Snibe Diagnostic

CE

REF 130204001M: 100 tests
130604001M: 50 tests

MAGLUMI® β_2-MG (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescent immunoassay for the quantitative determination of β_2-microglobulin (β_2-MG) in human serum or urine 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

β_2-Microglobulin (β_2M) also known as B2M is a component of MHC class I molecules, which are present on all nucleated cells (excludes red blood cells)[1]. β_2M is a single-chain aglycosyl protein composed of 100 amino acids. Its molecular mass is 11.8kDa, and it is now known to be the light-chain component of the histocompatibility antigens (HLAs). It is therefore found on all nucleated cells and is present in high concentrations on the lymphocyte cell surface. This small protein bears sequence homology with immunoglobulins and is hence classified as belonging to the superfamily of immunoglobulins[2-4].

Serum β_2M levels are elevated in the presence of a number of solid tumors and lymphomas[5-6]. However, a variety of nonmalignant conditions such as rheumatoid arthritis, AIDS, lupus, Crohn's disease, and renal tubular dysfunction cause elevated levels of the marker[7-10]. The level of serum β_2M also appears to be an indicator of acute renal transplant rejection[11]. The role of β_2M levels is less certain for solid tumors, either in monitoring the disease or as an indicator of prognosis. There appears to be a use for this marker in the lymphoid malignancies such as Hodgkin's and non-Hodgkin's lymphoma, multiple myeloma, and chronic lymphocytic leukemia. A high initial level of β_2M is an indicator of poor prognosis and an advanced stage of the disease. It is also useful for monitoring the course of the disease in these cancers, particularly in multiple myelomas[6-7,10-13].

PRINCIPLE OF THE TEST

The β_2-MG assay is a competitive chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), ABEI labeled with anti-β_2-MG monoclonal antibody, FITC labeled with purified β_2-MG antigen and magnetic microbeads coated with anti-FITC polyclonal antibody are mixed thoroughly and incubated, forming immuno-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 inversely proportional to the concentration of β_2-MG present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material Provided

Component	Contents	100 tests (REF: 130204001M)	50 tests (REF: 130604001M)
Magnetic Microbeads	Coated with anti-FITC polyclonal antibody, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	β_2-MG antigen, containing bovine serum, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator High	β_2-MG antigen, containing bovine serum, NaN_3 (<0.1%).	2.5 mL	2.0 mL
FITC Label	Purified β_2-MG antigen labeled FITC, containing BSA, NaN_3 (<0.1%).	10.5 mL	7.0 mL
ABEI Label	Anti-β_2-MG monoclonal antibody labeled ABEI, containing BSA, NaN_3 (<0.1%).	10.5 mL	7.0 mL
Diluent	0.9%NaCl.	25.0 mL	15.0 mL
Internal Quality Control	β_2-MG antigen, containing bovine serum, 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 representative.

CALIBRATION

Traceability: This method has been standardized against the WHO1st International Standard B2M.

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 (10 calibrations) and a master curve 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 ***β$_2$-MG (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 support provider or distributor for assistance.

SPECIMEN COLLECTION AND PREPARATION

Serum:

- Use standard sampling tubes or tubes containing separating gel. Collect blood aseptically followed the universal precautions for venipuncture.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some serum specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time.
- If the serum specimen is centrifuged before a complete clotting, the presence of fibrin may cause erroneous results. Serum specimens must be free of fibrin and other particulate substance.
- Do not use hemolyzed or grossly lipemic specimens as well as specimens containing particulate matter or exhibiting obvious microbial contamination. Inspect all specimens for bubbles, and remove bubbles before analysis for optimal results.
- Avoid repeated freezing and thawing. The serum sample can be frozen and thawed for two times.
- Serum specimens removed from the separator, red blood cells or clot may be stored up to 48 hours at 2-8°C, and stored up to 3 months frozen at -20°C or colder.
- Before shipping serum 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. Serum specimens should be shipped frozen.

Urine:

- Collect urine samples using standard procedures.
- The urine sample cannot be frozen and is stable for up to 4 days at 2-8°C.
- Stored samples should be thoroughly mixed prior to use (Vortex mixer).
- 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.
- The sample volume required for a single determination of β$_2$-MG is 10 µL.

WARNING AND PRECAUTIONS FOR USERS

- IVD
- For in *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 should be considered potentially able to transmit infectious agents. They should therefore be disposed of 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 container 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 sample.
- 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. It is still possible to keep on using the kit beyond the opened or on-board period if the controls are found within the expected ranges.
- 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. For further information please refer to the corresponding Analyzer Operating Instructions.

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.
The automatic sample dilution is available after dilution settings are done in the MAGLUMI and Biolumi series Fully-auto chemiluminescence immunoassay analyzer user software. Please refer to the corresponding Analyzer Operating Instructions.

LIMITATIONS

- A skillful operation and strict adherence to the instructions are necessary to obtain reliable results. Procedural directions should be followed exactly and careful operation should be used to obtain valid results. Any modification of the procedure is likely to alter the results.
- For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or received immunotherapy may contain human anti-mouse antibodies (HAMA), which may result in falsely elevated or decreased values. Moreover, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples as well.
- Additional clinical or diagnostic information may be required to determine patient status.

RESULTS

Calculation of Results
The analyzer automatically calculates the β_2-MG 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 corresponding Analyzer Operating Instructions.
Interpretation of Results
The expected ranges for the β_2-MG assay were obtained by testing 205 apparently healthy individuals in China, and gave the following reference values listed below:
Serum: 0.9-2.7 µg/mL (2.5^{th}-97.5^{th} percentiles).
Random urine: <0.195 µg/mL (95^{th} percentile).
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 β_2-MG assay was determined as described in the CLSI EP5-A2. 3 controls containing different concentration of analyte were assayed in duplicate at two independent runs per day for 20 testing days. The result is summarized in the following table:

Sample	Mean(µg/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(µg/mL)	%CV	SD(µg/mL)	%CV	SD(µg/mL)	%CV
Control 1	1.343	0.082	6.11	0.071	5.29	0.109	8.12
Control 2	3.325	0.174	5.23	0.107	3.22	0.204	6.14
Control 3	5.768	0.192	3.33	0.227	3.94	0.297	5.15

Limit of Blank (LoB)
The LoB for the β_2-MG assay is 0.03 µg/mL.

Limit of Detection (LoD)
The LoD for the β_2-MG assay is 0.05 µg/mL.

Measuring Range
0.03-10 µg/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as <0.03 µg/mL. Values above the measuring range are reported as >10 µg/mL.

Linearity
The assay is linear between 0.05 µg/mL and 10 µg/mL based on a study performed with guidance from CLSI EP6-A. Nine equally distributed levels of samples were prepared by spiking a serum sample containing β_2-MG 11 µg/mL with a serum sample free of β_2-MG (0.0 µg/mL). The mean sample recovery ranged between 90% to 110%..

Method Comparison
A total of 158 samples in the range of 0.146 to 9.886 µg/mL were tested by the β_2-MG assay and a commercially available immunoassay. The data from the resulting linear regressions are summarized as: $y=1.046x-0.0802$, $r^2=0.9803$.

Analytical Specificity
The specificity of the assay was obtained by adding IgG (17 mg/mL), IgA (3 mg/mL), IgM (2.5 mg/mL) and IgE (320 IU/mL) to two serum samples at the indicated concentrations. No interference was found.

Endogenous Interference
Substances up to the following concentrations did not interfere with the assay:
- Bilirubin 12.5 mg/dL
- Hemoglobin 500 mg/dL
- Triglyceride 1250 mg/dL

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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