D-DIMER-CHECK-1
Qualitative determination of D-Dimer in whole blood and plasma samples

I- INTENDED PURPOSE

The D-DIMER-CHECK-1 is a rapid screening test for the detection of D-Dimer in citrated plasma and whole blood samples as a tool to assess coagulation disorders by medical healthcare professionals. The determination of D-Dimers only is not sufficient to diagnose deep vein thrombosis nor pulmonary embolism.

II- PRINCIPLE

Fibrinogen is one of the main proteins of the blood coagulation system. As a result of the blood coagulation, thrombin is activating fibrinogen into fibrin monomers which are leading to clots formation (1). Fibrin clots are then digested by plasmin and D-Dimer, which is the main and the smallest component of fibrin clots lysis, is released into the bloodstream. The presence of D.Dimer in blood samples is an indicator of various coagulation disorders, including deep venous thrombosis (DVT), pulmonary embolism (PE) (2, 3) and atherosclerosis. D-Dimer assay is a widely used and simple exclusion method of DVT and PE (4) which is, in addition, not requiring any expensive laboratory instruments (5, 6). In healthy individuals, D-Dimer concentration in blood is less than 400 - 500 ng/mL FEU (FEU: Fibrin Equivalent Unit).

The D-DIMER-CHECK-1 is a rapid screening test for the detection of D-Dimer in citrated plasma and whole blood samples.
As the samples flows through the absorbent device, the anti-D-Dimer immunoglobulins dye conjugate binds to the D-Dimer, forming an antibody-antigen complex. This complex binds to the specific polyclonal antibodies directed against human D-Dimers in the positive reaction zone and produces a pink-rose coloured band, if the D-Dimer concentration in the sample is greater than 400 ng/mL FEU. In case of the concentration level is lower than 400 ng/mL FEU, there is no line in the positive reaction zone. The reaction mixture continues flowing through the absorbent device, past the reaction and control zones. Unbound conjugate binds to the reagents in the control zone, producing a pink-rose colour band, demonstrating that the reagents are functioning correctly.

III- D-DIMER-CHECK-1 KIT COMPONENTS

Each kit contains everything needed to perform 10 or 20 tests.

1- D-DIMER-CHECK-1 test devices:	10	20
2- Disposable plastic pipettes:	10	20
3- Diluent in a dropper bottle:	2.5mL	5 mL
4- Instructions leaflet:	1	1

CE

IV- STORAGE AND STABILITY

1- All D-DIMER-CHECK-1 kit components should be stored at any temperature between +4°C and +30°C in the sealed pouch.
2- ***Do not freeze the test kit.***
3- The D-DIMER-CHECK-1 kit is stable until the expiry date stated on the package label.

V- PRECAUTIONS

1- This test is designed for *in vitro* diagnostic use and professional use only.
2- Read carefully the instructions before using this test.
3- Handle all specimens as if they contained infectious agents. When the assay procedure is completed, dispose of specimens carefully after autoclaving them for at least one hour. Alternatively, they can be treated with 0.5% to 1% solution of sodium hypochlorite for one hour before disposal.
4- Wear protective clothing such as laboratory coats and disposable gloves while assaying samples.
5- Do not eat, drink or smoke in the area where specimens and kit reagents are handled.
6- Avoid any contact between hands and eyes or nose during specimen collection and testing.
7- Do not use beyond the expiry date which appears on the package label.
8- Do not use a test from a damaged protective wrapper.
9- When the test is to be performed with whole blood, fresh samples should be used (< 4 hours).
10- If plasma samples are to be assayed, please use only citrated samples.
11- Please dispose of used device, and pipette in the appropriate waste bin.

VI- SPECIMEN COLLECTION AND PREPARATION

1- D-DIMER-CHECK-1 test is performed on human citrated plasma or whole blood.
2- The specimen should be collected under the standard laboratory conditions (aseptically in such a way as to avoid haemolysis).
3- Each specimen should be treated as if potentially infectious.
4- Whole blood samples should be tested immediately (< 4 hours).
5- Plasma samples should be collected in citrated collection tubes, if anticoagulant is requested.
6- If the test is to be run within 48 hours after collection the specimen should be stored in the refrigerator (+2°C to +8°C). If testing is delayed more than 48 hours, the specimen should be frozen. The frozen specimen must be completely thawed, thoroughly mixed and brought to room temperature prior to testing. Avoid repeated freezing and thawing.

7- In case of cloudiness, high viscosity or presence of particulate matter into the citrated plasma specimen, it should be diluted with equal volume (V/V) of diluting buffer (not provided but available upon request) before testing.

VII- ASSAY PROCEDURE

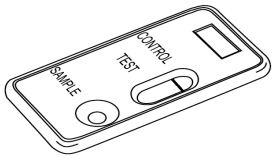
1- Allow samples and D-DIMER-CHECK-1 test devices to come to room temperature prior to testing.
2- Remove the reaction device from its protective wrapper by tearing along the split.
3- Label device with the patient's name or control number.
4- Fill the plastic pipette with specimen (citrated plasma) and, by holding it vertically, dispense one drop (25 µL) into sample well. If whole blood is used, dispense two drops (50 µL) into the sample well **and wait for the whole blood sample to be completely absorbed before adding diluent.**
5- Add 5 or 6 drops of diluent (200 µL) in the sample well.**with an interval of 2-3 seconds between each drop.**
6- Read the results after 10 to 15 minutes. For low positive samples, it is necessary to read the results at 15 minutes.

DO NOT INTERPRET AFTER 15 MINUTES.

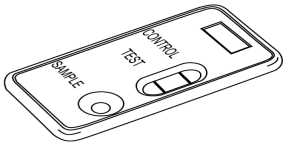
VIII- READING TEST RESULTS

WARNING: The D-DIMER-CHECK-1 rapid test is a qualitative test. Therefore no correlation should be made between the colour intensity of the test line and the D-Dimer concentration in the patient sample. Any visible line in the test area either strong or weak (even much weaker than the control line) should be interpreted as positive.

A. Negative
One coloured band appears in the control zone. No band is visible in the test zone.



B. Positive
In addition to the control band, a clearly distinguishable band also appears in the test zone. D-Dimer concentration is higher than 400 ng/mL FEU.



C. Inconclusive
If there is no distinct colour band visible in the control zone, the test is inconclusive. In this case, repeat the test.

IX- PERFORMANCES CHARACTERISTICS

a) Sensitivity and specificity
29 human plasmas (IN.VENT panel n°01019) and 20 human plasmas obtained from a local clinical laboratory were pre-assayed on VIDAS® BIOMERIEUX analyser and tested with the D-DIMER-CHECK-1. The 48 samples found positive on VIDAS® were also rendered positive by the D-DIMER-CHECK-1 test. The sensitivity is equal to 100%, which is mandatory for this deep venous thrombosis (DVT) exclusion test.
Only one sample was identified as negative on the BIOMERIEUX analyser. So it was not possible to calculate diagnostic specificity for the rapid test.
However, publication results (8) show that the level of specificity for D-Dimer tests is within 19 and 33 % (VIDAS, TINAQUANT and ELISA) for a 500 ng/mL FEU cut-off value.

b) Comparison with a reference method
29 human plasmas (IN.VENT n° 01019) and 20 other plasmas obtained from a local clinical lab were pre-assayed by an EIA method (VIDAS) and then been tested with the D-DIMER-CHECK-1 rapid test. Results are reported in table I.

Human plasmas identification	[D-Dimers] obtained values (VIDAS® BIOMERIEUX)		D-DIMER-CHECK-1
	in µg/mL FEU	Decision regarding the cut-off value	
IN.VENT panel			
1	3.79	+	+
2	2.66	+	+
3	2.82	+	+
4	4.13	+	+
5	2.23	+	+
6	3.90	+	+
7	4.69	+	+
8	2.18	+	+
9	3.16	+	+
10	3.04	+	+
11	1.70	+	+
12	2.68	+	+
13	2.89	+	+
14	1.07	+	+
15	1.43	+	+
16	0.90	+	+
17	0.93	+	+
18	0.56	+	+
19	1.42	+	+
20	1.07	+	+
21	1.72	+	+
22	0.54	+	+
23	1.38	+	+
24	1.20	+	+
25	5.36	+	+
26	1.22	+	+
27	1.40	+	+
28	2	+	+
29	4.35	+	+
Human plasmas panel (local clinical laboratory)			
30	2.67	+	+
31	0.46	-	+
32	10	+	+
33	2.74	+	+
34	0.77	+	+
35	0.54	+	+
36	0.47	-	+
37	1.32	+	+
38	5.04	+	+
39	2.05	+	+
40	5.64	+	+
41	5.07	+	+
42	0.59	+	+
43	1.82	+	+

Human plasmas identification	[D-Dimers] obtained values (VIDAS® BIOMERIEUX)		D-DIMER-CHECK-1
	in µg/mL FEU	Decision regarding the cut-off value	
Human plasmas panel (local clinical laboratory)			
44	1.6	+	+
45	1.65	+	+
46	0.17	-	+/-
47	1.34	+	+
48	1.14	+	+
49	1.08	+	+

Table I

Only sample n° 46 was found negative with the reference method and borderline with the D-DIMER-CHECK-1 rapid test. This discrepancy has no significant impact on the diagnosis as the D-DIMER-CHECK-1 is used as a tool for the exclusion of deep venous thrombosis (DVT), when value is lower than 400 ng/mL.

The diagnostic sensitivity is calculated as follows:
46 x100 = 100% (CI 95% [91.84 – 100]*)
46

The diagnostic specificity is not calculated as the number of negative samples is not significant.

The overall agreement is calculated as follows :
(46+1) x 100 = 95.9% (CI 95% [85.32 – 100]*)
49
**CI 95% : 95% Confidence Interval.*

c) Reference values
Normal values vary with age (10) or during pregnancy (11) and are shown in tables II and III respectively.

Age (years)	Cut-off in ng/mL
<50	450
50-60	600
60-70	700
70-80	850
80-90	950

Table II

Pregnancy trimesters	Cut-off in ng/mL
First	800 – 1,000
Second	1,300 – 1,500
Third	2,000 – 2,300

Table III

D-Dimers levels up to 10 times higher have been observed in patients with severe COVID-19 disease (12).

X- LIMITATIONS

1- The D-DIMER-CHECK-1 test is useful as a negative predictive diagnostic tool. A result lower than 400 ng/mL FEU excludes a DVT or a PE.

2- The specificity of the D-DIMER-CHECK-1 test decreases with the patient's age (700 ng/mL FEU, from 70 years old) and some physiological profiles (1500-2300 ng/mL FEU, in case of pregnancy). Normal pregnancy causes a progressive increase in circulating D-Dimer (5, 11). Therefore, the D-DIMER-CHECK-1 test results have no use in ruling out DVT in the third trimester.
3- The test should not be used for predicting DVT or PE for patients older than 80 years, suffering from cancer (leukaemia), experiencing an infectious or inflammatory process (hepatic cirrhosis, septicaemia, etc…) or having experienced a recent surgical act or trauma.
4- As for any diagnostic procedure, the physician should evaluate the data obtained using this kit in the light of the other clinical information available.
5- Patients presenting DVT symptoms and a high Wells score can show significantly higher false negative results (<20%) (9). Using this test in such circumstances is not advised.
6- If plasma samples are to be assayed, use only citrated samples.
7- Use only fresh whole blood samples (< 4 hours) when test is to be performed with blood samples.
8- If the reading time (maximum 15 minutes) is not strictly respected, wrong results will be obtained.

X1- BIBLIOGRAPHY

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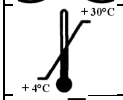
	Read the instructions before use		For *in vitro* diagnostic use
	Temperature limitations		Do not reuse
	Manufacturer		

 Manufactured by VEDALAB - France

CHANGES DESCRIPTION
Changes type:

- N/A — Not Applicable (creation)
- Technical change — Addition, revision and/or removal of information related to the product.
- Administrative — Implementation of non-technical changes noticeable to the end-user.

Changes type	**Change description**
Technical change	Chap IX Addition: CI 95%

Note: Minor typographical, grammar, spelling and formatting changes are not reported in the change details.