BIOLABO
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MANUFACTURER:
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D-DIMER Turbidimetric Immunoassay

Reagent for determination of D-Dimer in human plasma

REF K1210	**R1** 1 x 18 mL **R2** 1 x 11 mL **R3** 2 x 1 mL **R4** 1 x 20 mL **R5** 2 x 35 mL
REF K2210	**R1** 1 x 25 mL **R2** 1 x 15 mL **R3** 2 x 1 mL **R4** 1 x 20 mL **R5** 2 x 45 mL

TECHNICAL SUPPORT AND ORDERS
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CE

IVD

Made in France

I: corresponds to significant modifications

I INTENDED USE

This reagent is designated for professional use in laboratory (automated method).
This Latex immunoassay is a quantitative test is to determine D-Dimer in citrated human plasma. It can be used to exclude the presence of thrombosis in patients with suspected thrombotic disorders and as an aid in the management of patients with Covid-19 disease.
I This test should be used with other clinical and diagnostic information in order to diagnose and manage patients.

I GENERALITIES (3-6) (12-13)

Fibrin fragments containing D-Dimer antigen is always present in plasma because 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 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.
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 anticoagulant treatment of hospitalized Covid-19 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 at 400-800 nm which is proportional to the concentration of D-Dimer in the specimen.

I REAGENTS

R1 D-DIMER Reaction Buffer

Buffer

Sodium azide < 0.1%, 2-methylisothiazol-3(2H)-one < 0,0015%

R2 D-DIMER Latex Reagent

Polystyrene particles coated with monoclonal antibodies

Buffer, Sodium azide< 0.1%, 2-methylisothiazol-3(2H)-one < 0,0015%

EUH208: May produce an allergic reaction. EUH210: Safety data sheet available on request

R3 D-DIMER Calibrator

Freeze-dried citrated plasma enriched with D-Dimer. Human origin

Additives of components from bovine plasma

BSA < 4%, Sodium azide < 0,001%

R4 D-DIMER Dilution Buffer

To dilute D-DIMER Calibrator (calibration curve) and plasma of patients.

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

R5 D-DIMER Cleaning Solution

Classification due to sodium hydroxide
Met. Corr. 1: H290 - May be corrosive to metals.
Skin Corr. 1B: H314 - Causes severe skin burns and eye damage.
P280: Wear protective gloves/protective clothing/eye protection/face protection.
P301+P330+P331: IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P303+P361+P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water or shower.
P304+P340: IF INHALED: Remove person to fresh air and keep comfortable for breathing. P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310: Immediately call a poison center/doctor.

I SAFETY CAUTIONS (1) (2)

- Material Safety Data Sheet is available upon request.
- Each human donor unit used to manufacture this product was tested and found non-reactive for HbsAg, antibody to Hepatitis C and antibody to HIV-1/HIV-2.
- Products from animal origin were approved ante and post mortem by veterinarians inspection.
- However, no test method can offer complete assurance that infectious agents are absent. All specimens or reagents from biological origin should be handled as potentially infectious.
- Waste disposal: Respect legislation in force in the country.

Any serious incident that has occurred in connection with the device is notified to the manufacturer and the competent authority of the Member State in which the user and/or patient is based.

I REAGENTS PREPARATION

Reagents (R1, R2, R4, R5) are ready to use.

Swirl gently Latex reagent (R2) before each use to homogenise latex particles.

Calibrator (R3):

- Add 1 mL of demineralized water (15-25°C).
- Recap and wait for approximately 15 minutes at room temperature. Gently agitate until the content is completely dissolved.

I 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, R4, R5) are stable at least 8 weeks at 2-8°C
- Calibrator (R3) must be reconstituted without delay.

Once reconstituted,

- Calibrator (R3) is stable 7 days at 2-8°C and 24h at 20-25°C when free from contamination.

I SPECIMEN COLLECTION AND HANDLING (7)

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

I LIMITS (10)

Turbid or opalescent plasma may cause erratic results and should be interpreted with caution: dilute the sample and re-assay

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. Basic medical analysis laboratory equipment
2. Biochemistry Clinical Analyzer Kenza One, Kenza 240TX/ISE or Kenza 450TX/ISE
3. Demineralized water

I CALIBRATION (9) (11)

- REF 13210 D-DIMER Calibrator (R3) traceable to an In-House Reference Preparation which value was assigned using a working calibrator traceable according to ISO 17511:2020, section 5.6.
- Batch specific value is indicated in the certificate of analysis and on the label of the vial.
- Construct Standard curve as indicated in the application of KENZA analyser used

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

I REFERENCE INTERVAL (6) (8) (14) (15)

Plasma	< 200 ng/mL (DDU)

D-DIMER increase in patients with deep venous thrombosis (DVT), pulmonary embolism, disseminated intravascular coagulation, severe COVID-19 disease and trauma. D-DIMER increase also during pregnancy and with age.

As there is no internationally established standard for D DIMER, the concentration in any given specimen may differ when determined using D-DIMER assays from different manufacturers.

Each laboratory should establish its own reference intervals and cut off levels for the population that it serves.

PERFORMANCES

On automatic analyser SOLEA 100 at 37°C (DDU units):

Measuring 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).

I Cut-off : 200 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 Board stability:
Reagents (R1, R2, R4, R5) may be stored at 15°C (8 hours per day) for 7 days.

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.

Performances will depend on Instrument used.

Performances and stability data on Thrombolyzer Compact X and other instruments 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. Prepare a fresh control serum and repeat the test
2. If control is still out of range, use a new vial of fresh calibrator
3. If control is still out of range, use a new vial of reagent and reassay

If control is still out of range, please contact BIOLABO technical support or your local Agent.

I PROCEDURE

Refer to specific applications of KENZA Analyzer used.

Minimal Software revision required :

- KENZA 240TX/ISE : from 6.13
- KENZA 450TX/ISE : from 2.20
- KENZA ONE : from 2.04

Contact support@biolabo.fr for more details

CALCULATION

The analyzer provides directly final result (DDU units).
Refer to the user's manual of KENZA analyzer.

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

I Samples upper of the measuring range should be diluted with diluent (R4) and re-assayed. No result outside the measuring range should be used for diagnosing nor for patient management

REFERENCES

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(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*

(11) *EN ISO 17511 In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials*

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