



Instructions for Use

MRX Red D-dimer, K5073

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Instructions for Use [EN]

MRX Red D-dimer

REF K5073For *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 analysers with turbidimetric detection in the 600 - 800 nm wavelength range.

2 Valid combinations

This device is intended for use in combination with an instrument with turbidimetric detection.

Valid combinations are:

Reagent	Instrument	Instrument settings
K5073	Sysmex CS-series	Refer to your local distributor for instrument-specific application sheets
	Sysmex CN-series	

Note that if the device is used in combination with other instruments or other instrument-specific application sheets not provided by Nordic Biomarker, the combination must be validated in accordance with Regulation (EU) 2017/746.

3 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 over time, is proportional to the amount of D-dimer in the sample.

4 Components

MRX Red D-dimer consists of:

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

5 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 and Reaction Buffer contain material of animal origin and should be handled as potentially infectious.

The Latex Reagent contains synthetic polymer microparticles. Therefore, ensure that no residues are released into wastewater or the environment. Do not rinse the container before disposal.

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.

6 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.

7 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. For information regarding on-board stability, refer to the instrument-specific application sheet.
- 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. For information regarding on-board stability, refer to the instrument-specific application sheet.

8 Material required but not provided

- Analyser with turbidimetric detection in the 600 - 800 nm wavelength range (refer to section 2 for valid instruments) and pipettes.
- MRX D-dimer Calibrator for calibration.
- Control materials with different D-dimer levels for quality control.
- Phosphate buffered saline (PBS) for sample dilution.

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

Recommended materials are presented below:

Control material	REF
MRX Routine Normal Control and	K5039
MRX Routine Abnormal Control or	K5040
MRX Specialty Normal Control and	K5021
MRX Specialty Abnormal Control	K5022

Solutions for sample dilution	REF
MRX PBS Diluent	K5047

9 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. Invert 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

10 Procedure

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

10.1 Application settings

Enter the product specific settings in the instrument according to the instrument-specific application sheet.

10.2 Calibration

Each lot of MRX Red D-dimer must be calibrated prior to determination of D-dimer values in patients' plasma samples. Calibrate the assay according to the instrument-specific application sheet. The lot-specific D-dimer concentration of the calibrator is found in the Certificate of Analysis for the calibrator used (K5012/K5045).

Recalibration must be performed when a new lot of reagent is introduced and it is also suggested when controls are not within the acceptable range.

10.3 Quality control

To maintain consistent assay results, it is recommended that controls in different levels are analysed together at regular intervals. Each laboratory is recommended to establish its own acceptable 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. A new acceptable range must be determined for each individual lot of controls. Refer to section 8 "Material required but not provided" for recommended control materials.

10.4 Sample analysis

For analysis of samples, refer to the instrument operator's manual.

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).

Result in ng/mL DDU can be converted to ng/mL FEU by a conversion factor of 2.5.

Ex. 200 ng/mL DDU = 500 ng/mL FEU

Results in ng/mL can be converted to mg/L or µg/mL.

Ex. 500 ng/mL FEU = 0.5 mg/L FEU = 0.5 µg/mL FEU

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 500 ng/mL FEU.^{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}

Expected values in the normal population were estimated based on analysis of 120 healthy blood donors using MRX Red D-dimer on Sysmex CS-series instrument.

No. of samples	Expected values
120	0–556 ng/mL FEU ^a

^a 95% confidence interval

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. In addition, the expected values differ depending on the population being studied. Thus, each laboratory should establish its own expected values.

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-series instruments:

Interfering substance	Tolerance
Bilirubin	Up to 40 mg/dL
Haemoglobin	Up to 990 mg/dL
Triglycerides	Up to 1500 mg/dL
Unfractionated heparin	Up to 330 U/dL
Low molecular weight heparin	Up to 330 U/dL
Rheumatoid factor	Up to 1200 IU/mL

For interfering substances for other valid instruments in section 2, refer to the instrument-specific application sheet.

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 fragment D, or fibrinogen fragment E.

14 Analytical performance characteristics

Analytical performance characteristics for MRX Red D-dimer on Sysmex CS-series instruments:

Measuring range:

Limit	ng/mL FEU
Lower Limit	265
Upper Limit	9138
No prozone effect below	250 000

Precision:

Sample	Repeatability		Reproducibility	
	ng/mL FEU	CV %	ng/mL FEU	CV %
Level 1	1064	2.8	909	9.9
Level 2	2882	1.9	2250	2.5
Level 3	4229	1.4	3712	4.6

For analytical performance characteristics for other valid instruments in section 2, refer to the instrument-specific application sheet.

15 Clinical performance characteristics

The following clinical performance for exclusion of thrombosis in patients with suspected VTE was obtained using the diagnostic cut-off 500 ng/mL FEU.¹²

D-dimer assay	Sensitivity (95% CI)	Specificity (95% CI)	NPV
Medirox MRX (n=810)	0.94 (0.90–0.99)	0.66 (0.62–0.69)	0.99

Medirox MRX, current product name is MRX Red D-dimer; CI, confidence interval; NPV, negative predictive value.

The use of an age-adjusted cut-off, of age × 10 ng/mL FEU (for patients ≥ 50 years) increases the diagnostic specificity to 0.72 (95% CI 0.69–0.76), thus increasing the diagnostic utility of the assay.¹²

In patient management in Covid-19 disease, the D-dimer result shall only be used as one of several parameters.^{6,13} Thus, clinical performance characteristics based only on MRX Red D-dimer is not relevant.

16 Summary of Safety and Performance

The Summary of Safety and Performance (SSP) is available in the European database on medical devices (Eudamed), where it is linked to this Basic UDI-DI, 7350060320026N. The Eudamed public website is found on <https://ec.europa.eu/tools/eudamed>. In case Eudamed is not fully functional, the SSP is available from Nordic Biomarker on request.

17 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.

18 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.

19 References

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20 Definition of symbols

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

21 Revision history

Version	Changes to previous version
4.0	Section 5: Information on material of animal origin updated, and information on synthetic polymer microparticles added. Section 13 and 14: Addition of information for other instruments. Minor editorial revisions made.