



130256007M: 100 tests/kit
130656007M: 50 tests/kit
130756007M: 30 tests/kit

MAGLUMI® Aldosterone (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Aldosterone (ALD) in human serum, plasma and 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 and treatment of individuals with suspected or confirmed primary aldosteronism (a disorder caused by the excessive secretion of aldosterone by the adrenal gland), hypertension caused by primary aldosteronism, selective hypoaldosteronism, edematous states, and other conditions of electrolyte imbalance.

SUMMARY

ALD is a steroid hormone produced in the zona glomerulosa of the adrenal gland and plays a key role in balancing water and electrolytes levels¹⁻³. The production of ALD is mainly regulated by Ang II, potassium (K⁺), and adrenocorticotrophic hormone (ACTH)². ALD facilitates Na⁺ reabsorption and K⁺ excretion by the kidney, thereby contributing to the physiological regulation of electrolytes, water balance, and blood pressure⁴. Inappropriate secretion of aldosterone can lead to a number of diseases states, including hypertension and hypokalemia, and metabolic syndromes that can cause damage to target organs⁴. Autonomous overproduction of ALD leads to primary aldosteronism (PA), which is the most common form of secondary endocrine hypertension⁴. Selective hypoaldosteronism (SH) is a condition manifested by hyperkalemia due to low ALD secretion with normal cortisol. Selective hypoaldosteronism (SH) is an isolated deficiency of ALD without reduction in glucocorticoid or sex hormone secretion from the adrenal gland. It may manifest as hyperkalemia and hyperchloremic metabolic acidosis⁵. Restricting dietary salt leads to an increase in ALD and renin whereas a salt load results in their suppression⁷.

TEST PRINCIPLE

Sandwich chemiluminescence immunoassay.

The sample, buffer and magnetic microbeads coated with anti-ALD antibody are mixed thoroughly, incubating and performing a wash cycle after a precipitation in a magnetic field. ABEI labeled with another anti-ALD antibody are then added, reacting to form sandwich complexes and incubating. After precipitation in a magnetic field, the supernatant is decanted and then another 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 ALD present in the sample.

REAGENTS

Kit Contents

Component	Description	100 tests/kit	50 tests/kit	30 tests/kit
Magnetic Microbeads	Magnetic microbeads coated with anti-ALD antibody (~6.67 µg/mL) in PBS buffer, NaNa ₃ (<0.1%).	2.5 mL	1.5 mL	1.0 mL
Calibrator Low	A low concentration of ALD antigen in PBS buffer, NaNa ₃ (<0.1%).	1.0 mL	1.0 mL	1.0 mL
Calibrator High	A high concentration of ALD antigen in PBS buffer, NaNa ₃ (<0.1%).	1.0 mL	1.0 mL	1.0 mL
Buffer	Tris-HCl buffer, NaNa ₃ (<0.1%).	10.5 mL	6.0 mL	4.2 mL
ABEI Label	ABEI labeled with anti-ALD antibody (~0.500 µg/mL) in Tris-HCl buffer, NaNa ₃ (<0.1%).	17.5 mL	9.5 mL	6.3 mL
Diluent	Bovine serum, NaNa ₃ (<0.1%).	5.5 mL	3.5 mL	3.5 mL
Control 1	A low concentration of ALD antigen (65.0 pg/mL) in PBS buffer, NaNa ₃ (<0.1%).	1.0 mL	1.0 mL	1.0 mL
Control 2	A high concentration of ALD antigen (370 pg/mL) in PBS buffer, NaNa ₃ (<0.1%).	1.0 mL	1.0 mL	1.0 mL

All reagents are provided ready-to-use.

The control barcode labels are provided.

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 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
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SPECIMEN COLLECTION AND PREPARATION

Specimen Types

Only the specimens listed below were tested and found acceptable.

Specimen Types	Collection Tubes
Serum	Tubes without additive/accessory, or tubes containing clot activator or clot activator with gel.
Plasma	K2-EDTA
Urine	/

- 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 grossly hemolyzed/hyperlipidaemia specimens and specimens with obvious microbial contamination.
- 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.
- Samples must be free of fibrin and other particulate matter.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- The sample volume required for a single determination of this assay is 50 µL.

Serum and plasma sample

- 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.
- Specimens should be free of fibrin, red blood cells, or other particulate matter. Such specimens may give reliable results and 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.

Urine sample pre-treated by Sample release agent (REF: 130299034M)

Urine hydrolysis

- Label a glass or polypropylene tube for each urine sample.
- Add 1 part urine and 2 parts Sample release agent 1. Mix thoroughly by vortex or rotator.
- Cap tubes and incubate overnight for 18 hours at 30°C.

Urine Neutralization

- After hydrolysis, the urine sample must be neutralized before testing.
- Label a glass or polypropylene tube for each urine sample.
- Add 1 part hydrolyzed urine and 1 parts Sample release agent 2, mix well.

Specimen Storage

- Serum and plasma specimens removed from the separator, red blood cells or clot may be stored up to 8 hours at 10-30°C, or 5 days at 2-8°C, or 1 month frozen at -20°C. Frozen specimens subjected to up to 3 freeze/thaw cycles have been evaluated.
- Collect 24-hours urine, keeping the specimen refrigerated during collection, measure and record the volume. Add 1 g boric acid/100 mL urine. Mix well before withdrawing an aliquot to be assayed. Borate stabilized urine samples are stable for 8 hours at 10-30°C, or 5 days when stored at 2-8°C, or for 1 month when stored at -20°C. Samples are stable through 3 freeze thaw cycles.
- Hydrolyzed and neutralized urine preps are stable for 2 months when stored at 2-8°C.

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, ALD concentrations above the analytical measuring interval, can be diluted with Diluent either automated dilution protocol or manual dilution procedure. The recommended dilution ratio is 1:50. The concentration of the diluted sample must be >40.0 pg/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

Aldosterone (CLIA) assay, control barcode labels.

Materials Required (But Not Provided)

- General laboratory equipment.
- Sample release agent.
- 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 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 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 Aldosterone 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 system 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 Aldosterone (CLIA) Controls (REF: 160201295MT) from Snibe or our authorized distributors for more.

RESULTS

Calculation

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

Interpretation of Results

The expected range for the ALD assay was obtained by testing 551 serum samples healthy individuals in China, gave the following expected value:

Test subjects	N	Mean (pg/mL)	2.5 th percentile (pg/mL)	97.5 th percentile (pg/mL)
Upright	286	148.644	28	376
Supine	265	108.105	28	239

The expected range for the ALD assay was obtained by testing 297 urine samples apparently healthy individuals in China, gave the following expected value:

Test subjects	N	Mean (µg/day)	2.5 th percentile (µg/day)	97.5 th percentile (µg/day)
Urine (24 hours)	297	10.573	1.1	30

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 ALD results are inconsistent with clinical evidence, additional testing is needed to confirm the result.
- 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 observed⁹.
- Bacterial contamination 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 (pg/mL) (n=180)	Within-Run		Between-Run		Reproducibility	
		SD (pg/mL)	%CV	SD (pg/mL)	%CV	SD (pg/mL)	%CV
Serum Pool 1	40.431	1.433	3.54	0.971	2.40	2.287	5.66
Serum Pool 2	309.021	9.081	2.94	7.965	2.58	15.650	5.06
Serum Pool 3	806.361	25.306	3.14	14.475	1.80	34.539	4.28
Plasma Pool 1	39.957	1.309	3.28	1.032	2.58	2.067	5.17
Plasma Pool 2	298.795	11.504	3.85	4.281	1.43	14.969	5.01
Plasma Pool 3	797.638	26.470	3.32	17.501	2.19	36.571	4.58
Urine Pool 1	75.393	2.596	3.44	1.628	2.16	3.994	5.30
Urine Pool 2	397.321	11.743	2.96	7.528	1.89	21.676	5.46
Urine Pool 3	761.632	22.998	3.02	18.238	2.39	39.311	5.16
Control 1	66.082	2.645	4.00	0.907	1.37	3.645	5.52
Control 2	364.550	13.891	3.81	5.610	1.54	19.899	5.46

Linear Range

20.0-2000 pg/mL (defined by the Limit of Quantitation and the maximum of the master curve).

Reportable Interval

8.00-100000 pg/mL (defined by the Limit of Detection and the maximum of the master curve×Recommended Dilution Ratio).

Analytical Sensitivity

Limit of Blank (LoB) =5.00 pg/mL.

Limit of Detection (LoD) =8.00 pg/mL.

Limit of Quantitation (LoQ) =20.0 pg/mL.

Analytical Specificity

Interference

Interference was determined using the assay, three serum and urine 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	
	Serum	Urine		Serum	Urine
Bilirubin	40 mg/dL	40 mg/dL	Acetylsalicylic Acid	65.2 mg/dL	65.2 mg/dL
Hemoglobin	600 mg/dL	600 mg/dL	Salicylic Acid	59.9 mg/dL	59.9 mg/dL
Intralipid	2000 mg/dL	2000 mg/dL	Valproic Acid	57.6 mg/dL	57.6 mg/dL
Rheumatoid factor	1500 IU/mL	/	Propranolol	230 µg/dL	230 µg/dL
ANA	398 AU/mL	/	Metoprolol	1.28 mg/dL	1.28 mg/dL
Biotin	0.5 mg/dL	/	Triamterene	886 µg/dL	886 µg/dL
Urea	/	4 g/dL	Tetracycline	1.51 mg/dL	1.51 mg/dL

Boric Acid	/	2 g/dL	Alodipine besylate	13.9 µg/dL	13.9 µg/dL
Acetic Acid	/	2%	Verapamil	216 µg/dL	237 mg/dL
Tartaric Acid	/	1 g/dL	Furosemide	5.99 mg/dL	5.99 mg/dL
Uric Acid	/	100 mg/dL	Eplerenone	1.99 µg/dL	1.99 µg/dL
Glucose	10 mg/mL	10 mg/mL	Enalapril	42.4 µg/dL	46.6 mg/dL
Ascorbic Acid	6 mg/dL	200 mg/dL	Lisinopril	32.7 µg/dL	32.7 µg/dL
Acetaminophen	20 mg/dL	20 mg/dL	Losartan potassium	225 µg/dL	249 mg/dL
Valsartan	1.1 mg/dL	1.1 mg/dL	Prazosin HCl	120000 ng/mL	120000 ng/mL
Nifedipine	40 µg/dL	40 mg/dL	Prednisone	100000 ng/mL	100000 ng/mL
Androstenedione	10000 ng/mL	100000 ng/mL	Pregnenolone	100000 ng/mL	100000 ng/mL
17α-OH-Corticosterone	100000 ng/mL	100000 ng/mL	17α-Hydroxyprogesterone	100000 ng/mL	100000 ng/mL
Cortisol	100000 ng/mL	200000 ng/mL	Spirolactone	100000 ng/mL	100000 ng/mL
Cortisone	200000 ng/mL	200000 ng/mL	11-deoxycortisol	100000 ng/mL	100000 ng/mL
21-Hydroxyprogesterone	100000 ng/mL	100000 ng/mL	Dehydroepiandrosterone	100000 ng/mL	1000000 ng/mL
Dexamethasone	200000 ng/mL	200000 ng/mL	Estriol	10000 ng/mL	100000 ng/mL
Estradiol	100000 ng/mL	100000 ng/mL	Hydrochlorothiazide (HCTZ)	600 µg/dL	600 µg/dL
Fludrocortisone	200000 ng/mL	200000 ng/mL			

Cross-Reactivity

Cross-reactivity was determined using the assay, three serum and urine samples containing different concentrations of analyte were spiked with potential cross-reactants 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	
	Serum	Urine		Serum	Urine
Ketosteroid	100000 ng/mL	100000 ng/mL	Testosterone	100000 ng/mL	200000 ng/mL
Corticosterone	10000 ng/mL	100000 ng/mL	Oestrone	10000 ng/mL	100000 ng/mL
Progesterone	100000 ng/mL	100000 ng/mL			

High-Dose Hook

No high-dose hook effect was seen for ALD concentrations up to 100000 pg/mL.

Method Comparison

A comparison of the Aldosterone assay with a commercially available immunoassay, gave the following correlations (pg/mL):

Serum:

Number of samples measured: 116

Passing-Bablok: y=0.9943x-1.1137, r=0.978.

The clinical specimen concentrations were between 32.15 and 1984 pg/mL.

Urine:

Number of samples measured: 103

Passing-Bablok: y=1.0010x-0.5424, r=0.987.

The clinical specimen concentrations were between 457 and 44730 pg/mL.

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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		Authorized representative in the European Community
	<i>In vitro</i> diagnostic medical device		Kit component
	Catalogue number		Batch code
	CE marking with notified body ID number		

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