MAGLUMI CRP (CLIA)

REF 130216002M

Σ 100

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

EC REP

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 direct sunlight
	Keep upright for storage

INTENDED USE

The kit has been designed for the quantitative determination of C-reactive protein (CRP) in human serum.
The method can be used for samples over the range of 0-10000 ng/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

C-reactive protein (CRP) is a non-specific test. It is used by a doctor to detect inflammation if there is a high suspicion of tissue injury or infection somewhere in the body, but the test cannot tell where the inflammation is or what condition is causing it. CRP is not diagnostic of any condition, but it can be used together with signs and symptoms and other tests to evaluate an individual for an acute or chronic inflammatory condition.
For example, CRP may be used to detect or monitor significant inflammation in an individual who is suspected of having an acute condition such as:
A serious bacterial infection like sepsis or a fungal infection Pelvic inflammatory disease (PID)
The CRP test is useful in monitoring people with chronic inflammatory conditions to detect flare-ups and/or to determine if treatment is effective. Some examples include:
Inflammatory bowel disease
Some forms of arthritis
Autoimmune diseases, such as lupus or vasculitis
CRP may sometimes be ordered along with an Erythrocyte Sedimentation Rate (ESR), another test that detects inflammation. While the CRP test is not specific enough to diagnose a particular disease, it does serve as a general marker for infection and inflammation, thus alerting medical professionals that further testing and treatment may be necessary. Depending on the suspected cause, a number of other tests may be performed to identify the source of inflammation.
This test may be ordered when an individual is suspected of having a serious bacterial infection based on their medical history and signs and symptoms. It may be ordered, for example, when a newborn shows signs of infection or when an individual has symptoms of sepsis, such as fever, chills and rapid breathing and heart rate.
It may also be ordered on a regular basis to monitor conditions such as rheumatoid arthritis and lupus and is often repeated at intervals to determine whether treatment is effective. This is particularly useful for inflammation problems since CRP levels drop as inflammation subsides.

PRINCIPLES OF THE TEST

Sandwich immunoluminometric assay:
Use an anti-CRP monoclonal antibody to label ABEI, and use another monoclonal antibody to label FITC. Sample, Calibrator or Control are mixed thoroughly with FITC Label and nano magnetic microbeads in a cuvette incubated at 37°C, then cycle washing for 1 time. Then add ABEI Label and incubated to form a sandwich, after sediment in a magnetic field, suck the supernatant then cycle washing for the 2nd time. Subsequently, Starter 1+2 substrates 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 CRP present in controls or samples.

CONT

KIT COMPONENTS

Material Supplies

Reagent Integral for 100 determinations	
Nano magnetic microbeads: TRIS buffer, 1.2%(W/V), 0.2%NaN_3, coated with sheep anti- FITC polyclonal antibody.	2.5ml
Calibrator low: bovine serum, 0.2%NaN_3	2.5ml
Calibrator high : bovine serum, 0.2%NaN_3	2.5ml
FITC Label: anti-CRP monoclonal antibody labeled FITC, contains BSA, 0.2%NaN_3.	22.5ml
ABEI Label: anti-CRP monoclonal antibody labeled ABEI, contains BSA, 0.2%NaN_3.	12.5ml
Diluents: 0.9% NaCl.	25.0ml
All reagents are provided ready-to-use.	

*Please prepare 0.9% sodium chloride solution in case of insufficient diluents.

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 kit 1+2	REF:130299004M
MAGLUMI Light check	REF:130299005M
MAGLUMI Wash /System Liquid	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 Nano Magnetic Microbeads 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.

TRACEABILITY AND CALIBRATION

1)Traceability

To perform an accurate calibration, we have provided the test calibrators standardized against the WHO International Standard HUMAN C-REACTIVE PROTEIN 1st International Standard 85/506.

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 lots (Reagent Integral or Starter Reagents).
- Every 2 weeks 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.

Store at 2-8℃: 24 hours,for longer storage periods: freeze to below - 20℃.

Avoid repeated freezing and thawing cycles,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.

Prevent cross contamination when handling patient specimens. 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 that the silicon film still exists on the surface of the kit.

For 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 Chemilumi -nescence Analyzer Operating Instructions.

Auto-dilution 1:100	
Step one:	
20µl	Sample
+180µl	Diluent
Step two:	
20µl	Sample from step one
+180µl	Diluent
20µl	Auto-dil sample, calibrator or controls
+100µl	FITC Label
+20µl	Nano magnetic microbeads
10 min	Incubation
400µl	Cycle washing
200µl	ABEI
10 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. About 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

A skillful technique and strict adherence to the instructions are necessary to obtain reliable results. Bacterial contamination of samples or repeated freeze-thaw cycles may affect the test results. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

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 CRP assay, No high-dose hook effect was seen for CRP concentrations up to 50,000ng/ml.

RESULTS

1)Calculation of Results

The analyzer automatically calculates the CRP 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 Fully Auto Operator's Manual.

2)Interpretation of Results

Reference values：

This kit is HsCRP, mainly used to monitor the cardiovascular disease, the reference range of the adult < 700 ng/ml.

If this kit is used to monitor the infectious disease, It is suggested that the sample should be diluted 1:100 by 0.9% normal saline, then perform the assay on the analyzer, the result shown on the analyzer should be multiplied by 100 to get the real result. It is suggested that each laboratory should establish the corresponding reference range.

Results may differ between laboratories due to variations in population and test method. 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	385	22.64	5.88%
Level 2	2102	125.49	5.97%
Level 3	7105	428.43	6.03%

Inter-assay coefficient of variation was evaluated on three batches of kits. 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	392	35.48	9.05%
Level 2	2140	192.39	8.99%
Level 3	7083	649.51	9.17%

2) Analytical Sensitivity

The sensitivity is defined as the concentration of CRP 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 0.13 ng/ml.

3) Specificity

Any cross-reactivities with serum protein may be neglected in physiologically relevant concentration ranges.

Compound	Concentration	Cross reactivity
Serum protein	100ng/ml	0.5%

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
21.1ng/ml	20.4 ng/ml	97%

5) Linearity

Use CRP 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 exceed 0.9800.

Calibrator Point	Concentration ng/ml	Absolute linear correlation coefficient (r)
A	0.0	
B	0.5	r=0.9820
C	2.0	
D	10.0	
E	50.0	
F	100.0	

6) Method comparison

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

Linear regression
y = 1.08x-580
r = 0.977
Sy.x = 1446.4

Number of samples measured: 125
The sample concentrations were between 0.72 and 32000 ng/ml.

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