automatically read the test at the appropriate time and the result will be displayed after 4 minutes.
8. Press the eject button on the LabPad® Evolution and discard the test device in an appropriate biowaste container.

Procedure for venous whole blood samples:

3. Unscrew the cap of the diluent tube and discharge 20 µL of venous blood into it with a laboratory pipette.
4. Close the diluent tube and homogenise by successive inversion (about 30 seconds). Tilt the tube with a rapid downward movement three times to recover the entire volume of diluted sample.
   ⚠ Do not vortex the diluent tube.
5. Unscrew the cap of the diluent tube and collect 80 µL of diluted sample using the transfer pipette provided: insert the tip of the pipette in contact with the liquid and gently tilt the diluent tube horizontally **without pressing the bulb**. The pipette fills automatically by capillary action to the black mark.
6. Dispense the entire contents of the transfer pipette into the sample well of the Ksmart®. Avoid the formation of air bubbles during transfer.
7. Start the timer and leave the Ksmart® on the bench for 1 minute (until the migration front reaches the bottom of the cassette) and then insert it into the LabPad® Evolution. The reader will automatically read the test at the appropriate time and the result will be displayed after 4 minutes.
8. Press the eject button on the LabPad® Evolution and discard the test device in an appropriate biowaste container.



⚠ If the Ksmart® is inserted into the reader before the sample is fully absorbed into the well (i.e. before the end of the minute migration time), this may cause incorrect sample migration which may lead to an error message on the LabPad® Evolution. In this case, repeat the test with a new sample and a new Ksmart®.

9. INTERPRETATION OF RESULTS

- LabPad® Evolution automatically determines the D-dimer concentration in the sample and displays the quantitative result expressed as ng/mL Fibrinogen Equivalent Unit (FEU).
- If an error message is displayed by the LabPad® Evolution, please refer to the user manual of the meter.

10.QUALITY CONTROL

Quality control checks should be carried out at regular intervals to verify the validity of the test and confirm the results obtained. It is recommended that a quality check be performed every 100 measurements or every 6 months to ensure that the test is performing well.
Quality control materials are included in the assay kit and must be used with the Ksmart® D-DIMER cassettes provided in the same kit.

Procedure for quality controls:

The control beads provided in the Ksmart® D-DIMER + Controls kit allow the preparation of two D-DIMER control levels: a low D-DIMER control (Low) and a high D-DIMER control (High). To perform Quality control tests, it is mandatory to use the Quality Control (QC) mode of the LabPad® Evolution. Please refer to the chapter 8 of the LabPad® Evolution user manual for more information.

⚠ The same procedure applies to the Low D-DIMER Control (red cap) and High D-DIMER Control (green cap)

Procedure:

1. Allow the Ksmart® cassette and Control tube to reach room temperature (15-30°C) prior to testing.
2. Prepare the LabPad® Evolution: turn on the LabPad® Evolution analyser and go to the QC mode of the LabPad®:" Select « Settings », then « Measurements », then « Quality control » then «Continue». (Chapter 8 of the LabPad® Evolution user manual).
3. Unpack the Ksmart® cassette from the sealed pouch and place it horizontally on a clean, dry surface.
4. Unpack the lyophilized control bead from its sealed pouch.
5. Unscrew the cap of the buffer bottle and transfer the bead into the buffer bottle.
6. Recap the buffer bottle and shake about 30 seconds to dissolve the control bead.
7. Unscrew the control tube and transfer the diluted control onto the Ksmart®, using either the transfer pipette provided or a laboratory pipette calibrated to 80 µL.
   - With transfer pipette: insert the tip of the pipette in contact with the liquid and gently tilt the diluent tube horizontally without pressing the bulb. The pipette fills automatically by capillary action to the black mark. Then dispense the entire contents of the pipette into the sample well of the Ksmart®.
   - With laboratory pipette: collect 80 µL of liquid with the laboratory pipette then dispense into the sample well of the Ksmart®
8. Start the timer and leave the Ksmart® on the bench for 1 minute (until the migration front reaches the bottom of the cassette) and then insert it into the LabPad® Evolution. The reader will automatically read the test at the appropriate time and the result will be displayed after 4 minutes.
9. Discard the test device in an appropriate biowaste container by pressing the eject button on the LabPad® Evolution.

Target values:

To find out the target high and low values for this batch of Ksmart® cassettes, please refer to the card "Quality Control card" included in the kit. ("Target" = targeted D-dimer value; "Range" = range of expected value at a confidence interval of 95%).

⚠ If the values obtained for the controls are outside the confidence interval, please proceed to a 2nd control.

11.PERFORMANCE

Range of measurement

When used with the LabPad® Evolution instrument, the Ksmart® D-DIMER + Controls test provides a quantitative D-dimer value in the range of 250 to 5,000 ng/mL FEU. The instrument displays "< 250 ng/mL FEU" if the D-dimer concentration is less than 250 ng/mL FEU and displays "> 5000 ng/mL FEU" if the D-dimer concentration is greater than 5,000 ng/mL FEU.

Linearity

In the linearity range 250-5,000 ng/mL FEU, the linear regression coefficient is $r \geq 0.95$.

Limit of quantification (LoQ)

The limit of quantitation for the Ksmart® D-DIMER + Controls assay is 250 ng/mL FEU.

Hook effect

No hook effect was observed with the Ksmart® D-DIMER + Controls assay at D-dimer concentrations up to 40,000 ng/mL FEU.

Precision

Intra-run precision:
The intra-assay coefficient of variation is CV<15%.
Inter-run precision:
The inter-assay coefficient of variation is CV<20%.

Cross reactivity

No cross-reactivity was observed with human anti-mouse antibodies (HAMA) concentrations up to 200 ng/mL.

Interfering substances

The following potentially interfering substances were tested on samples containing different concentrations of D-dimer: triglycerides (1,000 mg/dL), bilirubin (20 mg/dL), haemoglobin (1,000 mg/dL) and rheumatoid factors (320 U/mL). None of the substances tested showed any interference.

Hematocrit

Hematocrit levels between 30% and 50% do not significantly affect Ksmart® D-DIMER + Controls results. However, the use of the Ksmart® D-DIMER + Controls test in subjects with hematocrit levels outside of the 30-50% range may result in an increase of more than 20% for hematocrit levels < 30% (anemia) or a decrease of more than 20% for hematocrit levels > 50% (polycythemia).

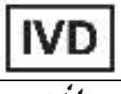
12.LIMITATIONS

- Failure to follow the testing procedure may adversely affect the performance of the test and/or invalidate the test result.
- Any clinical diagnosis based on the test result must be supported by the full judgment of the physician involved, including clinical symptoms and other relevant test results.
- It is the responsibility of each user to verify the appropriateness of the values obtained for their patient population.
- Human anti-mouse antibodies (HAMA) may be present in patients who have received immunotherapy with a murine monoclonal antibody. Although no cross-reactivity of HAMA has been observed with this test, it is recommended that results obtained in patients treated with HAMA be interpreted with caution.

13. LITERATURE

1. Myasoedova V A , Poggio P , Parolari A . A prominent role of D-Dimer in inflammation and atherosclerosis[J]. Vessel Plus, 2017.
2. Han-Xiao, Sun H , Ge Z Q , et al. Clinical laboratory investigation of a patient with an extremely high D-Dimer level: A case report[J]. World Journal of Clinical Cases, 2020, v.8(16):189-195.
3. Zhao J , Endocrinology D O . Effects of Alprostadil and Epalrestat Combined With Compound Three Dimensional B on Diabetic Peripheral Neuropathy[J]. China Continuing Medical Education, 2017.
4. Boissier E. et al., Recommandations préanalytiques en hémostase : stabilité des paramètres d'hémostase générale et délais de réalisation des examens., 2017.

14. INTERNATIONAL SYMBOLS

	Consult instructions for use or electronic instructions for use		Contains sufficient for <n> tests
	Catalogue number		*In vitro* diagnostic medical device
	Do not reuse		Keep dry
	Temperature limits		Use-by-date

	Manufacturer		Batch code
	Buffer		Importer
	Authorized representative in Switzerland		Do not use if package is damaged and consult the instructions for use
	Unique device identifier		Minivette® POCT 20 µL
	Transfer pipette 80 µL		Positive control

15. MANUFACTURER INFORMATION

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