

MAGLUMI[®] Testosterone (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Testosterone in human serum 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

Testosterone is a steroid from the androstane class containing a keto and hydroxyl groups at the three and seventeen positions respectively. It is biosynthesized in several steps from cholesterol and is converted in the liver to inactive metabolites¹. In humans and most other vertebrates, testosterone is secreted primarily by the testicles of males and, to a lesser extent, the ovaries of females. Small amounts are also secreted by the adrenal glands. On average, in adult males, levels of testosterone are about 7-8 times as great as in adult females². In men, testosterone plays a key role in the development of male reproductive tissues such as the testis and prostate, as well as promoting secondary sexual characteristics such as increased muscle and bone mass, and the growth of body hair³. In addition, testosterone is involved in health and well-being, and the prevention of osteoporosis. Insufficient levels of testosterone in men may lead to abnormalities including frailty and bone loss⁴⁻⁵. In plasma, 98% of testosterone is bound to protein, with 65% bound to sex hormone-binding globulin (SHBG) and 33% bound weakly to albumin⁶.

Determination of testosterone level is useful for the diagnosis of hepergonadism and heperpituitarism in men, and hirsutism, menstrual disorders and polycystic ovarian syndrome in women. It is still helpful for the characterization and follow-up of some cancers such as testicular, breast, ovarian and adrenal tumours⁷⁻¹⁰.

PRINCIPLE OF THE TEST

The Testosterone assay is a competitive chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), ABEI labeled with anti-TEST monoclonal antibody, magnetic microbeads coated with purified TEST antigen are mixed thoroughly and incubated, forming antibody-antigen 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 TEST present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material Provided

Components	Contents	100 tests (REF: 130202010M)	50 tests (REF: 130602010M)
Magnetic Microbeads	Magnetic microbeads coated with TEST antigen, containing BSA, NaN ₃ (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	Containing BSA and TEST antigen, NaN ₃ (<0.1%).	2.5 mL	2.0 mL
Calibrator High	Containing BSA and TEST antigen, NaN ₃ (<0.1%).	2.5 mL	2.0 mL
Buffer	Containing BSA, 0.25% ANS, NaN ₃ (<0.1%).	6.5 mL	4.0 mL
ABEI Label	Anti-TEST monoclonal antibody labeled with ABEI, containing BSA, NaN ₃ (<0.1%).	6.5 mL	4.0 mL
Internal Quality Control	Containing BSA and TEST antigen, 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 representatives.

CALIBRATION

Traceability: This method has been standardized against USP Testosterone Reference Material.

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 and a master curve (10 calibrations) 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 2 weeks 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 **Testosterone (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 supporters or distributors for assistance.

SPECIMEN COLLECTION AND PREPARATION

- Use standard sampling tubes or tubes containing separating gel. Collect blood aseptically following the universal precautions for venipuncture.
- 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 clotting, the presence of fibrin may cause erroneous results. Samples must be free of fibrin and other particulate matter.
- Do not use hemolyzed or grossly lipemic specimens as well as specimens containing particulate substance or exhibiting obvious microbial contamination. Inspect all specimens for bubbles, and remove bubbles before analysis for optimal results.
- Avoid repeating freeze-thaw cycles. The serum sample can be only frozen and thawed two times. Specimens must be mixed thoroughly after thawing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or a secondary tube. Care should be taken to transfer only the clarified specimen without the lipemic material.
- All samples (patient specimens and controls) should be tested within 3 hours when placed on board the MAGLUMI and Biolumi Systems. Refer to the SNIBE service for more details of onboard sample storage constraints.
- Specimens removed from the separator, cells or clot may be stored up to 24 hours at 2-8°C. Freeze samples at or below -20°C if the sample is not assayed within 24 hours.
- Before shipping specimens, it is recommended that specimens be removed from the serum separator, red blood cells or clot. 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. Specimens should be shipped frozen.
- The sample volume required for a single determination of testosterone is 20 µL.

WARNING AND PRECAUTIONS FOR USERS

- **IVD**
- For *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 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 containers 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 samples.
- 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 kit. For further information, please refer to the corresponding Analyzer Operating Instructions.

DILUTION

Sample dilution by analyzer is not available in this reagent kit.

Samples with concentrations above the measuring range can be diluted manually. After manual dilution, multiply the result by the dilution factor. Please choose applicable diluents or ask SNIBE for advice before manual dilution .

LIMITATIONS

- A skillful technique and strict adherence to the instructions are necessary to obtain reliable results.
- Bacterial contamination or heat inactivation of the specimens may affect the test results.
- A result within the expected range does not rule out the presence of disease and should be interpreted together with the patient's clinical picture and other diagnostic procedures.
- Test results are reported quantitatively. However, diagnosis of a disease should not be based on the result of a single test, but should be determined in conjunction with clinical findings in association with medical judgement.
- Any therapeutical decision should also be taken on a case-by-case basis.
- 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.
- A strong interaction with 19-nortestosterone (Nandrolone) was found. Do not use samples from patients receiving Nandrolone treatment.

RESULTS

Calculation of Results

The analyzer automatically calculates the Testosterone 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 corresponding Analyzer Operating Instructions.

Conversion factor: ng/mLx3.47= nmol/L.

Interpretation of Results

The expected ranges for the Testosterone assay were obtained by testing 180 males and 198 females apparently healthy individuals in China, and gave the following expected values:

Males: 2.2-10.5 ng/mL (2.5th-97.5th percentiles).

Females: <1.0 ng/mL (95th percentile).

Results may differ between laboratories due to variations in population and test method. It is recommended that each laboratory should establish its own expected ranges.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the Testosterone assay was determined as described in the CLSI EP5-A2. 3 controls and 3 human serum pools containing different concentration of analyte were assayed in duplicate at two independent runs per day for 20 testing days. The results are summarized in the following table:

Sample	Mean (ng/mL)	Within-Run		Between-Run		Total	
	(N=80)	SD (ng/mL)	%CV	SD (ng/mL)	%CV	SD (ng/mL)	%CV
Serum Pool 1	2.488	0.113	4.54	0.068	2.73	0.132	5.31
Serum Pool 2	10.069	0.220	2.19	0.313	3.11	0.382	3.79
Serum Pool 3	14.622	0.276	1.89	0.315	2.15	0.419	2.87
Control 1	1.549	0.082	5.29	0.097	6.26	0.127	8.20
Control 2	5.722	0.229	4.00	0.000	0.00	0.229	4.00
Control 3	7.994	0.277	3.47	0.309	3.87	0.415	5.19

Limit of Blank (LoB)

The LoB for the Testosterone assay is 0.09 ng/mL.

Limit of Detection (LoD)

The LoD for the Testosterone assay is 0.15 ng/mL.

Measuring Range

0.09-17 ng/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as <0.09 ng/mL. Values above the measuring range are reported as >17 ng/mL.

Linearity

The assay is linear between 0.15 ng/mL and 17 ng/mL based on a study performed with guidance from CLSI EP6-A. Nine equally distributed levels of samples were prepared by blending a serum sample containing Testosterone 18 ng/mL with a serum sample depleted of Testosterone (0.0 ng/mL). The mean sample recovery ranged from 90.0% to 110.0%.

Method Comparison

A total of 100 samples in the range of 0.16 to 17.68 ng/mL were tested by the Testosterone assay (y) and a commercially available immunoassay (x). The data from the resulting linear regressions are summarized as: $y=0.987x+0.068$, $r^2=0.977$.

Analytical Specificity

The specificity of the assay was obtained by adding PROG (100 ng/mL), E2 (3000 pg/mL), CORTISOL (600 ng/mL) and DHEAS (50000 ng/mL) to 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 30 mg/dL
- Hemoglobin 1800 mg/dL
- Triglyceride 2000 mg/dL

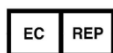
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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
	Temperature limit (Store at 2-8 °C)		Use-by date
	Contains sufficient for		Keep away from sunlight
	This way up		Authorized representative in the European Community
	In vitro diagnostic medical device		Kit components
	Catalogue number		Batch code