DIAGON
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INSTRUCTION FOR USE

Dia-D-Dimer B

CE

Cat.No.: 07912 Dia-D-Dimer B 4 x 3 ml

Intended use

Dia-D-Dimer B is an immunoturbidimetric assay used for the quantitative determination of the fibrin degradation products that contain D-dimer in human plasma. D-dimer containing moieties are formed by plasmin degradation of factor XIII a cross-linked fibrin. Elevated levels of D-dimer are found in clinical conditions such as deep vein thrombosis (DVT), pulmonary embolism (PE) and disseminated intravascular coagulation (DIC)[1-3]. Laboratory measurements of fibrin degradation products, including D-dimer, have significance in the initial assessment of these conditions. Dia-D-Dimer B is a turbidimetric assay that utilises antibody coated latex particles. In the presence of D-dimer, the particles aggregate and turbidity increases. The increase in scattered light is proportional to the amount of D-dimer in the sample. The latex particles are coated with a monoclonal antibody that reacts with fibrin D-dimer or fragment D of fibrin. The antibody has no cross reactivity with fibrinogen[4]. This allows for the determination of D-dimer in human plasma.

Warnings

The reagents contained in this kit are for *in vitro* diagnostic use only. **DO NOT INGEST!** Wear gloves when handling all kit components.

Precautions

Refer to the product safety data sheets for risk and safety phrases and disposal information. The D-Dimer Calibrator is of human origin. Plasma products have been screened and found negative (unless otherwise stated on the kit box or vial) for the presence of Hepatitis B Antigen (HbsAg) HIV 1 and 2 antibody and HCV antibody; however they should be handled with the same precautions as a human plasma sample.

Materials provided

Important: The reagents are lot-specific. Lots are not interchangeable.

Component	Content	Description	Preparation
D-Dimer Blue Latex	4 x 3 mL	Latex particles coated with anti-D-dimer monoclonal antibody.	Ready to use. The latex may sediment during storage. Mix thoroughly before use.
D-Dimer Blue Buffer	4 x 7 mL	Containing buffer and preservatives.	Ready to use.
D-Dimer Diluent	2 x 7 mL	Containing buffer and preservatives.	Ready to use.
D-Dimer Calibrator	2 x 1 mL	Lyophilised human plasma enriched with D-dimer.	Reconstitute each vial of the appropriate calibrator with 1 mL of D-Dimer Diluent. Swirl gently. Allow to stand for 15 minutes for complete dissolution and mix well before use.
Each kit contains instructions for use.			
Each kit contains lot specific reference values insert.			

Materials required but not provided

Analyser operable at 350-600 nm. Diagon Ltd. supplies the following controls available for use with this product:

Cat.No.: 09102 Dia-CONT Ddi N

Cat.No.: 09202 Dia-CONT Ddi P

Storage and stability

Unopened reagents are stable until the given expiry date when stored under storage conditions. Once reconstituted, the controls are stable for 8 hours when kept at $^{+}2$ –$^{+}8$°C. The lyophilised product should appear as a dry, straw coloured plug or pieces. Any deviation from this appearance should be advised to the manufacturer before use.

D-Dimer Latex	Once opened, the reagent is stable for 4 weeks at $^{+}2$ – $^{+}8$°C or 2 weeks at $^{+}20$°C.
D-Dimer Buffer	Once opened, the reagent is stable for 4 weeks at $^{+}2$ – $^{+}8$°C or 2 weeks at $^{+}20$°C.
D-Dimer Diluent	Store at $^{+}2$ –$^{+}8$°C and use within 4 weeks of opening.
D-Dimer Calibrator	Once reconstituted, the reagent is stable for 12 hours at $^{+}4$ –$^{+}25$°C.

Sample Collection and Preparation

Plastic or siliconised glass should be used throughout. Blood (9 parts) should be collected into 3.2% sodium citrate anticoagulant (1 part). Separate plasma after centrifugation at 1500 x g for 15 minutes[5]. Plasma should be kept at $^{+}2$ – $^{+}8$°C or $^{+}18$ –$^{+}24$°C.

Testing should be completed within 24 hours of sample collection, or plasma can be stored frozen at -20°C or -70°C for 24 months[6]. Thaw quickly at $^{+}37$°C prior to testing. Do not keep at $^{+}37$°C for more than 5 minutes.

Procedure

Preparation of Standard Curve

Use the lot-specific value for D-Dimer Calibrator to determine the exact D-dimer concentration in each standard dilution. Users must construct a standard curve each time a new kit lot is used, after any instrument change or service, or every 6 months, and if D-Dimer Control H/L is assayed out of range.

Automated method

Refer to the appropriate instrument operator manual for detailed instructions or contact Diagon Ltd for instrument specific application guides.

Interpretation of results

The test should be used in conjunction with clinical observations and results of other laboratory tests. Elevated levels are found in patients with confirmed DVT, PE, DIC, and trauma[1-3]. D-dimer levels rise during pregnancy and high levels are associated with complications[7]. The results may be reported either in D-dimer units or in fibrinogen equivalent units (FEU); 1 ng/mL of D-dimer is equivalent to approximately 2 ng/mL of FEU, however, a more accurate conversion factor, originating from the Fibrinogen/D-dimer weight ratio of 340 kDa/195 kDa, would be 1.74[8].

Limitations

Presence of rheumatoid arthritis factor may result in false-positive results (influence not quantified). Results from patients with heterophilic antibody should be interpreted with caution since this test kit contains mouse antibodies and interference may occur resulting in falsely elevated or decreased values. Turbid or opalescent plasma

may cause erratic results and should be interpreted with caution.

Quality control

Each laboratory should establish a quality control program. Normal and abnormal control plasmas should be tested prior to each batch of patient samples, to ensure satisfactory instrument and operator performance. If controls do not perform as expected, patient results should be considered invalid. It is recommended that the D-dimer low control and D-dimer high control are assayed at regular intervals in order to ensure consistent assay results. If the D-Dimer Control H/L result deviates from the D-dimer concentration given in the lot-specific Instruction for Use, a new standard curve should be constructed.

Reference values

The concentration of D-dimer in any given specimen may differ from the concentration determined using D-dimer assays from different manufacturers.

Reference values can vary between laboratories depending on the techniques and systems in use. For this reason each laboratory should establish its own reference ranges.

Performance characteristics

The following performance characteristics have been determined by Diagon Ltd using a photo-optical coagulation instrument. The user should establish product performance characteristics for the specific instrumentation used.

Reproducibility

		Intra-assay precision		Inter-assay precision	
Sample	***n***	***D-dimer (ng/mL)***	***CV (%)***	***D-dimer (ng/mL)***	***CV (%)***
Medium	42	1680	2.54	1622	1.21
Low	42	387	5.31	384,55	0.84

Dia-D-Dimer B is insensitive to the following substances: haemoglobin (up to 4 g/L), bilirubin (up to 0.1 g/L), triglycerides (up to 25 g/L), low molecular weight heparin (up to 100 U/mL), and non-fractionated heparin (up to 100 U/mL).

References

1. Declerck P *et al.* (1987) Fibrinolytic response and fibrin fragment D-dimer levels in patients with deep vein thrombosis, *Thrombosis and Haemostasis*,**58:**1024-1029
2. Lindahl T *et al.* (1998) Clinical evaluation of a diagnostic strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-dimer, *Scand. J. Clin. Lab. Invest*, **58:**307-316
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4. Holvoet P *et al.* (1989) Binding properties of monoclonal antibodies against human fragment D-dimer of cross-linked fibrin to human plasma clots in an in vivo model in rabbits, *Thrombosis and Haemostasis*,**61:**307-313

5. Clinical and Laboratory Standards Institute (2008) Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Haemostasis Assays: Approved Guideline, 5th edn. CLSI: H21-A5
6. Clinical and Laboratory Standards Institute (2011) Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease; Approved Guideline, CLSI: H59-A
7. Ballegeer V *et al.* (1987) Fibrinolytic response to venous occlusion and fibrin fragment D-dimer levels in normal and complicated pregnancy, *Thrombosis and Haemostasis*, **58:**1030-1032
8. Edlund B, Nilsson TK (2006) A proposed stoichiometrical calibration procedure to achieve transferability of D-dimer measurements and to characterize the performance of different methods, *ClinBiochem*,**39(2):**137-142

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Symbols			
IVD	In vitro diagnostics devices		Check in user manual
	Biohazard		Temperature range
	Manufacturer		Expiry date
LOT	LOT number	CE	CE conformity sign
REF	Catalogue number		