D-dimer Rapid Test Cassette (Whole Blood/Plasma) Package Insert

REF CDM-402 English

A rapid test for the qualitative detection of D-dimer in whole blood or plasma.
For professional in vitro diagnostic use only.

INTENDED USE

The D-dimer Rapid Test Cassette (Whole Blood/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of human D-dimer in whole blood or plasma as an aid in the diagnosis of Disseminated Intravascular Coagulopathy (DIC), deep venous thrombosis (DVT) and pulmonary embolism (PE).

SUMMARY

D-dimer (or D dimer) is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two cross linked D fragments of the fibrin protein.[1,2] D-dimer concentration may be determined by a blood test to help diagnose thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients with suspected thrombotic disorders. While a negative result practically rules out thrombosis, a positive result can indicate thrombosis but does not rule out other potential causes. Its main use, therefore, is to exclude thromboembolic disease where the probability is low. In addition, it is used in the diagnosis of the disorder Disseminated Intravascular Coagulopathy.[3,4]

The D-dimer Rapid Test Cassette (Whole Blood/Plasma) is a simple test that utilizes a combination of anti-D-dimer antibody coated particles and capture reagents to qualitatively detect D-dimer in whole blood or plasma. The minimum detection level is 500ng/mL .

PRINCIPLE

The D-dimer Rapid Test Cassette (Whole Blood/Plasma) is a qualitative, membrane based immunoassay for the detection of D-dimer in whole blood or plasma. The membrane is pre-coated with specific capture antibodies in the test line region of the test. During testing, the whole blood or plasma specimen reacts with the particle coated with specific antibodies. The mixture migrates upward on the membrane chromatographically by capillary action to react with specific capture antibodies on the membrane and generate a colored line. The presence of this colored line in the specific test line region indicates a positive result, while its absence indicates a negative result. To serve as a procedural control, a colored line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

The test contains anti-D-dimer antibody conjugated colloid gold particles and capture antibodies coated on the membrane.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after expiration date.
- Do not eat, drink or smoke in the area where the specimens or kits are handled.
- Do not use test if pouch is damaged.
- Handle all specimens as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimens.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
- The used test should be discarded according to local regulations.
- Humidity and temperature can adversely affect results.

STORAGE AND STABILITY

Store as packaged in the sealed pouch either at room temperature or refrigerated (2-30 °C). The test is stable through the expiration date printed on the sealed pouch. The test must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use after the expiration date.

SPECIMEN COLLECTION AND PREPARATION

- The D-dimer Rapid Test Cassette (Whole Blood/Plasma) can be performed using whole blood (from venipuncture or fingerstick) or plasma.
- To collect **Fingerstick Whole Blood specimens**:
  - Wash the patient's hand with soap and warm water or clean with an alcohol swab. Allow to dry.
  - Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
  - Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
  - Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
  - Add the Fingerstick Whole Blood specimen to the test by using **a capillary tube**:
    - Touch the end of the capillary tube to the blood until filled to approximately 25µL. Avoid air bubbles.
    - Place the bulb onto the top end of the capillary tube, then squeeze the bulb to dispense the whole blood to the specimen area of the test cassette.
- To collect **Whole Blood from venipuncture**:
  - Collect blood from venipuncture with the anticoagulants tube (EDTA, Heparin, Citrate and Oxalate) use it directly for the test.
- Separate plasma from blood as soon as possible to avoid hemolysis. Use only clear non-hemolyzed specimens.
- Testing should be performed immediately after the specimens have been collected. Do not leave the specimens at room temperature for prolonged periods. Plasma specimens may be stored at 2-8 °C for up to half-day, for long term storage, specimens should be kept below -20 °C. Whole blood collected by venipuncture should be stored at 2-8 °C if the test is to be run within half day of collection. Do not freeze whole blood specimens. Whole blood collected by fingerstick should be tested immediately.
- Bring specimens to room temperature prior to testing. Frozen specimens must be completely thawed and mixed well prior to testing. Specimens should not be frozen and thawed repeatedly.
- If specimens are to be shipped, they should be packed in compliance with local regulations covering the transportation of etiologic agents.
- EDTA K2, Heparin sodium, Citrate sodium and Potassium Oxalate can be used as the anticoagulant for collecting the specimen.

MATERIALS

Materials provided

- Test Cassettes
- Droppers
- Buffer
- Package insert

Materials required but not provided

- Specimen collection containers
- Centrifuge (for plasma only)
- Lancets(For fingerstick Whole Blood Only)
- Timer
- Heparinized Capillary Tubes and Dispensing Bulb(For fingerstick Whole Blood Only)

DIRECTIONS FOR USE

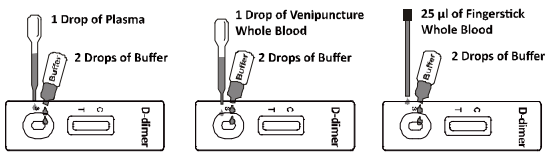
Allow the test, specimen, buffer and/or controls to reach room temperature (15-30 °C) prior to testing.

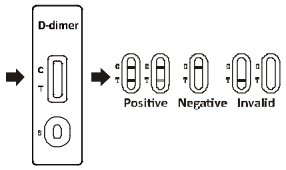
1. Bring the pouch to room temperature before opening it. Remove the test cassette from the sealed pouch and use it within one hour.
2. Place the cassette on a clean and level surface.
   For **Plasma** specimen:
   - Hold the dropper vertically and transfer **1 drop of plasma** (approximately 25µL) to the specimen area, then **add 2 drops of buffer** (approximately 80µL), and start the timer. See illustration below.

   For **Venipuncture Whole Blood** specimen:
   - Hold the dropper vertically and transfer **1 drop of whole blood** (approximately 25 µL) to the specimen area, then **add 2 drops of buffer** (approximately 80 µL), and start the timer. See illustration below.

   For **Fingerstick Whole Blood** specimen:
   - To use a capillary tube: Fill the capillary tube **and transfer approximately 25 µL of fingerstick whole blood specimen** to the specimen area of test cassette, then **add 2 drops of buffer** (approximately 80 µL) and start the timer. See illustration below.
3. Wait for the colored line(s) to appear. Read result at **10 minutes.** Do not interpret the result after 20 minutes.

Note: It is suggested not to use the buffer, beyond 6 months after opening the vial.





INTERPRETATION OF RESULTS

POSITIVE:* A colored line in the control line region (C) and the presence of one colored line in the test line region indicate a positive result. This indicates that the concentration of D-dimer is above the minimum detection level.

***NOTE:** The intensity of the color in the test line region will vary depending on the concentration of D-dimer, present in the specimen. Therefore, any shade of color in the test line region should be considered positive.

NEGATIVE: One colored line appears in the control line region (C). No line appears in the test line region (T).This indicates that the concentration of D-dimer are below the minimum detection levels.

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

QUALITY CONTROL

A procedural control is included in the test. A colored line appearing in the control line region(C) is considered an internal quality procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Control standards are not supplied with this kit; however, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

LIMITATIONS

1. The D-dimer Rapid Test Cassette (Whole Blood/Plasma) is for *in vitro diagnostic use* only. This test should be used for the detection of D-dimer in whole blood or plasma specimens only. Neither the quantitative value nor the rate of increase in D-dimer can be determined by this qualitative test.
2. The D-dimer Rapid Test Cassette (Whole Blood/ Plasma) will only indicate the qualitative level of D-dimer in the specimen and should not be used as the sole criteria for the diagnosis of Disseminated Intravascular Coagulopathy (DIC), Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE).
3. The D-dimer Rapid Test Cassette (Whole Blood/Plasma) cannot detect less than 500ng/mL D-dimer in specimens. A negative result at any time does not preclude the possibility of Disseminated Intravascular Coagulopathy (DIC), Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE).
4. False negative readings can occur if the sample is taken either too early after thrombus formation, if testing is delayed for several days or if the sample was take too later after the occurrence of thromboembolic infarction, because the D-dimer concentration may decrease to normal values after one week already. Additionally, a treatment with anti-coagulants prior sample collection can render the test negative because it prevents thrombus extension.[3,4]
5. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.E.g. use "Wells score" for DVT resp. PE, Ultrasound, quantitative laboratory D-dimer results etc.[2]
6. There is a slight possibility that some whole blood specimens with very high viscosity or which have been stored for more than 2 days may not run properly on the test cassette. Repeat the test with a plasma specimen from the same patient using a new test cassette.
7. The hematocrit of the whole blood should be between 25% and 65%.

EXPECTED VALUES

Increased D-dimer concentration above the widely accepted cut-off value of 500ng/ml FEU (Fibrinogen Equivalent Unit) is a sign of an active fibrinolysis and has been verified at patients with DIC, DVT and PE. Such increased concentrations after surgery and injury and during sickle cell anaemia, liver disease, heavy infections, sepsis, inflammation, malignant disease or in older people too. The concentration of D-dimer rises also during a normal pregnancy.

PERFORMANCE CHARACTERISTICS

Sensitivity and Specificity

421 clinical specimens with known status of D-dimer above or below cut-off value of 500ng/mL collected from local hospitals were tested with D-dimer Rapid Test Cassette (Whole Blood/Plasma) in house. Results indicated relative sensitivity was 97.2%, relative specificity was 94.0%, and the overall accuracy was 96.4% compared with ITM.

Clinical Study Result （In-house）

Method		ITM		Total Results
D-dimer Rapid Test Cassette (Whole Blood/Plasma)	Results	Positive	Negative	
	Positive	312	6	318
	Negative	9	94	103
Total Results		321	100	421

Relative sensitivity: 97.2% (95%CI*: 94.7%~98.7%);
Relative specificity: 94.0% (95%CI*: 87.4%~97.8%);
Accuracy: 96.4% (95%CI*:94.2%~98.0%). *Confidence Intervals

396 clinical specimens were evaluated with D-dimer Rapid Test Cassette (Whole Blood/Plasma) at a German site, results indicated relative sensitivity was 92.0%, relative specificity was 89.9%, and the overall accuracy was 90.2% compared with ITM.

Clinical Study Result (At German site)

Method		ITM			
D-dimer Rapid Test Cassette (Whole Blood/ Plasma)	Results	0-250 ng/ml	250-500 ng/ml	500-2500 ng/ml	>2500 ng/ml
	Positive	5	30	35	11
	Negative	104	207	4	0
Total Results		109	237	39	11
Accuracy:		95.4%	87.3%	89.7%	100%

Relative Sensitivity: 92.0% (95%CI*: 80.8%-97.8%)
Relative Specificity: 89.9% (95%CI*: 86.2%-92.9%)
Accuracy: 90.2% (95%CI*: 86.8%-92.9%) *Confidence Intervals

Precision

Intra-Assay

Within-run precision has been determined by using 10 replicates of below five specimens: D-dimer specimen levels at 0ng/ml, 500ng/ml, 1,000ng/ml, 1,500ng/ml and 3,000ng/ml. The specimens were correctly identified at the prescribed reading time.

Inter-Assay

Between-run precision has been determined by 3 independent assays on the same five specimens: 0ng/ml, 500ng/ml, 1,000ng/ml, 1,500ng/ml and 3,000ng/ml of D-dimer. Three different lots of the D-dimer Rapid Test Cassette (Whole Blood/Plasma) have been tested using these specimens. The specimens were correctly identified at the prescribed reading time

Cross-reactivity

The D-dimer Rapid Test Cassette (Whole Blood/Plasma) has been tested with HBsAg, anti-syphilis, RF, anti-HIV, anti-HCV, anti-H.pylori, anti-Rubella IgG, anti-CMV IgG and anti-Toxo IgG positive specimens. The results showed no cross-reactivity.

Interfering Substances

The following potentially interfering substances were added to D-dimer negative and positive specimens, respectively.

Acetaminophen: 20 mg/dL	Caffeine: 20 mg/dL
Acetylsalicylic Acid: 20 mg/dL	Gentisic Acid: 20 mg/dL
Ascorbic Acid: 20mg/dL	Albumin: 10,500mg/dL
Creatin: 200 mg/dL	Hemoglobin: 1,000 mg/dL
Bilirubin: 1,000mg/dL	Oxalic Acid: 600mg/dL
Cholesterol: 800mg/dL	Triglycerides: 1,600mg/dL

None of the substances at the concentration tested interfered in the assay.

BIBLIOGRAPHY

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3. Dempfl e, Carl-Erik (2005): Bestimmung des D-dimer-Antigens in der klinischen Routine, DeutschesÄrzteblatt Jg. 102, Heft 7, 18. Februar 2005: A428-A432.
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Index of Symbols

	Attention, see instructions for use	Σ	Tests per kit	EC REP	Authorized Representative
IVD	For in vitro diagnostic use only		Use by		Do not reuse
2°C 30°C	Store between 2-30°C	LOT	Lot Number	REF	Catalog #
	Do not use if package is damaged		Manufacturer		Consult Instructions For Use

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