IVD

CE

MediRox

Instructions for Use [EN]

MRX Red D-dimer

REF K5034

For *In vitro* Diagnostic Use.

1 Intended use

Latex immunoassay for quantitative determination of D-dimer in citrated human plasma. Can be used to exclude the presence of thrombosis in patients with suspected venous thromboembolism (VTE) and as an aid in patient management in Covid-19 disease. Intended to be used by professional laboratory personnel using coagulation analysers with turbidimetric detection in the 600 - 800 nm wavelength range.

2 Background and principle of method

Fibrin fragments containing D-dimer antigen is always present in plasma as a result of plasmin degradation of cross-linked fibrin. After an injury, or when suffering from conditions associated with increased haemostatic activity, there is an increase in plasma D-dimer concentration. D-dimer determination has become a common aid in the diagnosis of thrombosis. Elevated levels of D-dimer are found in clinical conditions such as deep vein thrombosis (DVT), pulmonary embolism (PE) and disseminated intravascular coagulation (DIC).[1-4]
A negative D-dimer test result from a patient with a suspected thrombotic disorder has a high negative predictive value.

In patients with Covid-19 disease, increasing plasma D-dimer concentration is seen with worsening disease. Markedly elevated D-dimer is a prognostic marker for mortality and can be used as an aid in managing anti-coagulant treatment of hospitalized Covid-19 patients.[5,6]

MRX Red D-dimer consists of D-dimer specific monoclonal antibodies coupled to sub-micron sized polystyrene particles. When the reagent is exposed to a plasma sample containing D-dimer, the particles will agglutinate, giving rise to increased light-scattering. When exposed to the appropriate wavelength of light, the increase in measured turbidity, or light-scattering, is proportional to the amount of D-dimer in the sample.

3 Components

MRX Red D-dimer consists of:

- Latex Reagent: 5 × 4 mL polystyrene particles, coated with monoclonal antibodies, suspended in buffer with stabilisers and preservatives.
- Reaction Buffer: 5 x 7 mL containing buffer, Heterophilic Blocking Reagent (HBR), and preservatives.

4 Warnings and precautions

Wear suitable clothing for protection. Avoid contact with skin and eyes. Do not empty into drains. Waste must be disposed of in accordance with local regulations.

The Latex Reagent contains Bovine Serum Albumin. The animals were approved by veterinarians by ante- and post-mortem inspections. However, as no method can offer complete assurance, this material should be handled as potentially infectious.

The Latex Reagent and Reaction Buffer contain sodium azide (less than 0.1%) and 2-methylisothiazol-3(2H)-one (less than 0.0015%) to prevent microbial growth; use proper disposal procedures.

EUH208: Contains 2-methylisothiazol-3(2H)-one. May produce an allergic reaction.

EUH210: Safety data sheet available on request.

5 Preparation

- Latex Reagent: Ready to use. As the microparticles will settle during storage, swirl the vial gently a few times every day before use to ensure a homogenous suspension. Do not shake.
- Reaction Buffer: Ready to use. Swirl the vial gently a few times before use.

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6 Storage and stability

- Latex Reagent: Store at 2 - 8 °C. Do not freeze. After opening, stable for 8 weeks at 2 - 8 °C in the closed original vial, provided no contamination occurs. On-board stability: 7 days on Sysmex CS-2100i and ACL TOP.
- Reaction Buffer: Store at 2 - 8 °C. Do not freeze. After opening, stable for 8 weeks at 2 - 8 °C in the closed original vial, provided no contamination occurs. On-board stability: 7 days on Sysmex CS-2100i and ACL TOP.

7 Specimen collection and preparation

Venous blood is collected in 3.2% sodium citrate at a ratio of 9 parts blood to 1 part anticoagulant (1:10 ratio). The ratio is critical. Trauma or stasis during blood sampling should be avoided. Inverse immediately after sampling. The presence of any clots in a specimen is a cause for rejection. Centrifuge to produce platelet-poor plasma and use for analysis. Refer to CLSI guideline H21-A5 for further instructions on specimen collection, handling and storage.[7]

8 Procedure

For each instrument, refer to its operator's manual and to the instrument-specific application sheet.

9 Material required but not provided

Coagulation analyser capable of turbidimetric detection in the 600 - 800 nm wavelength range, pipettes, and the following:

Calibrator	REF
MRX D-dimer DDU Calibrator or MRX D-dimer FEU Calibrator	K5012 or K5045

Control material	REF
MRX Routine Normal Control MRX Routine Abnormal Control	K5039 K5040

Solutions	REF
Phosphate buffered saline (PBS) for dilution, e.g. MRX PBS Diluent	K5047
Deionised water for reconstitution e.g. MRX Laboratory Water	K5036

10 Quality control

To maintain consistent assay results, it is recommended that control plasmas are assayed at regular intervals. MRX Routine Controls (K5039/K5040) are recommended for MRX Red D-dimer. Each laboratory should establish a control range to determine the allowable variation in the day-to-day performance of the test, as well as appropriate intervals for analysing controls in accordance with good laboratory practice. Recalibration is suggested at least when control plasmas are not within the acceptable range and each time a new batch of reagent is used.

11 Results

The results are reported in ng/mL D-dimer Units (DDU) or Fibrinogen Equivalent Unit (FEU) depending on the calibrator used (K5012/K5045).

Samples that are reported above the measuring range should be manually diluted and re-analysed. No result outside the measuring range should be used in forming a diagnosis or for patient management.

12 Expected values

The normal level of D-dimer in the population is typically below 200 ng/mL DDU.[4,8] Elevated levels of D-dimer are found in patients with deep venous thrombosis (DVT), pulmonary embolism, disseminated intravascular coagulation, severe Covid-19 disease and trauma.[5,9] D-dimer levels increase during pregnancy and with age.[10,11]

As there is no internationally established standard for D-dimer, the concentration of D-dimer in any given specimen may differ when determined using D-dimer assays from different manufacturers. Thus, each laboratory should establish its own reference intervals or cut-off levels.

13 Limitations and interfering substances

The results should be used together with other clinical and diagnostic information in forming a diagnosis and for patient management.

Turbid or opalescent plasma may cause erratic results and should be interpreted with caution: dilute the sample and re-assay. MRX Red D-dimer is insensitive to the following substances on Sysmex CS-instrument series:

Interfering substance	Tolerance
Bilirubin	Up to 40 mg/dL
Haemoglobin	Up to 1000 mg/dL
Triglycerides	Up to 1000 mg/dL
Unfractionated heparin	Up to 330 U/dL
Low molecular weight heparin	Up to 330 U/dL

Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain anti-mouse antibodies (HAMA), which may cause over-estimation of D-dimer values. The presence of rheumatoid factor may also result in falsely elevated D-dimer values. The reaction buffer includes HBR that reduces unspecific reactions, but users should be aware that there still is a possibility of over-estimated D-dimer values for samples with HAMA or rheumatoid factor.

The monoclonal antibody in MRX Red D-dimer has been screened for its specificity against cross-linked fibrin degradation products. MRX Red D-dimer has more than 100-fold specificity for D-dimer (fibrin or purified D-dimer), over fibrinogen, fibrinogen D, or fragment E.

14 Analytical performance characteristics

The following performance data was obtained with a Sysmex CS-2100i instrument. Performance will depend on the instrument used.

MRX Red D-dimer has a measuring range of 230 - 8800 ng/mL FEU. There is no prozone effect below 250 000 ng/mL FEU.

Precision:

Sample	Mean FEU	Repeatability CV
Level 1	1060 ng/mL	3.5%
Level 2	2880 ng/mL	2.0%
Level 3	4230 ng/mL	1.4%

15 Reporting of incidents

Any serious incidents that occur in relation to this device shall be reported to Nordic Biomarker as well as the national competent authority in which the user is established.

16 Additional information

A paper copy of these Instructions for Use is available on request. Contact your local distributor.
The instrument-specific application sheet is available from your local distributor.

17 References

1. HEIT, John A., et al. Determinants of plasma fibrin D-dimer sensitivity for acute pulmonary embolism as defined by pulmonary angiography. *Archives of Pathology and Laboratory Medicine*, 1999, 123.3: 235-240.
2. BOUNAMEAUX, Henri, et al. Plasma measurement of D-dimer as diagnostic aid in suspected venous thromboembolism: an overview. *Thrombosis and haemostasis*, 1994, 71.01: 001-006.
3. PFITZNER, Susanne A., et al. Fibrin Detected in Plasma of Patients with Disseminated intravascuiar Coagulation by Fibrin-specific Antibodies Consists Primarily of High Molecular Weight Factor XIIIa-crosslinked and Plasmin-modified Complexes Partially Containing Fibrinopeptide A. *Thrombosis and haemostasis*, 1997, 78.09: 1069-1078.
4. LINDAHL, T. L., et al. Clinical evaluation of a diagnostic strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-dimer. *Scandinavian journal of clinical and laboratory investigation*, 1998, 58.4: 307-316.
5. ROSTAMI, Mehrdad; MANSOURITORGHABEH, Hassan. D-dimer level in COVID-19 infection: a systematic review. Expert review of hematology, 2020, 13.11: 1265-1275.
6. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed [2022-05-05].
7. CLSI. Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline – Fifth Edition. CLSI document H21-A5. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
8. GARDINER, Chris, et al. An evaluation of rapid D-dimer assays for the exclusion of deep vein thrombosis. *British journal of haematology*, 2005, 128.6: 842-848.
9. MEISSNER, Mark H.; CHANDLER, Wayne L.; ELLIOTT, Jennifer S. Venous thromboembolism in trauma: a local manifestation of systemic hypercoagulability?. *Journal of Trauma and Acute Care Surgery*, 2003, 54.2: 224-231.
10. BALLEGEER, V., et al. Fibrinolytic response to venous occlusion and fibrin fragment D-dimer levels in normal and complicated pregnancy. *Thrombosis and haemostasis*, 1987, 58.08: 1030-1032.
11. KARIO, Kazuomi; MATSUO, Takefumi; KOBAYASHI, Hiroko. Which factors affect high D-dimer levels in the elderly?. *Thrombosis research*, 1991, 62.5: 501-508.

18 Definition of symbols

	Manufacturer	 nordicbiomarker.com/IFU	Consult electronic instructions for use
	CE mark		Use-by date
	In vitro diagnostic medical device		Temperature limit
	Catalogue number		Biological risks
	Batch code		Contains biological material of animal origin

19 Revision history

Version	Changes to previous version
4.0	Added translation into German.