Snibe Diagnostic

CE REF 130206008M: 100 tests
130606008M: 50 tests

MAGLUMI® D-Dimer (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of D-Dimer in human plasma using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer (including Maglumi 600, Maglumi 800, Maglumi 1000, Maglumi 1000 Plus, Maglumi 2000, Maglumi 2000 Plus, Maglumi 4000, Maglumi 4000 Plus, MAGLUMI X8, MAGLUMI X3 and MAGLUMI X6) and Biolumi series Integrated System (including Biolumi CX8).

SUMMARY AND EXPLANATION OF THE TEST

D-Dimer (or D dimer) is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two D fragments of the fibrin protein joined by a cross-link. D-Dimers are not normally present in human blood plasma, except when the coagulation system has been activated, for instance because of the presence of thrombosis or disseminated intravascular coagulation[1]. D-Dimer concentration may be determined by a blood test to help diagnose thrombosis. Since its introduction in the 1990s, it has become an important test performed in patients with suspected thrombotic disorders. While a negative result practically rules out thrombosis, a positive result can indicate thrombosis but does not rule out other potential causes. Its main use, therefore, is to exclude thromboembolic disease where the probability is low. In addition, it is used in the diagnosis of the blood disorder disseminated intravascular coagulation[1-2]. The D-Dimer assay depends on the binding of a monoclonal antibody to a particular epitope on the D-Dimer fragment. Several detection kits are commercially available; all of them rely on a different monoclonal antibody against D-Dimer. For some of these, the area of the D-Dimer to which the antibody binds is known. The binding of the antibody is then measured quantitatively by one of various laboratory methods[1].
D-Dimer is commonly used to exclude thromboembolic disease in outpatients suspected of having deep venous thrombosis (DVT) and pulmonaryembolism (PE). DVT and PE is relatively common and can cause sudden, fatal embolic events in the pulmonary arteries and other regions[3-5]. Measurement of the D-Dimer level in plasma has been used as a screening strategy for subclinical DVT. A systematic review reported that a normal range of a highly sensitive D-Dimer level accurately ruled out DVT in patients classified as having a low or moderate clinical probability of DVT. The DVT is a high-risk factor for the stroke because of advanced age, hemiplegia, and coagulation disorders, and DVT can cause paradoxical embolic stroke via a right-toleft shunt. Thus, it is important to monitor the level of D-Dimer the incidence and characteristics of DVT in acute stroke patients[6-8]. The Plasma D-Dimer level has proven to be useful for DVT screening in chronic stroke patients undergoing rehabilitation[9-10].
National and international scientific organizations have suggested the use of these markers when implementing new diagnostic strategies in patients with coronary syndrome. Since D-Dimer is well known to be an important prognostic indicator of heart diseases, its most definitive role is on monitoring post-treatment clinical status and the post therapeutic evaluation of patients[11-12].

PRINCIPLE OF THE TEST

The D-Dimer assay is a sandwich chemiluminescence immunoassay.
The sample (or calibrator/control, if applicable), ABEI labeled with anti-D-Dimer monoclonal antibody, buffer and magnetic microbeads coated with another anti-D-Dimer monoclonal antibody are mixed thoroughly and incubated to form a sandwich; after precipitation in a magnetic field, decant the supernatant, and perform a wash cycle. Subsequently, the Starter 1+2 are added to initiate a flash chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which is proportional to the concentration of D-Dimer present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material provided

Components	Contents	100 tests (REF: 130206008M)	50 tests (REF: 130606008M)
Magnetic Microbeads	Magnetic microbeads coated with anti-D-Dimer monoclonal antibody, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	D-Dimer antigen containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator High	D-Dimer antigen containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Buffer	Containing BSA, NaN_3 (<0.1%).	6.5 mL	4.0 mL
ABEI Label	Anti-D-Dimer monoclonal antibody labeled with ABEI, containing BSA, NaN_3 (<0.1%).	6.5 mL	4.0 mL
Internal Quality Control	D-Dimer antigen containing BSA, NaN_3 (<0.1%).	2.0 mL	2.0 mL
All reagents are provided ready-to-use.			

Accessories Required But Not Provided

MAGLUMI and Biolumi Series:

Reaction Module	REF: 630003
Starter 1+2	REF: 130299004M, 130299027M
Wash Concentrate	REF: 130299005M
Light Check	REF: 130299006M
Reaction Cup	REF: 130105000101

Please order accessories from Shenzhen New Industries Biomedical Engineering Co., Ltd. (SNIBE) or our authorized representatives.

CALIBRATION

Traceability: This method has been standardized against the SNIBE internal reference substance.

Test of assay specific calibrators allows the RLU values to adjust the assigned master curve. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve (10 calibrations) provided via the reagent Radio Frequency Identification (RFID) CHIP.

Recalibration is recommended if any of the following conditions occurs:

- After each change of lots (Reagent or Starter 1+2).
- Every week and/or each time a new reagent kit is used (recommended).
- After instrument service is required.
- If controls lie outside the expected range.

QUALITY CONTROL

Follow government regulations or accreditation requirements for quality control frequency.

Internal quality control is only applicable with MAGLUMI and Biolumi systems. For instructions for use and target value refer to ***D-Dimer (CLIA) Quality Control Information***. User needs to judge results with their own standards and knowledge.

For detailed information about entering quality control values, refer to the corresponding Analyzer Operating Instructions.

To monitor system performance and chart trends, commercially available quality control materials are required. Treat all quality control samples the same as patient samples. A satisfactory level of performance is achieved when analyte values obtained are within the acceptable Control Range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme. If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical supporters or distributors for assistance.

SPECIMEN COLLECTION AND PREPARATION

- Plasma collected using EDTA anticoagulant tubes or sodium citrate tubes. Collect blood aseptically following the universal precautions for venipuncture.
- Ensure that complete clot formation in specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time.
- If the specimen is centrifuged before a complete clotting, the presence of fibrin may cause erroneous results.
- Do not use hemolyzed or grossly lipemic specimens as well as specimens containing particulate substance or exhibiting obvious microbial contamination. Inspect all specimens for bubbles, and remove bubbles before analysis for optimal results.
- Avoid repeated freezing and thawing. The plasma sample can be frozen and thawed for once .Stored samples should be thoroughly mixed prior to use (Vortex mixer). Frozen specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing. Please ask local representative of SNIBE for more derails if you have any doubt.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care should be taken to transfer only the clarified specimen without the lipaemic material.
- All samples (Patient specimens or controls) should be tested within 3 hours when placed on board the MAGLUMI and Biolumi Systems. Refer to the SNIBE service for more detailed discussion of onboard sample storage constraints.
- Plasma was stable at 2-8 °C for 7 days. If preserved more than 4 days, please seal the samples, -20°C can be stored for 1 month.
- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator. When shipped, specimens should be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens should be shipped frozen.
- The sample volume required for a single determination of D-Dimer is 20 µL.

WARNING AND PRECAUTIONS FOR USERS

- IVD
- For *In Vitro* Diagnostic Use.
- Follow the package insert carefully. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION**: This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the 29 CFR 1910.1030 Occupational exposure to bloodborne pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed in accordance with the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.
- This product contains Sodium Azide. Dispose of contents and containers must be in accordance with all local, regional and national regulations.
- Refer to safety data sheets which are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not interchange reagent components from different reagents or lots.
- Prior to loading the reagent kit on the system for the first time, the reagent kit requires mixing to re-suspend magnetic microbeads that have settled during shipment.
- For magnetic microbeads mixing instructions, refer to the Preparation of the Reagent section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and samples.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

STORAGE AND STABILITY

- Sealed: Stored at 2-8°C until the expiration date.
- Opened at 2-8°C: Minimum stability is 4 weeks.
- On-board: Minimum stability is 4 weeks.
- To ensure the best kit performance, it is recommended to place opened kits in the refrigerator after the end of the intraday test work.
- Keep upright for storage to facilitate later proper resuspension of magnetic microbeads.
- Keep away from sunlight.

TEST PROCEDURE

Preparation of the Reagent

- Resuspension of the magnetic microbeads takes place automatically when the kit is loaded successfully, ensuring the magnetic microbeads are totally resuspended homogenous prior to use.
- To ensure proper test performance, strictly adhere to the corresponding Analyzer Operating Instructions. Each test parameter is identified via a RFID CHIP on the Reagent kit. For further information please refer to the corresponding Analyzer Operating Instructions.

DILUTION

Sample dilution by analyzer is not available in this reagent kit.

Samples with concentrations above the measuring range can be diluted manually. After manual dilution, multiply the result by the dilution factor. Please choose applicable diluents or ask SNIBE for advice before manual dilution.

High-Dose Hook

No high-dose hook effect was seen for D-Dimer concentrations up to 500 µg FEU/mL.

LIMITATIONS

- A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
- Bacterial contamination or heat inactivation of the specimens may affect the test results.
- A result within the expected range does not rule out the presence of disease and should be interpreted together with the patient's clinical picture and other diagnostic procedures.
- Diagnosis of a disease should not be based on the result of a single test, but should be determined in conjunction with clinical findings in association with medical judgement.
- Any therapeutical decision should also be taken on a case-by-case basis.
- Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA plasma concentrations may occasionally influence results.

RESULTS

Calculation of Results

The analyzer automatically calculates the D-Dimer concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in µg FEU/mL. For further information please refer to the corresponding Analyzer Operating Instructions.

Interpretation of Results

The expected range for the D-Dimer assay was obtained by testing 205 apparently healthy individuals in China, and gave the following reference values listed below:

<0.5 µg FEU/mL (95th percentile).

Conversion factor: µg FEU/mL×1=mg FEU/L

µg FEU/mL×1000=ng FEU/mL

Results may differ between laboratories due to variations in population and test method. It is recommended that each laboratory establish its own expected ranges.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the D-Dimer assay was determined as described in the CLSI EP5-A2. 3 human plasma pools and 2 controls containing different concentration of analyte were assayed in duplicate at two independent runs per day for 20 testing days. The results are summarized in the following table:

Sample	Mean (µg FEU/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(µg FEU/mL)	%CV	SD(µg FEU/mL)	%CV	SD(µg FEU/mL)	%CV
Plasma Pool 1	1.100	0.051	4.64	0.073	6.64	0.089	8.09
Plasma Pool 2	5.132	0.233	4.54	0.256	4.99	0.346	6.74
Plasma Pool 3	9.803	0.401	4.09	0.178	1.82	0.439	4.48
Control 1	6.992	0.243	3.48	0.324	4.63	0.405	5.79
Control 2	35.023	0.890	2.54	0.866	2.47	1.242	3.55

Limit of Blank (LoB)

The LoB for the D-Dimer assay is 0.05 µg FEU/mL.

Limit of Detection (LoD)

The LoD for the D-Dimer assay is 0.1 µg FEU/mL.

Measuring Range

0.05-100 µg FEU/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as <0.05 µg FEU/mL. Values above the measuring range are reported as >100 µg FEU/mL.

Linearity

The assay is linear between 0.1 μg FEU/mL and 100 μg FEU/mL. Nine equally distributed levels of samples were prepared by spiking a plasma sample containing D-Dimer 110 μg FEU/mL with a plasma sample free of D-Dimer (0.0 μg FEU/mL).The mean sample recovery ranged between 90% to 110%.

Method Comparison

A total of 100 samples in the range of 0.26 and 49.69 μg FEU/mL were tested using the D-Dimer assay (y) and a commercially available immunoassay (x). The data from the resulting linear regressions are summarized as: y=0.991x-0.022, r^2=0.989.

Analytical Specificity

The specificity data of the assay was obtained by adding the cross-reactant at the indicated concentrations to plasma samples. The D-Dimer assay does not show any significant cross reactions with Troponin Ⅰ (50 μg/mL).

Endogenous Interference

The assay is not affected by hemoglobin≤500 mg/dL, jaundice bilirubin≤30 mg/dL, rheumatoid factor≤100 IU/mL, or heparin≤100 IU/mL.

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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
2°C 8°C	Temperature limit (Store at 2-8 °C)		Use-by date
Σ	Contains sufficient for		Keep away from sunlight
	This way up	EC REP	Authorized representative in the European Community
IVD	*In vitro* diagnostic medical device	CONTENTS	Kit components
REF	Catalogue number	LOT	Batch code