



130218005M:100 tests/kit
130618005M: 50 tests/kit

MAGLUMI® Fibrin/fibrinogen degradation products (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Fibrin/fibrinogen degradation products (FDP) in human plasma using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer and Biolumi series Integrated System, and the assay is used for an aid in the diagnosis of individuals with suspected or confirmed primary and secondary hyperfibrinolysis related diseases.

SUMMARY

Blood flow is maintained by the proper balance of hemostasis and fibrinolysis¹, fibrinolysis process is accurately regulated by activators, inhibitors and cofactors to maintain a delicate balance². Hemostasis, the physiological cessation of bleeding, involves the interaction of vasoconstriction, platelet aggregation and coagulation¹, the end result of coagulation is the deposition of cross-linked fibrin polymers to form blood clots¹. Fibrinolysis is the process which results in enzymatic dissolution of fibrinogen and fibrin clots³.

When fibrin is laid down intravascularly to form a hemostatic barrier or when it is formed extravascularly in exudates in inflammatory tissues for the localization of infections, foreign bodies or tumor cells, it is subjected to proteolysis. Most of this is carried out by the fibrinolytic enzyme plasmin. The resulting breakdown products are particles of different molecular sizes collectively know as fibrin degradation products⁴. In addition, plasma fibrinogen itself can also be subjected to the proteolytic action of plasmin whenever there is excessive fibrinolytic activity in blood⁴. FDP includes cross-linked fibrin and non-cross-linked fibrin or fibrinogen degradation products, which are formed and released upon plasmin-mediated thrombus degradation⁵. Therefore, FDP values reflect the coagulation and fibrinolysis status in the body, and can be useful for the diagnosis of thrombosis disorders and prediction of the effects of anticoagulant therapy⁶.

Although low levels of D-dimer and fibrinogen/fibrin degradation products (FDP) can be detected in the circulation of healthy individuals, their levels are significantly elevated in patients with deep venous thrombosis (DVT) , pulmonary embolism (PE) , disseminated intravascular coagulation , myocardial infarction , cancer , sepsis or other complications^{6,7}. FDP has been regarded as one of the most useful parameters to evaluate the hyperfibrinolytic state, especially for the diagnosis of DIC⁸. In clinical practice, simultaneous measurements of FDP and D-dimer are useful for more accurate estimation of hyperfibrinolytic states and to avoid possible misinterpretations due to lack of information about D-dimer in cases of elevated FDP values⁵.

TEST PRINCIPLE

Sandwich chemiluminescence immunoassay.

The prediluted sample, buffer, magnetic microbeads coated with FDP monoclonal antibody and ABEI labeled with another FDP monoclonal antibody are mixed thoroughly and incubated, reacting to form sandwich complexes. After precipitation in a magnetic field, the supernatant is decanted and then a wash cycle is performed. Subsequently, the Starter 1+2 are added to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which is proportional to the concentration of FDP present in the sample.

REAGENTS

Kit Contents

Component	Description	100 tests/kit	50 tests/kit
Magnetic Microbeads	Magnetic microbeads coated with FDP monoclonal antibody(~10.00 µg/mL) in PBS buffer, NaN ₃ (<0.1%).	2.5 mL	1.5 mL
Calibrator Low	A low concentration of FDPs antigen in PBS buffer, NaN ₃ (<0.1%).	1.0 mL	1.0 mL
Calibrator High	A high concentration of FDPs antigen in PBS buffer, NaN ₃ (<0.1%).	1.0 mL	1.0 mL
Buffer	BSA, NaN ₃ (<0.1%).	11.5 mL	6.5 mL
ABEI Label	ABEI labeled with FDP monoclonal antibody (~500 ng/mL) in Tris-HCl buffer, NaN ₃ (<0.1%).	7.5 mL	4.5 mL
Diluent	PBS buffer, NaN ₃ (<0.1%).	5.5 mL	3.5 mL
Control 1	A low concentration of FDPs antigen (4.00 µg/mL) in PBS buffer, NaN ₃ (<0.1%).	1.0 mL	1.0 mL
Control 2	A high concentration of FDPs antigen (20.0 µg/mL) in PBS buffer, NaN ₃ (<0.1%).	1.0 mL	1.0 mL

Warnings and Precautions

- For *in vitro* diagnostic use.
- For professional use only.
- Exercise the normal precautions required for handling all laboratory reagents.
- Personal protective measures should be taken to prevent any part of the human body from contacting samples, reagents, and controls, and should comply with local operating requirements for the assay.
- A skillful technique and strict adherence to the package insert are necessary to obtain reliable results.
- Do not use kit beyond the expiration date indicated on the label.
- Do not interchange reagent components from different reagents or lots.
- Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).
- All waste associated with biological samples, biological reagents and disposable materials used for the assay should be considered potentially infectious and should be disposed of in accordance with local guidelines.
- This product contains sodium azide. Sodium azide may react with lead or copper plumbing to form highly explosive metal azides. Immediately after disposal, flush with a large volume of water to prevent azide build-up. For additional information, see Safety Data Sheets available for professional user on request.

Note: If any serious incident has occurred in relation to the device, please report to Shenzhen New Industries Biomedical Engineering Co., Ltd. (Snibe) or our authorized representative and the competent authority of the Member State in which you are established.

Reagent Handling

- To avoid contamination, wear clean gloves when operating with a reagent kit and sample. When handling reagent kit, replace the gloves that have been in contact with samples, since introduction of samples will result in unreliable results.
- Do not use kit in malfunction conditions; e.g., the kit leaking at the sealing film or elsewhere, obviously turbid or precipitation is found in reagents (except for Magnetic Microbeads) or control value is out of the specified range repeatedly. When kit in malfunction conditions, please contact Snibe or our authorized distributor.
- To avoid evaporation of the liquid in the opened reagent kits in refrigerator, it is recommended that the opened reagent kits to be sealed with reagent seals contained within the packaging. The reagent seals are single use, and if more seals are needed, please contact Snibe or our authorized distributor.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.
- Use always the same analyzer for an opened reagent integral.
- For magnetic microbeads mixing instructions, refer to the Preparation of the Reagent section of this package insert.
- For further information about the reagent handing during system operation, please refer to Analyzer Operating Instructions.

Storage and Stability

- Do not freeze the integral reagents.
- Store the reagent kit upright to ensure complete availability of the magnetic microbeads.
- Protect from direct sunlight.

Stability of the Reagents	
Unopened at 2-8°C	until the stated expiration date
Opened at 2-8°C	6 weeks
On-board	4 weeks

Stability of Controls	
Unopened at 2-8°C	until the stated expiration date
Opened at 10-30°C	24 hours
Opened at 2-8°C	6 weeks
Frozen at -20°C	3 months
Frozen and thawed cycles	no more than 1 time

SPECIMEN COLLECTION AND PREPARATION

Specimen Types

Only the specimens listed below were tested and found acceptable.

Specimen Types	Collection Tubes
Plasma	Sodium citrate anticoagulant tube(1:9)

- The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. Follow tube manufacturers' instructions carefully when using collection tubes.

Specimen Conditions

- Do not use heat-inactivated samples or grossly hemolyzed/hyperlipidaemia specimens and specimens with obvious microbial contamination.
- Samples must be free of fibrin and other particulate matter.
- To prevent cross contamination, use of disposable pipettes or pipette tips are recommended.

Preparation for Analysis

- Inspect all specimens for foam. Remove foam with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- Frozen specimens must be completely thawed before mixing. Mix thawed specimens thoroughly by low speed vortexing or by gently inverting. Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous. If specimens are not mixed thoroughly, inconsistent results may be obtained.
- For reliable results, specimens should be free of fibrin, red blood cells, or other particulate matter. Specimens must be centrifuged prior to testing, transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- The sample volume required for a single determination of this assay is 5 µL.

Specimen Storage

Specimens removed from the separator, red blood cells or clot may be stored up to 4 hours at 10-30°C or 24 hours at 2-8°C, or 1 month frozen at -20°C. Frozen specimens subjected to 1 freeze/thaw cycle have been evaluated.

Specimen Shipping

- Package and label specimens in compliance with applicable local regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

Specimen Dilution

- Samples, with FDP concentrations above the analytical measuring interval, can be diluted with Diluent either by following automated dilution protocol or manual dilution procedure. The recommended dilution ratio is 1:10 (sample volume:total volume). The concentration of the diluted sample must be >8 µg/mL.
- For manual dilution, multiply the result by the dilution factor. For dilution by the analyzers, the analyzer software automatically takes the dilution into account when calculating the sample concentration.

PROCEDURE

Materials Provided

Fibrin/fibrinogen degradation products (CLIA) assay, control barcode labels.

Materials Required (But Not Provided)

- General laboratory equipment.
- Fully-auto chemiluminescence immunoassay analyzer Maglumi 600, Maglumi 800, Maglumi 1000, Maglumi 2000, Maglumi 2000 Plus, Maglumi 4000, Maglumi 4000 Plus, MAGLUMI X3, MAGLUMI X6, MAGLUMI X8, MAGLUMI X10, or Integrated System Biolumi 8000 and Biolumi CX8.
- Additional accessories of test required for the above analyzers include Reaction Module, Starter 1+2, Wash Concentrate, Light Check, Tip, and Reaction Cup. Specific accessories and accessories' specification for each model refer to corresponding Analyzer Operating Instructions.
- Please use accessories specified by Snibe to ensure the reliability of the test results.

Assay Procedure

Preparation of the Reagent

- Take the reagent kit out of the box and visually inspect the integral vials for leaking at the sealing film or elsewhere. If there is no leakage, please tear off the sealing film carefully.
- Open the reagent area door; hold the reagent handle to get the RFID label close to the RFID reader (for about 2s); the buzzer will beep; one beep sound indicates successful sensing.
- Keeping the reagent straight insert to the bottom along the blank reagent track.
- Observe whether the reagent information is displayed successfully in the software interface, otherwise repeat the above two steps.
- 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.

Assay Calibration

- Select the assay to be calibrated and execute calibration operation in reagent area interface. For specific information on registering calibrations, refer to the calibration section of Analyzer Operating Instructions.
- Execute recalibration according to the calibration interval required in this package insert.

Quality Control

- When new lot used, check or edit the quality control information.
- Scan the control barcode, choose corresponding quality control information and execute testing. For specific information on registering quality controls, refer to the quality control section of the Analyzer Operating Instructions.

Sample Testing

- After successfully loading the sample, select the sample in interface and edit the assay for the sample to be tested and execute testing. For specific information on registering samples, refer to the sample section of the Analyzer Operating Instructions.

To ensure proper test performance, strictly adhere to Analyzer Operating Instructions.

Calibration

Traceability: This method has been standardized against the Snibe internal reference standard.

Test of assay specific calibrators allows the detected relative light unit (RLU) values to adjust the master curve.

Recalibration is recommended as follows:

- Whenever a new lot of Reagent or Starter 1+2 is used.
- Every 7 days.
- The analyzer has been serviced.
- Control values lie outside the specified range.

Quality Control

Controls are recommended for the determination of quality control requirements for this assay and should be run in singlicate to monitor the assay performance. Refer to published guidelines for general quality control recommendations, for example Clinical and Laboratory Standards Institute (CLSI) Guideline C24 or other published guidelines⁹.

Quality control is recommended once per day of use, or in accordance with local regulations or accreditation requirements and your laboratory's quality control

procedures, quality control could be performed by running the Fibrin/fibrinogen degradation products assay:

- Whenever the kit is calibrated.
- Whenever a new lot of Starter 1+2 or Wash Concentrate is used.

Controls are only applicable with MAGLUMI and Biolumi systems and only used matching with the same top eight LOT numbers of corresponding reagents. For each target value and range refer to the label.

The performance of other controls should be evaluated for compatibility with this assay before they are used. Appropriate value ranges should be established for all quality control materials used.

Control values must lie within the specified range, whenever one of the controls lies outside the specified range, calibration should be repeated and controls retested. If control values lie repeatedly outside the predefined ranges after successful calibration, patient results must not be reported and 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 package insert.
- If necessary, contact Snibe or our authorized distributors for assistance.

If the controls in kit are not enough for use, please order Fibrin/fibrinogen degradation products (CLIA) Controls (REF: 1602011023MT) from Snibe or our authorized distributors for more.

RESULTS

Calculation

The analyzer automatically calculates the FDP 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/mL. For further information please refer to the Analyzer Operating Instructions.

Interpretation of Results

The expected range for the FDP assay was obtained by testing 331 apparently healthy individuals, gave the following expected value:

<5 µg/mL (95th percentile).

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

LIMITATIONS

- Results should be used in conjunction with patient’s medical history, clinical examination and other findings.
- If the FDP results are inconsistent with clinical evidence, additional testing is needed to confirm the result.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies^{10,11}. Additional information may be required for diagnosis.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or animal serum products can be prone to this interference and anomalous values may be observed¹².
- Bacterial contamination or heat inactivation of the specimens may affect the test results.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

Precision

Precision was determined using the assay, samples and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): duplicates at two independent runs per day for 5 days at three different sites using three lots of reagent kits (n = 180). The following results were obtained:

Sample	Mean (µg/mL) (n=180)	Within-Run		Between-Run		Reproducibility	
		SD (µg/mL)	%CV	SD (µg/mL)	%CV	SD (µg/mL)	%CV
Plasma Pool 1	4.732	0.173	3.66	0.081	1.72	0.345	7.28
Plasma Pool 2	19.701	0.524	2.66	0.556	2.82	1.298	6.59
Plasma Pool 3	39.740	1.236	3.11	0.937	2.36	2.443	6.15
Control 1	3.906	0.156	4.01	0.082	2.09	0.280	7.18
Control 2	20.258	0.615	3.04	0.499	2.46	1.324	6.53

Based on internal testing on the MAGLUMI and Biolumi systems, the overall repeatability (% CV) is estimated to be ≤ 5% for samples tested, the overall reproducibility (%CV) is estimated to be ≤ 10%. Performance of the assay at individual laboratories may vary.

Linear Range

2.50-80.0 µg/mL (defined by the Limit of Quantitation and the maximum of the master curve).

Reportable Interval

1.50-800 µg/mL (defined by the Limit of Detection and the maximum of the master curve×Recommended Dilution Ratio).

Analytical Sensitivity

Limit of Blank (LoB) =0.80 µg/mL.

Limit of Detection (LoD) ≈1.50 µg/mL.

Limit of Quantitation (LoQ) ≈2.50 µg/mL.

Analytical Specificity

Interference

Interference was determined using the assay, three samples containing different concentrations of analyte were spiked with potential endogenous and exogenous interferences in a protocol (EP7-A2) of the CLSI. The measurement deviation of the interference substance is within ±10%. The following results were obtained:

Interference	No interference up to
Bilirubin	90 mg/dL
Hemoglobin	1000 mg/dL
Intralipid	3000 mg/dL
HAMA	40 ng/mL
Rheumatoid factor	2500 IU/mL
ANA	398 AU/mL

High-Dose Hook

No high-dose hook effect was seen for FDP concentrations up to 800 µg/mL.

Method Comparison

A comparison of the Fibrin/fibrinogen degradation products assay with a commercially available immunoassay, gave the following correlations (µg/mL):

Number of samples measured: 119

Passing-Bablok: y=1.0081x-0.0122, r=0.961.

The clinical specimen concentrations were between 2.51 and 78.14 µg/mL.

REFERENCES

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SYMBOLS EXPLANATIONS



Consult instructions for use



Temperature limit
(Store at 2-8°C)



Contains sufficient for<n> tests



This way up



In vitro diagnostic medical device



Catalogue number



CE marking with notified body ID number



Manufacturer



Use-by date



Keep away from sunlight



Authorized representative in the European Community



Kit component



Batch code

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