Instructions for Use

Thyroid Stimulating Hormone (CLIA)

[Product Name]

Thyroid Stimulating Hormone (CLIA)

[Packing Size]

24×1 Tests/Pkg (Calibrators included); 60×1 Tests/Pkg (Calibrators included); 60×1 Tests/Pkg

[Intended Use]

Thyroid stimulating hormone (TSH) assay is a chemiluminescent immunoassay (CLIA) used for the quantitative determination of human thyroid stimulating hormone (TSH) in human serum, plasma, or whole blood, and it is mainly used for the auxiliary evaluation of pituitary-thyroid function.

Thyroid stimulating hormone (TSH) is a glycoprotein hormone synthesized and secreted by the anterior pituitary gland to regulate thyroid function. It contains 211 amino acids with a molecular weight of 28000 Da, and is composed of two peptide chains - α chain and β chain [1, 2]. The synthesis and secretion of TSH are promoted by thyrotropin-releasing hormone (TRH) secreted by hypothalamus, and also negatively regulated by the concentration of free triiodothyronine (FT3) and free thyroxine (FT4), which form the hypothalamic-pituitary-thyroid axis. TSH stimulates the synthesis and secretion of thyroxine (T4) and triiodothyronine (T3) with metabolic activity by interacting with specific receptors on the surface of thyroid cells [3]. TSH fluctuates more rapidly and significantly than thyroid hormone when thyroid function changes. It is a sensitive indicator reflecting the function of hypothalamus-pituitary-thyroid axis. Measurement of TSH is mainly used to diagnose clinical or subclinical hyperthyroidism (decreased TSH level) and hypothyroidism (increased TSH level), monitor T4 replacement therapy in primary hypothyroidism or antithyroid therapy in hyperthyroidism, diagnosis of pathological syndromes of normal thyroid function, central hypothyroidism (pituitary and hypothalamic), and inappropriate TSH secretion syndrome (thyroid hormone resistance syndrome) [4-7]. The 3rd generation TSH assay can be used to distinguish patients with true hyperthyroidism from those with subclinical hyperthyroidism or TSH suppression caused by some non-thyroid diseases [8].

[Principle of the Assay]

This assay takes the double-antibody sandwich format. The detection principle is described below:

(1) Mix the sample with magnetic microparticle coated with an anti-TSH antibody, add another acridinium labeled anti-TSH antibody. After mixing and incubation, TSH in the sample will react with anti-TSH antibody coated on the microparticle, acridinium labeled anti-TSH antibody will react with another site on TSH, forming antigen-antibody complex;

(2) A magnet captures microparticle, and then unbound substance is washed off. Add pre-trigger and trigger solution to the reaction mixture sequentially to initiate chemiluminescence reaction;

(3) A photomultiplier tube is used to measure photons generated from the reaction. Signal is amplified exponentially. The count is proportional to TSH concentration in the sample. TSH concentration is determined by an internal calibration curve.

[Main Components]

Packing Size

Component \ Packing Size	Fill Volume		
	24×1 Tests/Pkg (Calibrators included)	60×1 Tests/Pkg (Calibrators included)	60×1 Tests/Pkg
TSH Reagent Cartridge – Microparticle (R1)	24×50 μL	60×50 μL	60×50 μL
TSH Reagent Cartridge – Conjugate (R2)	24×100 μL	60×100 μL	60×100 μL
TSH Calibrator C1	1×1.0 mL	1×1.0 mL	/
TSH Calibrator C2	1×1.0 mL	1×1.0 mL	/
Calibration Card	1 pcs	1 pcs	/

Main Composition

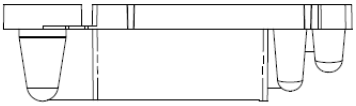
Component	Main Composition	
TSH Reagent Cartridge	Microparticle (R1)	Mouse anti-TSH antibody coated microparticle, ~0.3 g/L; MES buffer, 50 mmol/L; ProClin 300, 0.5 g/L
	Conjugate (R2)	Acridinium labeled mouse anti-TSH antibody, ~200 μg/L; MES buffer, 50 mmol/L; ProClin 300, 0.5 g/L
TSH Calibrator C1	TSH (recombinant); Phosphate buffer, 50 mmol/L; ProClin 300, 0.5 g/L	
TSH Calibrator C2	TSH (recombinant); Phosphate buffer, 50 mmol/L; ProClin 300, 0.5 g/L	
Calibration Card	Calibration curve and calibrator information	

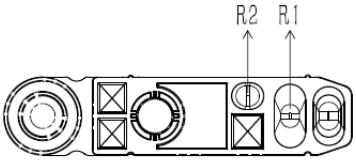
Note: (1) Components in different lots of reagent cannot be mixed or exchanged for use.

(2) Traceability: This quantification method can be traced back to TSH National Standard Reference Materials code 150530, which can be traced back to the 3rd IRP WHO Reference Standard 81/565.

(3) Information about the calibrators (such as lot number and concentration etc.) can be found on the instrument interface after scanning the Calibrator Card.

The position of each component in the reagent pack is shown in the front view (Upper) and vertical view (Down) of the reagent cartridge.





Instruments and accessories needed but not supplied (Medcaptain has the supplies)

(1) Medcaptain Immu F6/F6S Automatic Chemiluminescent Immunoassay Analyzers;

(2) Pre-trigger solution;

(3) Trigger solution;

(4) Washing solution;

(5) 500 μL pipette tips;

(6) Thyroid Function Controls.

[Storage and Shelf-life]

Storage: Store sealed reagent cartridges and calibrators at 2~8℃ in upright position, and avoid freezing.

Shelf life: 14 months.

Stability of Calibrators: Sealed vial of calibrators can be kept at 2~8℃ in dark for 14

months. After calibrator C1 and C2 is uncapped and sealed again, it can be stored at 10~30℃ for 5 days, and at 2~8℃ for 60 days.

The dates of manufacturing and expiration can be found on the labels.

[Matched Instruments]

Medcaptain Immu F6/F6S Automatic Chemiluminescent Immunoassay Analyzers

[Specimen Types]

Serum, plasma, and whole blood (collected with EDTA-K_2, EDTA-K_3, lithium heparin, and sodium heparin as the anti-coagulants) can be used in the testing.

Sample volume for each test: 100 μL.

The collected sample should be tested as soon as possible.

Whole blood must be tested within 4 hours after sample collection. Serum and plasma can be kept at 10~30℃ for 24 hours, at 2~8℃ for 7 days, and at -20℃ or below for 60 days. Frequent freeze-thaw cycles should be avoided, and only one freeze-thaw cycle is allowed. If the sample contains precipitate or frozen floccule, centrifugation is needed to clear the sample before testing.

Sample collection tubes from different manufacturers may lead to variation in testing results, due to the difference in tube material and additives in the tubes. Medcaptain has not evaluated all types of sample collection tubes from different manufacturers. Each laboratory should make its own judgment about the usability of sample collection tubes.

[Test Procedure]

Reagent Preparation

Reagent: TSH reagent cartridge (containing magnetic microparticle R1, and acridinium labeled conjugate R2) is ready for use. It can be loaded directly into the instrument after opening the package.

Calibrators: Calibrator C1 and C2 are ready for use. Each calibrator can be added to a sample cup, and the cups are loaded to a sample rack. The sample rack can be pushed directly into the instrument for calibrator testing.

Calibration

Refer to the relevant chapters in the operation manual of each chemiluminescent immunoassay analyzer. Calibration tests should be ordered before the first time use of TSH assay. Medcaptain provides TSH reagent pack and matched calibrators to calibrate the instrument.

Before calibration, scan the calibration card provided in the kit, and the calibration curve and calibrator information will be scanned into the system. Before calibration, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

Put calibrators on a sample rack, load the sample rack into the instrument.

On the screen interface of “Reagent > Request Calibration”, select test name and lot number to request a calibration. Select the position of each calibrator on the sample rack, set the number of repeat tests, start calibration.

Automatic immunoassay analyzer makes use of calibration data to validate the calibration, and adjust the calibration curve automatically. Instrument calibration is effective for 60 days. A new calibration is needed in the following situation:

(1) Change into a new lot of reagent;

(2) Control test results are out of the target range;

(3) The lot of reagent has been used on the same instrument for more than 60 days.

Refer to the Chapter of “Calibration” in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about calibration.

Control Testing

Thyroid Function Controls are matched with TSH reagent pack. There are two levels of controls: Low Control (L) and High Control (H).

Test two levels of controls with TSH reagent on the instrument in accordance with any local applicable regulations. Control testing is highly recommended every time the lot of reagent has been changed, the instrument has been re-calibrated, or after trouble shooting/ maintenance service.

Before the control testing, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

Put controls on a sample rack, and load the sample rack into the instrument; Select “Control” on the interface of test menu, select test name and control lot; Click on “Start” and begin the testing. Check the results after control test is finished.

Control test results should fall into a specific range. If it is out of the target range, the user should check the system, such as expiration date of the controls, storage condition, instrument performance and status. After root cause analysis and correction, the user should test controls again. If the same problem exists, please contact customer service of Medcaptain.

Each laboratory should set up its own control range and frequency of control testing, based on its own practice. Refer to the Chapter of “Control Testing” in instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about control testing.

Sample Testing

Before sample testing, take out reagent cartridges from the package, and load them into the instrument. The instrument scans two-dimensional barcode on the reagent pack automatically to obtain information of the reagent (reagent name, Lot No., and expiration date etc.);

If a sample collection tube is directly loaded to the instrument for testing, the sample volume should be at least 1.0 mL; Un-cap sample collection tubes, put samples on a sample rack, and push the sample rack into the instrument; Select “Sample” on the interface of test menu, enter information of samples, select test name; Click on “Start” and begin the testing. Check the results after sample test is finished.

The reagent usage for each test is: R1 50 μL, and R2 100 μL. The instrument aspirates and mixes each component in the reagent cartridge and incubates at 37℃. Time duration from sampling to result is about 15 min.

Refer to the Chapter of “Sample Testing” in instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about sample testing.

Result Calculation

Based on the built-in calibration curve, the instrument automatically calculate TSH concentration of each sample, in a unit of μIU/mL.

[Reference Intervals]

Samples for the study of reference intervals come from local area in Guangdong Province. A total of 248 healthy and normal people have been recruited (Male: 128; Female: 120), age ranges from 12 to 85 years old. Serum tests give a reference interval of 2.5th percentile to 97.5th percentile as: 0.32~4.50 μIU/mL.

Due to the differences in geography, race, sex, and age of tested population, the reference interval may vary in different laboratories. It is highly recommended for each clinical lab to establish its own reference intervals.

[Interpretation of Test Results]

The test data is for clinical reference only. It cannot be used as the only confirmatory evidence nor to eliminate the possibility of diseases. Clinical diagnosis of patients should take clinical symptoms, body sign, disease history, other lab test results, and treatment response into comprehensive consideration.

The measurement range of this assay is: 0.005~100 μIU/mL. If TSH concentration is lower than LoD, it will be reported as <0.005 μIU/mL; If TSH concentration is over the upper limit, it will be reported as >100 μIU/mL. For a sample with TSH concentration of >100 μIU/mL, sample diluent can be used to dilute the sample

manually (a dilution factor of 1:10 is recommended). Test the diluted sample in duplicate to obtain more accurate results.

When the instrument shows a warning sign of "SMPL", it means there is insufficient sample volume. Make sure enough sample is added for repeating the test. When the instrument shows a warning sign of "SMPJ", it means the sample probe has been blocked. Clean sample clot in the probe before repeating the test.

Some results are tagged with other signs. Refer to the Chapter of "Result Signs" in the instruction manual of Automatic Chemiluminescent Immunoassay Analyzer for detailed information about results tagged with signs.

[Limitation of the Test Method]

The test data is for clinical reference only. It cannot be used individually as the evidence to confirm or eliminate the possibility of diseases.

There is no Hook effect for a sample with TSH concentration of ≤5000 μIU/mL. For each endogenous interference substance with concentration less than the value shown in the table below, measurement error caused by interference is within ±10%.

Endogenous interference substance	Concentration of interference substance
Total Protein	≤12 g/dL
Bilirubin	≤20 mg/dL
Hemoglobin	≤500 mg/dL
Triglyceride	≤1500 mg/dL

For potential cross-reactant with concentration less than the value shown in the table below, the test result of TSH is less than 0.005 μIU/mL.

Cross-reactant	Concentration
LH	≤3000 mIU/mL
FSH	≤1000 mIU/mL
HCG	≤1000000 mIU/mL
β-TSH	≤200 μIU/mL
α-TSH	≤200 μIU/mL

Heterophilic antibodies in human serum may react with immunoglobulin in the reagent or sample, and interfere with immunoassay *in vitro*. More clinical or diagnostic information is needed to confirm disease diagnosis of patients. Some patients have frequent contact with animals, or have been treated or diagnosed with mouse monoclonal antibodies. They may have generated heterophilic antibodies. For example, some patients under monoclonal antibody treatment may have human anti-mouse antibodies (HAMA) in blood circulation, leading to false positive or false negative results. Anti-interference components are added to this reagent formulation to minimize the impact of HAMA and ANA, but the problem may not be totally eliminated, and some sample testing may still be impacted. More clinical and diagnostic information is needed to make a solid conclusion.

Samples with the titer of no less than 1:1000 by anti-nuclear IgG test kit (indirect immune-fluorescence method) were studied in interference tests. It has shown less than ±10% error in the test results. For RF at a concentration of less than 1500 IU/mL, and for multiple representative human HAMA samples, the measurement error caused by the interference is within ±10%.

[Property and Performance]

1 Limit of Blank

LoB ≤ 0.001 μIU/mL.

2 Limit of Detection

LoD ≤ 0.005 μIU/mL.

3 Limit of Quantitation

LoQ ≤0.005 μIU/mL. LoQ is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 10%, meeting the requirements of the 3rd generation TSH assay.

4 Accuracy

Accuracy should meet at least one of the following criteria:

a) Relative Deviation: take TSH National Standard to make reference samples for routine evaluation. The relative deviation between the measured result and the target concentration is less than ±10.0 %.

b) Relative Deviation: measure two levels of accuracy reference samples with traceability. The relative deviation between the measured result and the target concentration is less than ±10.0%.

5 Linearity

Test TSH samples with concentration in the range of 0.005~100 μIU/mL, the linearity correlation coefficient r≥0.9900.

6 Repeatability

Coefficient of variation (CV) for the test results of low (0.2±0.1 μIU/mL) and high (5±1 μIU/mL) corporate reference sample is less than 8.0%.

7 Lot-to-lot Variation

Coefficient of variation (CV) for the test results of low (0.2±0.1 μIU/mL) and high (5±1 μIU/mL) corporate reference sample with three batches of reagents is less than 10.0%.

8 Accuracy of Calibrator Value Assignment

Use primary calibrators with assigned values from higher level measurement procedure, calibrate the immunoassay analyzer, and use the same lot of reagent to measure the value of each product calibrator. The measured value of Calibrator C1 and C2 has a relative deviation within ±10.0% from its assigned value.

9 Homogeneity of Calibrators

9.1 Within-vial Homogeneity

Within-vial homogeneity of Calibrator C1 or C2 is represented with coefficient of variation, and CV≤8.0 %.

9.2 Between-vial Homogeneity

Between-vial homogeneity of calibrator C1 or C2 is represented with coefficient of variation, and CV≤5.0%.

[Attention Notes]

1 It is for in-vitro diagnosis only.
2 It can only be used by professionals.
3 Never use expired reagent kit.
4 Never mix components from different kits, or from different reagent lots.
5 Do not put the reagent cartridges upside down.
6 Measurement of TSH in a sample using different detection systems may yield different results, due to difference in test methods, assay specificity, and factors of interference. The measured values from different systems should not be directly compared to avoid inappropriate clinical interpretation.
7 Strictly follow the protocol in the package insert, and operate according to the lab guidelines.
8 The test results can only be used for clinical reference. Clinical diagnosis of patients should take symptoms, body sign, disease history, other laboratory test results, and response to treatment for comprehensive assessment.
9 User should wear gloves and lab coat. Rinse with water if the skin is in contact with the reagent. Flush eyes with copious of water if eyes are in touch with the reagent, and see a doctor immediately.
10 Take all samples and reaction waste as potential biohazards. All waste must be handled following the local government regulation.
11 This product is a single-use cartridge. Reagent cartridge should be put back into refrigerator and stored at 2~8℃ if they have been placed at room temperature but not opened yet.

[Interpretation of Signs]

	Temperature limit		Date of manufacturing
	In-vitro diagnostic medical device		Catalogue number
	Batch Code		Consult instruction for use
	Use-by Date		Authorized representative in the European Community
	This way up		CE marking of conformity
	Manufacturer		Unique device identifier
	Biological risks		

[References]

[1] Pierce JG. The Subunits of Pituitary Thyrotropin. Their Relationship to other Glycoprotein Hormones. Endocrinology 1971; 89:1331-1344.

[2] Rees Smith B, Pyle GA, Petersen VB, Hall R. Interaction of Thyrotropin with the Human Thyrotropin Receptor. J Endocrinol 1977; 75:391-400.

[3] Mariusz W, Szkudlinski, Valerie Fremont, Catherine Ronin, Bruce D, Weintraub. Thyroid-Stimulating Hormone and Thyroid-Stimulating Hormone Receptor Structure-Function Relationships. Physiol Rev 2002; 82: 473–502.

[4] White GH. Recent advances in routine thyroid function testing. CRC –Critical Reviews in Clinical Laboratory Sciences 1987; 24: 315-362.

[5] Spencer CA. Thyroid status: trends in testing – selective test use cuts cost. Clin Chem. 1989; News, 15, No. 11: 9-14.

[6] Meng Zhao wei, Tan Jian．Reading and analysis on management guidelines for hypothyroidism published in 2012 by American Thyroid Association and American Association of Clinical Endocrinologists. International Journal of Radiation Medicine and Nuclear Medicine, 2013, 37(2): 124-127.

[7] Chinese Thyroid Association, Chinese Collage of Surgeons, Chinese Medical Doctor Association; Chinese Research Hospital Association Thyroid Disease Committee; Clinical Practical Technology Committee of China International Exchange and Promotive Association for Medical and Health Care. Chinese expert consensus on surgical treatment of hyperthyroidism (2020 edition). Chinese Journal of Practical Surgery, 2020, 40 (11): 1229-1233.

[8] Christine R Squire and William D Fraser. Thyroid stimulating hormone measurement using a third generation immunometric assay. Ann Clin Biochem. 1995; 32: 307-313.

[Basic Information]

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