BIOLABO
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D-DIMER Turbidimetric Immunoassay

Reagent for determination of D-Dimer in human plasma

REF 13210	**R1** 3 x 7 mL	**R2** 3 x 4 mL
	R3 2 x 1 mL	**R4** 2 x 7 mL

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CE

IN VITRO DIAGNOSTIC USE

CLINICAL SIGNIFICANCE (3-6)

Fibrin fragments containing D-Dimer antigen is always present in plasma as a result of plasmin degradation. After an injury or in case of conditions associated with increased haemostatic activity, the D-Dimer concentration increases in plasma. The determination of D-Dimer concentration is an aid in the diagnosis of thrombosis. Deep vein thrombosis (DVT), pulmonary embolism (PE) and disseminated intravascular coagulation (DIC) are associated with elevated level of D-Dimer. A negative D-Dimer test result has a high negative predictive value for patient with a suspected thrombotic disorder.
This test should be used with other clinical and diagnostic information in order to diagnose and manage patients.

PRINCIPLE

D-DIMER reagent consists in sub-micron sized polystyrene particles coupled to monoclonal antibodies specific for D-Dimer. When plasma specimen containing D-Dimer is exposed to the reagent, the particles will agglutinate, giving rise to increased light-scattering. This phenomenon leads to an increase of absorbance measured at 600-800 nm which is proportional to the concentration of D-Dimer in the specimen.

REAGENTS

R1 D-DIMER Reaction Buffer

Buffer
Preservatives < 0.1%

R2 D-DIMER Latex Reagent

Polystyrene particles coated with monoclonal antibodies
Buffer
Preservatives < 0.1%

R3 D-DIMER Standard

Human Origin

Lyophilised plasma enriched with D-Dimer
The concentration of this standard is batch-specific
(See **Assigned value on the label of the vial**)

R4 D-DIMER Dilution Buffer

For dilution of D-DIMER Standard when constructing the standard curve. May also be used to dilute plasma of patients.

These reagents are not classified as harmful regarding 1272/2008/ EC Regulation

SAFETY CAUTIONS (1) (2)

BIOLABO reagents are designated for professional, in vitro diagnostic use (do not pipette with mouth).
- Refer to current Material Safety Data Sheet available on request or on www.biolabo.fr
- Verify the integrity of the contents before use.
- Waste disposal: Respect legislation in force in the country.

All specimens or reagents of biological origin should be handled as potentially infectious. Respect legislation in force in the country.

REAGENTS PREPARATION

Reagents (R1, R2, and R4) are ready to use
Vial R3: Add 1 mL of demineralised water. Re-close the vial and let stand for complete dissolution. Then mix gently by swirling before use.

STABILITY AND STORAGE

Stored away from light, well caped in the original vial at 2-8°C, reagents are stable when stored and used as described:

Unopened:
- Until expiry date stated on the label of the Kit

Once opened:
- Reagents R1, R2, and R4 are stables 4 weeks at 2-20°C
- Lyophilisate R3 must be reconstituted without delay.
- Once reconstituted, standard R3 is stable 12 hours at 2-25°C, 1 week at 2-8°C and 6 months at -20°C.

SPECIMEN COLLECTION AND HANDLING (7)

Plasma (citrate).
Mix freshly drawn blood (9 Volumes) with buffered tri-sodium citrate solution 0.109M (1 volume). Centrifuge for 10 min. at 3000g and extract supernatant.

LIMITS (10)

Patients who have received mouse monoclonal antibodies for diagnosis or therapy may have plasmas containing anti-mouse antibodies (HAMA). Such antibodies may lead to false enhance D-Dimer concentration. The same may occur with Rheumatoid Factor.
For a more comprehensive review of factors affecting this assay refer to the publication of Young D.S.

MATERIAL REQUIRED BUT NOT PROVIDED

1. Medical analysis laboratory equipment
2. Coagulation analyzer with turbidimetric detection between 600-800nm
3. Demineralised water for reconstitution of standard R3

Manufacturer	Expiry date	In vitro diagnostic	Storage temperature	Demineralized water	Biological risk
Product Reference	See Insert	Batch number	Store away from light	Sufficient for	Dilute with

CALIBRATION (9)

- REF 13210 D-DIMER Standard (R3) traceable to an In-House Reference Preparation which underwent a one-time value assignment to align with another commercially available assay which reports results in ng/mL (DDU).

The calibration frequency depends on proper instrument functions and on the preservation of the reagent.

EXPECTED VALUES (6) (8)

Plasma	< 200 ng/mL (DDU)

D-Dimer concentrations increase during pregnancy and with age.

Each laboratory should establish its own normal ranges for the population that it serves.

PERFORMANCES at 37°C on SOLEA 100

Linearity Range: between 100 and 3200 ng/mL

Detection limit: approx. 98 ng/mL

Precision:

Within-run N = 20	*Low level*	*Normal level*	*High level*
Mean (ng/mL)	214	409	1092
S.D. ng/mL	6.2	8.9	43.5
C.V. %	2.9	2.2	4.0

Between run N = 20	*Low level*	*Normal level*	*High level*
Mean (ng/mL)	408	1029	3210
S.D. ng/mL	10	46	97
C.V. %	2.4	4.4	3.0

Comparison studies with commercially available reagent:
On SOLEA 100 and Sysmex CA-1500 with human specimens (n=50) between 114 and 3095 ng/mL

y = 0.95 x r = 0.9466

Prozone effect: Tested up to 12800 ng/mL, no prozone effect is detected in the measuring range (between 100 and 3200 ng/mL).

Cut-off : 150 ng/mL

Interferences

Triglycerides	Negative interference from 3.31 mmol/L
Total bilirubin	No interference up to 855 µmol/L
Heparin	No interference up to 100 U/mL
Fragmin	No interference up to 100 U/mL
Haemoglobin	Negative interference from 1.86 mmol/L

Other substances may interfere (see § Limits)

On the board stability: at 15°C, in the opened vial stored on the board 8h/day, the rest of time in closed vial at 2-8°C, reagents R1, R2, R4 are stable 4 weeks.

Calibration Stability: Make a new calibration when changing reagent batch, if quality control results are found out of the established range and after maintenance operations.

<u>On a Sysmex CA-1500 instrument</u>

Clinical Sensitivity: 95%

Negative Predictive value: 98%

Performances and stability data on Thrombolyzer Compact X and Sysmex CA-1500 are available on request.

QUALITY CONTROL

- REF 13211 D-DIMER Control 1
- REF 13212 D-DIMER Control 2
- External quality control program

It is recommended to control in the following cases:

- At least once a run.
- At least once within 24 hours.
- When changing vial of reagent.
- After maintenance operations on the instrument.

If control is out of range, apply following actions:

1. Repeat the test with the same control.
2. If control is still out of range, prepare a fresh control serum and repeat the test.
3. If control is still out of range, use a new vial of calibrator or a fresh calibrator and repeat the test.
4. If control is still out of range, calibrate with a new vial of reagent.
5. If control is still out of range, please contact BIOLABO technical support or your local Agent.

PROCEDURE

Automated procedure

Refer to Operator's manual and validated instrument specific application.

CALCULATION

The analyzer provides directly final result.
Refer to the manual of instrument used.

To convert results in Fibrinogen equivalent units (FEU), multiply the result (DDU) by 2.5

REFERENCES

(1) *Occupational Safety and Health Standards; Bloodborne pathogens (29CFR1910.1030) Federal Register July 1, (1998) ; 6, p.267-280*

(2) *Directive du conseil de l'Europe (90/679/CEE) J. O. de la communauté européenne n°L374 du 31.12.1990, p.1-12*

(3) *Heit, J.A. et al. Determinants of plasma fibrin D-Dimer sensitivity for acute pulmonary embolism as defined by pulmonary angiography. Arch Pathol Lab Med, 123:235-239,1999*

(4) *Bounameaux, H., et al. Plasma measurement of D-Dimer as diagnosis aid in suspected venous thromboembolism: an overview. Thromb Haemostas, 71:1-6,1994*

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(6) *Lindhal T. et al. Clinical evaluation of a diagnosis strategy for deep venous thrombosis with exclusion by low plasma levels of fibrin degradation product D-Dimer. Scan J Lab Invest, 58: 307-316, 1998*

(7) *CLSI Approved Guideline H21-A5*

(8) *Gardiner, C. Et al. An evaluationof rapid D-Dimer assays for the exclusion of deep vein thrombosis. British Journal of Haematology, 128:842-848, 2005*

(9) *Section 5.6 of ISO 17511- Measurements of quantities in biological samples- metrological traceability of values assigned to calibrators and controls*

(10) *YOUNG D.S., Effect of Drugs on Clinical laboratory Tests, 4th Ed. (1995) p 3-216 to 3-216*