MAGLUMI S-Troponin I (CLIA)

REF 130206009M

Σ 100

EC REP

Shenzhen New Industries Biomedical Engineering Co., Ltd
4F,Wearnes Tech Bldg,
Science & Industry Park,
Nanshan,Shenzhen,518057CHINA
Tel. + 86-755-86028224
Fax.+ 86-755-26654850

Lotus Global Co., Ltd
15 Alexandra Road
London
NW8 0DP
UK
Tel. + 44-20-75868010
Fax.+ 44-20-79006187

CE

FOR PROFESSIONAL USE ONLY
Store at 2-8°C

COMPLETELY READ THE INSTRUCTIONS BEFORE PROCEEDING

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SYMBOLS EXPLANATIONS

EC REP	Authorized Representative in Europe
	Manufacturer
	Attention. See Instructions For Use
CONT	Contents of kit
IVD	In vitro diagnostic medical device (In vitro diagnostic use)
LOT	Lot number
REF	Catalogue Code
	Expiry date (Use by…)
8°C 2°C	Temperature limitation (store at 2...8 °C)
Σ	Number of tests
	Keep away from sunlight
	Keep upright

INTENDED USE

The kit has been designed for the quantitative determination of Troponin I (high sensitive) in human serum.
The method can be used for samples over the range of 0-50ng/ml. The test has to be performed on the MAGLUMI chemiluminescence immunoassay (CLIA) fully auto analyzer (Including MAGLUMI 1000, MAGLUMI 2000, MAGLUMI 2000 Plus and new developed models).

SUMMARY AND EXPLANATION OF THE TEST

The highest share（94 - 97%）of the troponin complex is localised on the (thin) actin filament in the sarcomers of cardiac and skeletal muscles. The troponin complex consists of three different proteins: troponin I, troponin C, and troponin T. Three tissue-specifics troponin I subunits have been identified, each coded by different genes:
- Two of these subunits are rapid and slow isoforms of troponin I (sTnI) derived from the rapid and slow fibres of skeletal muscles.
-The third is the myocardial form known as cardiac troponin I (cTnI) whose primary structure differs considerably from that of the two skeletal muscle isoforms.
Troponin I is a specific and sensitive marker for the detection of myocardial damage. As early as 4 to 12 hours after acute cardiac ischaemia, elevated troponin I levels (above the specific cut-off) allow diagnosing acute myocardial infarction with high specificity and sensitivity. According to the Joint Consensus of the ESC and ACC – Myocardial infarction redefined-for the definition of myocardial infarction and the IFCC C-SMCD quality specifications for cTnI assays, AMI should be defined as my cardiac Troponin I concentration exceeding the 99th percentile of a, reference control group. Accordingly,the acceptable imprecision (total) at the 99th percentile for each assay should be defined as not exceeding 10%.
Peak troponin I concentations are reached after 14 to 36 hours and remain at a high level for up to 7 days after the acute event.
Serial testing of troponin I concentrations is recommended in patients with suspected myocardial damage. According to the recommendation of the IFCC Committee for the use of cardiac markers in coronary artery diseases, troponin I should be determined at admission as well as 4, 8 and 12 hours (or in the next morning) after hospitalisation. Ample data suggests that patients with unstable angina pectoris (UAP), in whom troponin I levels are concomitantly elevated (above the reference range) have a significantly increased risk of mortality due to cardiovascular disease. Therefore, troponin I is a suitable parameter for risk stratification of such patients.
Successful risk stratification requires, however, analytical methods sensitive enough to detect even minor elevations of troponin I (above the reference range) early and with high precision.

PRINCIPLE OF THE TEST

Sandwich immunoluminometric assay.
Use an anti-Troponin I monoclonal antibody to label ABEI, magnetic microbeads coated with anti- Troponin I monoclonal antibody. Sample, Calibrator or Control with ABEI Label and magnetic microbeads are mixed thoroughly and incubated at 37℃, forming a sandwich; after sediment in a magnetic field, then cycle washing for 1 time. Subsequently, the starter reagents are added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU within 3 seconds and is proportional to the concentration of Troponin I present in controls or samples.

CONT KIT COMPONENTS

Material Supplies

Reagent Integral for 100 determinations	
Nano magnetic microbeads: microbeads coated with sheep anti-Troponin I monoclonal antibody, TRIS buffer, 0.2%NaN_3.	2.5ml
Calibrator Low: bovine serum, 0.2%NaN_3.	3.0ml
Calibrator High: bovine serum, 0.2%NaN_3	3.0ml
ABEI Label: anti-Troponin I monoclonal antibody labeled ABEI, contains BSA, 0.2%NaN_3.	7.5ml
All reagents are provided ready-to-use.	

Reagent Vials in kit box	
Internal Quality Control: containing BSA, 0.2%NaN_3. (target value refer to Quality Control Information date sheet)	2.0ml

Accessories Required But Not Provided

MAGLUMI Reaction Module	REF: 630003
MAGLUMI Starter 1+2	REF: 130299004M
MAGLUMI Wash Concentrate	REF: 130299005M
MAGLUMI Light Check	REF: 130299006M

Preparation of the Reagent Integral

Before the sealing is removed, gentle and careful horizontal shaking of the Reagent Integral is essential (avoid foam formation!) Remove the sealing and turn the small wheel of the magnetic microbeads compartment to and fro, until the colour of the suspension has changed into brown. Place the Integral into the reagent area and let it stand there for 30 min. During this time, the magnetic microbeads are automatically agitated and completely resuspended.

Do not interchange integral component from different reagents or lots!

Storage and Stability

- Sealed: Stored at 2-8 ℃ until the expiry date.
- Opened: Stable for 4 weeks. To ensure the best kit performance, it is recommended to place opened kits in the refrigerator if it's not going to be used on board during the next 12 hours.
- Keep upright for storage.
- Keep away from direct sunlight.

CALIBRATION AND TRACEABILITY

1)Traceability

To perform an accurate calibration, we have provided the test calibrators standardized against the SNIBE internal reference substance

Calibrators in the Reagent Kit are from Biodesign.

2) 2-Point Recalibration

Via the measurement of calibrators, the predefined master curve is adjusted (recalibrated) to a new, instrument-specific measurement level with each calibration.

3) Frequency of Recalibration

- After each exchange of lot (Reagent Integral or Starter Reagents).
- Every week and/or each time a new Integral is used (recommendation).
- After each servicing of the MAGLUMI Fully Auto analyzer.
- If controls are beyond the expected range.

SPECIMEN COLLECTION AND PREPARATION

Sample material: serum

Collect samples using standard procedures (Procedures should be finished in 2 hours).

Store at 2-8 ℃: 24 hours, for lo

below - 20 ℃

Freezing and thawing is only allowed for 1cycle, stored samples should be thoroughly mixed prior to use (Vortex mixer).

Please ask local representative of SNIBE for more details if you have any doubt.

Vacuum Tubes

(a) Blank tubes are recommended type for collecting samples.

(b) Please ask SNIBE for advice if special additive must be used in sample collecting.

Specimen Conditions

- Do not use specimens with the following conditions:
  (a) heat-inactivated specimens;
  (b) Cadaver specimens or body fluids other than human serum;
  (c) Obvious microbial contamination.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- Serum specimens should be free of fibrin, red blood cells or other particulate matter.
- Ensure that complete clot formation in serum 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 clot forms, the presence of fibrin may cause erroneous results.

Preparation for Analysis

- Patient specimens with a cloudy or turbid appearance must be centrifuged prior to testing. Following centrifugation, avoid the lipid layer (if present) when pipetting the specimen into a sample cup or secondary tube.
- Specimens must be mixed **thoroughly** after thawing by **low** speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results. Multiple freeze-thaw cycles of specimens should be avoided.
- All samples (patient specimens or controls) should be tested within 3 hours of being placed on board the MAGLUMI System. Refer to the SNIBE service for a more detailed discussion of onboard sample storage constraints.

Storage

- If testing will be delayed for more than 8 hours, remove serum or plasma from the serum or plasma separator, red blood cells or clot. Specimens removed from the separator gel, cells or clot may be stored up to 24 hours at 2-8°C.
- Specimens can be stored up to 30 days frozen at -20°C or colder.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the serum or plasma separator, red blood cells or clot. When shipped, specimens must be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical

specimens and infectious substances. Specimens must be shipped frozen (dry ice). Do not exceed the storage time limitations identified in this section of the package insert.

WARNING AND PRECAUTIONS FOR USERS

IVD

- For use in *IN-VITRO* diagnostic procedures only.
- Package insert instructions must be carefully followed. 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.

- The calibrators in this kit are prepared from bovine serum products. However, because no test method can offer complete assurance that HIV, Hepatitis B Virus or other infectious agents are absent; these reagents should be considered a potential biohazard and handled with the same precautions as applied to any serum or plasma specimen.
- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be autoclaved using an overkill approach (USP 24, 2000, p.2143). A minimum of one hour at 121 ℃ is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.
- It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens13. Biosafety Level 214 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- This product contains Sodium Azide; this material and its container must be disposed of in a safe way.
- Safety data sheets are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not mix reagents from different reagent kits.
- Prior to loading the Reagent Kit on the system for the first time, the microbeads requires mixing to re-suspend microbeads that have settled during shipment.
- For microbeads mixing instructions, refer to the KIT COMPONENTS, Preparation of the Reagent Integral section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and sample.
- Over time, residual liquids may dry on the kit surface, please pay attention the silicon film still exists on the surface of the kit.
- For a detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

TEST PROCEDURE

To ensure proper test performance, strictly adhere to the operating instructions of the MAGLUMI Fully Auto analyzer. Each test parameter is identified via a RFID tag on the Reagent Integral. For further information please refer to the MAGLUMI Chemiluminescence Analyzer Operating Instructions.

100μl	Sample, calibrator or controls
+50μl	ABEI label
+20μl	Nano magnetic microbeads
15 min	Incubation
400μl	Cycle washing
3 s	Measurement

DILUTION

Samples with concentrations above the measuring range can be diluted. After manual dilution, multiply the result by the dilution factor. After dilution by the analyzers, the analyzer software automatically takes the dilution into account when calculating the sample concentration.

Availability of sample dilution by analyzer please refers to the MAGLUMI analyzer user software program. Dilution settings please follow MALGUMI analyzer operating instructions.

QUALITY CONTROL

- Observe quality control guidelines for medical laboratories
- Use suitable controls for in-house quality control. Controls should be run at least once every 24 hours when the test is in use, once per reagent kit and after every calibration. The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined ranges. Each laboratory should establish guidelines for corrective measures to be taken if values fall outside the range.

LIMITATIONS OF THE PROCEDURE

1) Limitations

Increased troponin concentrations should not be used by themselves to diagnose or rule out a heart attack. A physical exam, clinical history, and ECG are also important as is whether the troponin levels from a series of tests are stably elevated or show a rise and/or fall over several hours. Very rarely, people who have a heart attack will have normal troponin concentrations, and some people with increased troponin concentrations have no apparent heart injury. Troponin levels may also be elevated with acute or chronic conditions such as myocarditis (heart inflammation), congestive heart failure, severe infections, kidney disease, and certain chronic inflammatory conditions of muscles and skin.

2) Interfering Substances

No interference with test results is seen by concentrations of bilirubin<0.06mg/ml, haemoglobin<16mg/dl or triglycerides< 12.5mg/ml.

3) HAMA

Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

4) High-Dose Hook

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For the MAGLUMI Troponin I assay, no high dose hook effect was observed when samples containing up to 1000 ng/ml.

RESULTS

1) Calculation of Results

- The analyzer automatically calculates the Troponin I 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 ng/ml. For further information please refer to the MAGLUMI Chemiluminescence Analyzer Operating Instructions.

2) Interpretation of Results

- Results of study in clinical centers with group of individuals, 95% of the results were：< 0.1ng/ml.
- Results may differ between laboratories due to variations in population and test method. If necessary, each laboratory should establish its own reference range.

PERFORMANCE CHARACTERISTICS

1) Precision

Intra-assay coefficient of variation was evaluated on 3 different levels of control serum repeatedly measured 20 times in the same run, calculating the coefficient of variation.

Intra-assay precision			
Control	Mean(ng/ml)	SD(ng/ml)	CV%
Level 1	0.64	0.03	4.69%
Level 2	1.59	0.07	4.40%
Level 3	4.91	0.26	5.30%

Inter-assay coefficient of variation was evaluated on three batches of kit. Repeatedly measured 3 different levels of control serum 21 times, calculating the coefficient of variation.

Inter-assay precision			
Control	Mean(ng/ml)	SD(ng/ml)	CV%
Level 1	0.74	0.06	8.11%
Level 2	1.69	0.15	8.61%
Level 3	4.86	0.41	8.43%

2) Analytical Sensitivity

The sensitivity is defined as the concentration of Troponin I equivalent to the mean RLU of 20 replicates of the zero standard plus two standard deviations corresponding to the concentration from the standard curve. The sensitivity is typically less than 4pg/ml.

3) Specificity

The specificity of the Troponin I assay system was assessed by measuring the apparent response of the assay to various potentially cross reactive analytes.

Compound	Concentration	Cross reactivity
hemoglobin	200 ng/ml	0.02%

4) Recovery

Consider calibrator high of known concentration as a sample, dilute it by 1:2 ratio with diluents, and measure its diluted concentration for 10 times. Then calculate the recovery of measured concentration and expected concentration. The recovery should be within 90% -110%.

Expected	Mean Measuring	Recovery
4.259 ng/ml	4.210 ng/ml	98.8%

5) Linearity

Use Troponin I calibrator to prepare the six point standard curve, measuring all points' RLU except point A, and then do four parameter linear fitting in double logarithm coordinate, the absolute linear correlation coefficient(r) should be bigger than 0.9800.

Calibrator Point	Concentration ng/ml	Absolute linear correlation coefficient (r)
A	0	
B	0.05	r=0.984
C	0.2	
D	0.5	
E	1.5	
F	5.0	

6) Method comparison

A comparison of MAGLUMI Troponin I (y) with a commercially available Troponin I test (x) using clinical samples gave the following correlations (ng/ml):

Linear regression
y = 0.98x-0.14
r = 0.969
Sy.x =0.21

Number of samples measured: 185
The sample concentrations were between 0.017 and 4.5ng/ml.

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