Snibe Diagnostic

CE REF 130203001M: 100 tests
130603001M: 50 tests

MAGLUMI® TSH (CLIA)

INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of thyroid-stimulating hormone (TSH) 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

Thyroid-stimulating hormone (TSH, thyrotropin) is a glycoprotein with a molecular weight of approx. 30000 daltons and is composed of two non-covalently bound subunits[1,2]. The alpha subunit has an identical amino acid sequence to the α-chains of luteinizing hormone (LH), follicle-stimulating hormone (FSH) and human chorionic gonadotropin (hCG)[3]. The beta subunit of TSH is unique, and confers biological as well as immunological specificity[4].

TSH is produced by the pituitary gland, a tiny organ located below the brain and behind the sinus cavities[5]. It is part of the body's feedback system to maintain stable amounts of the thyroid hormones thyroxine (T_4), triiodothyronine (T_3), free T_4 and free T_3 in the blood[6]. Thyroid hormones help control the rate at which the body uses energy. When concentrations decrease in the blood, the hypothalamus releases thyrotropin releasing hormone (TRH)[7]. This stimulates the release of TSH by the pituitary gland. The TSH in turn stimulates the production and release of T_4 and T_3 by the thyroid gland, a small butterfly-shaped gland that lies in the neck flat against the windpipe. When all three organs are functioning normally, thyroid production turns on and off to maintain constant blood thyroid hormone levels.

The TSH test is often important in evaluating thyroid function and/or symptoms of hyperthyroidism or hypothyroidism[8]. It is frequently ordered along with or preceding a T_4 test. Other thyroid tests that may be ordered include a T_3 test and thyroid antibodies (if autoimmune-related thyroid disease is suspected).

It may be ordered at regular intervals to monitor the effectiveness of treatment when someone is being treated for a known thyroid disorder.

PRINCIPLE OF THE TEST

The TSH assay is a sandwich chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), ABEI labeled with anti-TSH monoclonal antibody, magnetic microbeads coated with another anti-TSH monoclonal antibody are mixed thoroughly and incubated, forming sandwich of 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 proportional to the concentration of TSH present in the sample (or calibrator/control, if applicable).

KIT COMPONENTS

Material Provided

Component	Contents	100 tests (REF: 130203001M)	50 tests (REF: 130603001M)
Magnetic Microbeads	Magnetic microbeads coated with anti-TSH monoclonal antibody, containing BSA, NaN_3 (<0.1%).	2.5 mL	2.0 mL
Calibrator Low	TSH antigen, bovine serum, NaN_3 (<0.1%).	3.0 mL	2.0 mL
Calibrator High	TSH antigen, bovine serum, NaN_3 (<0.1%).	3.0 mL	2.0 mL
Buffer	Tris buffer, HAMA Blocker, containing BSA, NaN_3 (<0.1%).	6.5 mL	4.0 mL
ABEI Label	ABEI labeled with anti-TSH monoclonal antibody (mouse), containing BSA, NaN_3 (<0.1%).	6.5 mL	4.0 mL
Internal Quality Control	TSH antigen, 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 representatives.

CALIBRATION

Traceability: This method has been standardized against WHO 3rd International Standard 81/565.

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 exchange of lots (Reagent or Starter 1+2).
- Every two 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 ***TSH (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. Freeze samples only once. 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 detailed of onboard sample storage constraints.
- Specimens removed from the separator, cells or clot may be stored up to 48 hours at 2-8°C.
- 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 when shipped, 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 TSH is 100 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 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 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 for 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

Dilutions are not generally needed due to the broad assay measuring range. In the rare instance when sample dilution is requested, please refer to your laboratory procedures.

High-Dose Hook

For the the TSH assay, no high dose hook effect was observed when samples containing TSH up to 3,000 µIU/mL.

LIMITATIONS

- Whether high or low, an abnormal TSH result indicates an excess or deficiency in the amount of thyroid hormone available to the body, but it does not indicate the reason. An abnormal TSH test result is usually followed by additional testing to investigate the cause of the increase or decrease.

- Many medications—including aspirin and thyroid-hormone replacement therapy—may affect thyroid gland function test results and their use should be discussed with the doctor prior to testing.
- When a doctor adjusts a person's thyroid hormone replacement dosage, it is important to wait at least one to two months before checking the TSH again so that the new dose can have its full effect.
- Extreme stress and acute illness may also affect TSH test results. Results may be low during the first trimester of pregnancy
- 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.
- Serum TSH levels alone give no evidence of the presence or absence of thyroid disease. They must always be interpreted in context with the clinical picture and other diagnostic procedures.
- A high TSH result often means an underactive thyroid gland that is not responding adequately to the stimulation of TSH due to some type of acute or chronic thyroid dysfunction. Rarely, a high TSH result can indicate a problem with the pituitary gland, such as a tumor producing unregulated levels of TSH. A high TSH value can also occur when someone with a known thyroid disorder or who has had their thyroid gland removed is receiving too little thyroid hormone medication.
- A low TSH result can indicate an overactive thyroid gland (hyperthyroidism) or excessive amounts of thyroid hormone medication in those who are being treated for an underactive (or removed) thyroid gland. Rarely, a low TSH result may indicate damage to the pituitary gland that prevents it from producing adequate amounts of TSH.
- The following table summarizes test results and their potential meaning.

TSH	T4	T3	Interpretation
High	Normal	Normal	Mild (subclinical) hypothyroidism
High	Low	Low or normal	Hypothyroidism
Low	Normal	Normal	Mild (subclinical) hyperthyroidism
Low	High or normal	High or normal	Hyperthyroidism
Low	Low or normal	Low or normal	Non-thyroidal illness; rare pituitary (secondary) hypothyroidism

RESULTS

Calculation of Results

The analyzer automatically calculates the TSH 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 µIU/mL. For further information please refer to the corresponding Analyzer Operating Instructions.

Interpretation of Results

The expected range for the TSH assay was obtained by testing 164 apparently healthy individuals in China, gave the following expected value:
0.3-4.5 µIU/mL (2.5^{th}-97.5^{th} percentiles).
Results may differ between laboratories due to variations in population and test method. It is recommended that each laboratory should establish its own reference range.

PERFORMANCE CHARACTERISTICS

Precision

Precision for the TSH 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(µIU/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(µIU/mL)	%CV	SD(µIU/mL)	%CV	SD(µIU/mL)	%CV
Serum Pool 1	1.227	0.031	2.53	0.025	2.04	0.040	3.26
Serum Pool 2	11.864	0.209	1.76	0.166	1.40	0.267	2.25
Serum Pool 3	64.187	1.359	2.12	1.119	1.74	1.760	2.74
Control 1	0.620	0.019	3.07	0.012	1.94	0.023	3.71
Control 2	6.543	0.137	2.09	0.100	1.53	0.170	2.60
Control 3	17.214	0.345	2.00	0.294	1.71	0.453	2.63

Limit of Blank (LoB)

The LoB for the TSH assay is 0.001 µIU/mL.

Limit of Detection (LoD)

The LoD for the TSH assay is 0.006 µIU/mL.

Limit of Quantitation (LoQ)

Limit of Quantitation is tested as described in CLSI EP17-A2. It is defined as the concentration of TSH that can be measured with an inter assay CV of 20%. The LoQ for the TSH assay is 0.01 µIU/mL.

Measuring Range

0.001-100 µIU/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as <0.001 µIU/mL. Values above the measuring range are reported as >100 µIU/mL.

Linearity

The assay is linear between 0.01 µIU/mL and 100 µIU/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 TSH 110 µIU/mL with a serum sample depleted of TSH (0.0 µIU/mL). The mean sample recovery ranged from 90% to 110%.

Method Comparison

A total of 160 clinical samples in the range of 0.056 to 93.001 µIU/mL were tested using the TSH assay (y) and a commercially available immunoassay (x). The data from the resulting linear regressions are summarized as: $y=0.953x+0.3274$, $r^2=0.9596$.

Analytical Specificity

The specificity of the assay was obtained by adding hCG (500 mIU/mL), FSH (1500 mIU/mL) and LH (600 mIU/mL) to serum samples at the indicated concentrations. No interference was found.

Endogenous Interference

Interference substances were tested as described in CLSI EP7-A2.The result shows that no interference at the levels indicated below.

Interference	Concentration
Conjugate Bilirubin	60 mg/dL
Unconjugate bilirubin	40 mg/dL
Hemoglobin	2000 mg/dL
Triglycerides	1000 mg/dL
HAMA	300 ng/mL
Rheumatoid factor	124 IU/mL
Total protein	12.5 g/dL
Acetaminophen	20 mg/dL
Ibuprofen	50 mg/dL
Aspirin	50 mg/dL
Biotin	10 ng/mL

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SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
8°C 2°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