Snibe Diagnostic

CE 0123 REF 130254002M:100 tests/kit
130654002M: 50 tests/kit
130754002M: 30 tests/kit

# MAGLUMI® Albumin (CLIA)

## INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Albumin (ALB) in human urine 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 kidney diseases.

## SUMMARY

Albumin is an anionic single-chain protein with a molecular mass of 67 kDa, synthesized by liver cells and secreted into the plasma, where it is the most abundant protein[1]. It consists of a single polypeptide chain of 585 amino acid residues and contains 17 disulfide bonds. The chain is folded into a heart-shaped molecule consisting of three homologous domains, each of which has two subdomains[2]. This highly soluble protein is present in human plasma，and the half-life of albumin is approximately 19 days and accounts for at least 10% of liver protein synthesis[3].

Although it is not essential to life, a number of important and very diverse functions have been ascribed to this protein, including the maintenance of the oncotic pressure and blood volume, acid/ base buffer functions, antioxidant functions and the transport of a number of different substances like fatty acids, bilirubin, ions such as Ca2+ and Mg2+, drugs, hormones, and lipophilic as well as hydrophilic vitamins, for example, vitamin A, riboflavin, vitamin B6, ascorbic acid, and folate，Both serum and urinary albumin levels are important prognostic indicators in renal disease[4].The current definition of microalbuminuria (MA) is an amount of urinary albumin that is greater than the normal value, but also lower than what is detected by a conventional dipstick[5]. Proteinuria, which reflects primarily urinary albumin, is well recognized not only as a marker but also a risk factor for progressive glomerular disease[6]. Diabetic kidney disease is identified clinically through the presence of albuminuria, impaired glomerular filtration rate (GFR), or both, and these two biomarkers have been used for the diagnosis, severity classification, and outcome prediction of CKD (Chronic kidney disease)[7]. The presence of albumin indicates early damage to the glomerular blood vessels; however, in diabetics it also could indicate failure of renal autoregulation[8].

## TEST PRINCIPLE

Competitive chemiluminescence immunoassay.

The prediluted sample, ABEI labeled with ALB monoclonal antibody, buffer and magnetic microbeads coated with ALB antigen are mixed thoroughly and incubated. ALB present in the sample compete with ALB antigen immobilized on the magnetic microbeads for binding ALB monoclonal antibody labeled with ABEI, 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 ALB present in the sample.

## REAGENTS

**Kit Contents**

| Component | Description | 100 tests/kit | 50 tests/kit | 30 tests/kit |
|---|---|---|---|---|
| **Magnetic Microbeads** | Magnetic microbeads coated with ALB antigen (~8.00 μg/mL) in PBS buffer, $NaN_3$ (<0.1%). | 2.5 mL | 1.5 mL | 1.0 mL |
| **Calibrator Low** | A low concentration of ALB antigen, BSA, $NaN_3$ (<0.1%). | 1.0 mL | 1.0 mL | 1.0 mL |
| **Calibrator High** | A high concentration of ALB antigen, BSA, $NaN_3$ (<0.1%). | 1.0 mL | 1.0 mL | 1.0 mL |
| **Buffer** | Tris-HCl buffer, $NaN_3$ (<0.1%). | 6.5 mL | 4.0 mL | 3.0 mL |
| **ABEI Label** | ABEI labeled with ALB monoclonal antibody (~83.3 ng/mL) in Tris-HCl buffer, $NaN_3$ (<0.1%). | 7.5 mL | 4.5 mL | 3.3 mL |
| **Diluent** | 0.9% NaCl. | 25.0 mL | 13.5 mL | 8.0 mL |
| **Control 1** | A low concentration of ALB antigen (20.0 μg/mL), BSA, $NaN_3$ (<0.1%). | 1.0 mL | 1.0 mL | 1.0 mL |
| **Control 2** | A high concentration of ALB antigen (100 μg/mL), BSA, $NaN_3$ (<0.1%). | 1.0 mL | 1.0 mL | 1.0 mL |
| All reagents are provided ready-to-use. | | | | |

**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 | 6 hours |
| Opened at 2-8°C | 6 weeks |
| Frozen at -20°C | 3 months |
| Frozen and thawed cycles | no more than 3 times |

## SPECIMEN COLLECTION AND PREPARATION

**Specimen Types**

Collect 24-hour urine sample or other timed urine sample, such as 6-hour or 8-hour urine sample without preservative.

**Specimen Conditions**

- Recording the time, duration and total volume of the collection. Mix well and retain an aliquot for analysis.
- Samples should not be acidified, and no need to add preservatives to the samples.
- To prevent cross contamination, use of disposable pipettes or pipette tips are recommended.
- Bloody specimens are unsuitable for use, even if cleared by centrifugation, since blood contain a large amount of albumin much more than urine.

**Preparation for Analysis**

- The urine containing sediment should be cleared by filtration or centrifugation before use.
- 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.
- The sample volume required for a single determination of this assay is 20 μL.

**Specimen Storage**

Specimens may be stored up to 8 hours at 10-30°C or 14 days at 2-8°C, or 3 months frozen at -20°C. Frozen specimens subjected to up to 2 freeze/thaw cycles 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 ALB concentrations above the analytical measuring interval, can be diluted with manual dilution procedure. The recommended dilution ratio is 1:10. The concentration of the diluted sample must be >48.0 μg/mL.
- For manual dilution, multiply the result by the dilution factor.
- Please choose applicable diluents or ask Snibe for advice before manual dilution.

## PROCEDURE

**Materials Provided**

Albumin (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 X8, MAGLUMI X3, MAGLUMI X6 or Integrated System Biolumi 8000, 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 ordering 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 ordering 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 ordering patient specimens, refer to the sample ordering 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 28 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 guidelines[9].

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 Albumin 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 seven 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 Albumin (CLIA) Controls (REF: 160201488MT) from Snibe or our authorized distributors for more.

## RESULTS

**Calculation**

The analyzer automatically calculates the ALB 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.
Excretion rates = Result from analyzer in μg/mL × urine volume (in mL) / the duration of the collection (in min)
ALB in mg/24-hour = Result from analyzer in μg/mL× 24 hours urine volume (in mL) × $10^{-3}$.

**Interpretation of Results**

The expected range for the Albumin assay was obtained by testing 1722 apparently healthy individuals in China, gave the following expected value:
Excretion rates: ≤19.6 μg/min (95$^{th}$ percentile).
574 out of 1722 samples were 24-hour urine, and gave the following expected value:
24-hour urine: ≤28.4 mg/24-hour (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 reference interval.

## LIMITATIONS

- Results should be used in conjunction with patient's medical history, clinical examination and other findings.
- If the ALB results are inconsistent with clinical evidence, additional testing is needed to confirm the result.
- Bacterial contamination of the specimens may affect the test results.
- There are other potential causes of microalbuminuria besides incipient diabetic nephropathy. Consideration must be given to exercise, poor diabetic control and nondiabetic renal or systemic diseases, including hypertension. Urinary tract infections and congestive heart disease are also possible causes of subclinical elevations in the albumin excretion rate.

## 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 |
| Urine Pool 1 | 19.934 | 0.680 | 3.41 | 0.101 | 0.51 | 0.904 | 4.53 |
| Urine Pool 2 | 50.530 | 1.112 | 2.20 | 0.389 | 0.77 | 1.659 | 3.28 |
| Urine Pool 3 | 99.340 | 1.184 | 1.19 | 0.910 | 0.92 | 2.815 | 2.83 |
| Control 1 | 19.876 | 0.620 | 3.12 | 0.359 | 1.81 | 0.903 | 4.54 |
| Control 2 | 98.196 | 2.521 | 2.57 | 0.566 | 0.58 | 3.193 | 3.25 |

**Linear Range**

2.50-480 μg/mL (defined by the Limit of Quantitation and the maximum of the master curve).

**Reportable Interval**

1.00-4800 μg/mL (defined by the Limit of Detection and the maximum of the master curve×Recommended Dilution Ratio).

**Analytical Sensitivity**

Limit of Blank (LoB) =0.200 μg/mL.
Limit of Detection (LoD) =1.00 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 interferents 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 | Interference | No interference up to |
|---|---|---|---|
| Bilirubin | 50 mg/dL | Biotin | 0.5 mg/dL |
| Glucose | 5000 μg/mL | Gentamycin sulfate | 120 μg/mL |
| Urea | 625 μg/mL | Bovine serum albumin | 10000 μg/mL |

**Cross-Reactivity**

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

| Cross-reactant | No interference up to | Cross-reactant | No interference up to |
|---|---|---|---|
| Alpha-fetoprotein | 20 μg/mL | Transferrin | 100 μg/mL |
| Creatinine | 2500 μg/mL | Human IgG | 500 μg/mL |
| Apotransferrin | 100 μg/mL | Human IgM | 40 μg/mL |

**Method Comparison**

A comparison of the Albumin assay with a commercially available immunoassay, gave the following correlations (μg/mL):
Number of samples measured: 117
Passing-Bablok: $\hat{y}$=1.0035*x*-0.0298, τ=0.980.
The clinical specimen concentrations were between 2.53 and 479.68 μg/mL.

## REFERENCES


1. Donadio C, Tognotti D, Donadio E. Albumin modification and fragmentation in renal disease[J]. Clinica Chimica Acta, 2012, 413(3–4): 391–395.
2. Prinsen B H C M T, de Sain-van der Velden M G M. Albumin turnover: experimental approach and its application in health and renal diseases[J]. Clinica Chimica Acta, 2004, 347(1–2): 1–14.
3. Kanno S-I, Itoh K, Suzuki N, et al. Exogenous albumin inhibits sorafenib-induced cytotoxicity in human cancer cell lines[J]. Molecular and Clinical Oncology, 2013, 1(1): 29–34.
4. Birn H, Christensen E I. Renal albumin absorption in physiology and pathology[J]. Kidney International, 2006, 69(3): 440–449.
5. Prasad R M, Tikaria R. Microalbuminuria[A]. See: Microalbuminuria[M]. Treasure Island (FL): StatPearls Publishing, 2021.
6. Agrawal S, Smoyer W E. Role of albumin and its modifications in glomerular injury[J]. Pflügers Archiv - European Journal of Physiology, 2017, 469(7–8): 975–982.
7. Sheen Y-J. Risks of rapid decline renal function in patients with type 2 diabetes[J]. World Journal of Diabetes, 2014, 5(6): 835.
8. Weir M R. Microalbuminuria in Type 2 Diabetics: An Important, Overlooked Cardiovascular Risk Factor[J]. The Journal of Clinical Hypertension, 2004, 6(3): 134–143.
9. CLSI. Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions. 4th ed. CLSI guideline C24. Wayne, PA: Clinical and Laboratory Standards Institute; 2016.
10. Robert W. Schroff, Kenneth A. Foon, Shannon M. Beatty, et al. Human Anti-Murine Immunoglobulin Responses in Patients Receiving Monoclonal Antibody Therapy[J]. Cancer Research, 1985, 45(2):879-85.
11. Primus F J, Kelley E A, Hansen H J, et al. "Sandwich"-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy[J]. Clinical Chemistry, 1988, 34(2):261-264.




## SYMBOLS EXPLANATIONS

| | | | |
|---|---|---|---|
|  | Consult instructions for use |  | Manufacturer |
|  | Temperature limit (Store at 2-8°C) |  | Use-by date |
|  | Contains sufficient for<n> tests |  | Keep away from sunlight |
|  | This way up | EC REP | Authorized representative in the European Community |
| IVD | *In vitro* diagnostic medical device | CONTENTS | Kit component |
| REF | Catalogue number | LOT | Batch code |
| CE 0123 | CE marking with notified body ID number | | |



**Shenzhen New Industries Biomedical Engineering Co., Ltd.**
No.23, Jinxiu East Road, Pingshan District, 518122 Shenzhen, P.R. China
Tel: +86-755-21536601 Fax:+86-755-28292740

EC REP **Shanghai International Holding Corp. GmbH (Europe)**
Eiffestrasse 80, 20537 Hamburg, Germany
Tel: +49-40-2513175 Fax: +49-40-255726