Hormone

ichroma™ TSH

INTENDED USE

ichroma™ TSH is a fluorescence immunoassay (FIA) for the quantitative determination of TSH (Thyroid stimulating hormone) in human whole blood/serum/plasma. It is useful as an aid to the diagnosis of thyroid disorders.

For *in vitro* diagnostic use only.

INTRODUCTION

The determination of whole blood or serum or plasma level of thyroid stimulating hormone (TSH or thyrotropin) is recognized as an important measurement in the assessment of thyroid function[1,2]. TSH is secreted by the anterior lobe of the pituitary gland, and induces the production and release of triiodothyronine (T3) and thyroxine (T4) by the thyroid gland which is primarily responsible for body metabolism[3]. TSH is a glycoprotein with a molecular weight of approximately 28,000 daltons, consisting of two chemically different subunits, alpha (89 amino acids) and beta (115 amino acids)[4,5]. Although the concentration of TSH in the blood is extremely low, it is essential in the maintenance of normal thyroid function. The release of TSH by the anterior pituitary gland is regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus. Blood levels of TRH and TSH are inversely related to those of the thyroid hormones. When there is a high level of thyroid hormones in the blood, less TRH is released by the hypothalamus, so that less TSH is secreted by the anterior pituitary gland. The opposite action will occur when there are decreased levels of thyroid hormones in the blood. This process, known as a negative feedback mechanism, is responsible for maintaining the proper blood levels of these hormones[6,7,8].

PRINCIPLE

The test uses a sandwich immunodetection method.

The detector antibodies in buffer bind to antigens in the sample, forming antigen-antibody complexes, and migrate onto nitrocellulose matrix to be captured by the other immobilized-streptavidin on a test strip.

More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by the instrument for ichroma™ tests to show TSH concentration in the sample.

COMPONENTS

ichroma™ TSH consists of 'cartridge', 'detector tube' and 'detector diluent'.

- The cartridge contains the membrane called a test strip which has streptavidin at the test line and chicken IgY at the control line. All cartridges are individually sealed in an aluminum foil pouch containing a desiccant, and they are further packaged in a box.
- The detector tube has a granule containing anti-beta TSH-biotin conjugate, anti-TSH-fluorescence conjugate, anti-chicken Igy-fluorescence conjugate and sodium azide as a preservative in Tris-HCl. All detector tubes are packed in a pouch.
- The detector diluent contains and sodium azide as a preservative in Tris-HCl and it is pre-dispensed in a vial. The detector diluent is packed in box.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, detector tube, detector diluent and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges and detector tubes. A cartridge should be used for testing one sample only. A detector tube should be used for processing of one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use cartridge, if the pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- If test components and/or sample are stored in refrigerator, then allow cartridge, detector tube, detector diluent and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ichroma™ tests may generate slight vibration during use.
- Used cartridges, detector tubes, detector diluent, capillary tubes and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The detector tube and the detector diluent contain sodium azide (NaN_3), and it may cause certain health issue like convulsions, low blood pressure, low heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- No Biotin interference was observed in **ichroma™ TSH** when biotin concentration in the sample was below 5 ng/mL. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.
- **ichroma™ TSH** will provide accurate and reliable results subject to the below conditions.
  - **ichroma™ TSH** should be used only in conjunction with the instrument for ichroma™ tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
Sodium heparin

LIMITATION OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the antigens to the antibodies which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the antigens with time and/or temperature may also cause false negative result as it makes antigens unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

STORAGE AND STABILITY

Storage condition			
Component	Storage Temperature	Shelf life	Note
Cartridge	2 - 30 °C	20 months	Disposable
Detector tube	2 - 30 °C	20 months	Unopened
Detector diluent	2 - 30 °C	20 months	Unopened
	2 - 30 °C	20 months	Opened

- After the cartridge pouch is opened, the test should be performed immediately.

MATERIALS SUPPLIED

REF CFPC-22

Components of **ichroma™ TSH**

- Cartridge box:
  - Cartridge 25
  - Detector tube 25
  - Detector diluent 1
  - 35 µL Capillary tube 25
  - ID chip 1
  - Instructions for use 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ichroma™ TSH**.

Please contact our sales division for more information.

- Instrument for ichroma™ tests
  - **ichroma™ Reader** REF FR203
  - **ichroma™ II** REF FPRR021
  - **ichroma™ III** REF FPRR037
  - **ichroma™ M3** REF FPRR035
  - **ichroma™-50** REF FPRR022
  - **ichroma™-50 PLUS** REF FPRR036
- **Printer** REF FPRR007
- **Boditech TSH Control** REF CFPO-228
- **Boditech Hormone Control** REF CFPO-95

SAMPLE COLLECTION AND PROCESSING

The sample type for **ichroma™ TSH** is human whole blood/serum/plasma.

- It is recommended to test the sample within 24 hours after collection when collected sample is stored at room temperature.
- The samples (serum, plasma) should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The samples (whole blood, serum, plasma) may be stored for 2 weeks at 2-8 °C prior to being tested. If testing will be delayed more than 2 weeks, samples (serum, plasma) should be frozen at -20 °C.
- The samples (serum, plasma) stored frozen at -20 °C for 3 months showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect
- Whole blood sample may be used to collect according to below:

  ①Wear disposable gloves and protective equipment for safety.

  ②Open the zipper bag which has capillary tubes.

  ③Take out the capillary tube and check for damage or contamination.

  ④Hold the handle of the capillary tube and touch the surface of blood with the capillary tube.

  ⑤Fill it with blood completely.
  (Make sure that no air bubbles are present in the capillary tube. Do not get blood on the surface of the capillary tube. If the blood gets on the surface of the capillary tube, remove it gently with gauze.)

TEST SETUP

- Check the contents of **ichroma™ TSH**: Sealed cartridges, detector tubes, a detector diluent, 35 µL capillary tubes, an ID Chip and an instructions for use.
- Ensure that the lot number of the cartridge matches that of the detector tube, the detector diluent as well as an ID chip.
- If the sealed cartridge, the detector tube and the detector diluent have been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Turn on the instrument for ichroma™ tests.
- Insert the ID chip into the 'ID chip port'.

※ **Please refer to the instrument for ichroma™ tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

▶ **ichroma™ Reader, ichroma™ II, ichroma™ M3**

Multi test mode

1) Take 150 µL of detector diluent using a pipette and dispense it to the detector tube containing a granule. When the granule form is completely dissolved in the

tube, it becomes detection buffer.
(The detection buffer must be used immediately.
Do not exceed 30 seconds.)

2) Take 10 µL of sample (serum/plasma/control) using a pipette and dispense it to the detector tube.

※ If the test uses whole blood, transfer the whole blood collected in a capillary tube to a detector.

3) Close the lid of the detector tube and mix the sample thoroughly by shaking it about 10 times.
(The sample mixture must be used immediately.
Do not exceed 30 seconds.)
4) Take 75 µL of the sample mixture and dispense it into the sample well of the cartridge.
5) Leave the cartridge at room temperature for 12 minutes.

⚠ *Scan the sample-loaded cartridge immediately when the incubation time is over. If not, it will cause inaccurate test result.*

6) To scan the sample-loaded cartridge, insert it into the cartridge holder of the analyzer for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
7) Press the 'Select' or tap the 'Start' button on the analyzer for ichroma™ tests to start the scanning process.
(ichroma™ M3 will start the test automatically after inserting.)
8) The instrument for ichroma™ tests will start scanning the sample-loaded cartridge immediately.
9) Read the test result on the display screen of the instrument for ichroma™ tests.

Single test mode

1) The test procedure is same with the 'Multi test mode 1) -4)'.
2) Insert the sample-loaded cartridge into the holder of the instrument for ichroma™ tests. Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder. An arrow is marked on the cartridge especially for this purpose.
3) Press the 'Select' or tap the 'Start' button on the instrument for ichroma™ tests.
(ichroma™ M3 will start the test automatically after inserting.)
4) The cartridge goes inside the instrument for ichroma™ tests and will automatically start scanning the sample-loaded cartridge after 12 minutes.
5) Read the test result on the display screen of the instrument for ichroma™ tests.

▶ **ichroma™ III**

1) The test procedure is same with the 'Single test mode'.

▶ **ichroma™-50, ichroma™-50 PLUS**

1) Insert the tip array in the tip station.
2) Insert the detector tube in the reagent station and cover the reagent station to hold the detector tubes in place.
3) Open the lid of the detector diluent and insert the detector diluent in the diluent station.
4) Insert the cartridge magazine with the cartridges into the magazine station.
5) Insert the sample tube into the blood collection tube rack and load the blood collection tube rack into the sampling station (loading part).
6) Tap the button located in the upper side of the No. of test cartridge region to select the ID chip what you want to use.
7) When the selected cartridge slot is activated, set the number of test cartridge by tapping.
8) Set the number of pipette tips by tapping.
9) Tap the 'Start' button on the left upper of the main screen to start test.

INTERPRETATION OF TEST RESULT

- The instrument for ichroma™ tests calculates the test result automatically and displays TSH concentration of the test sample in terms of µIU/mL.
- Reference range: 0.4 - 4.0 µIU/mL
- Working range: 0.09 - 100 µIU/mL

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ichroma™ TSH**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
(Please refer to the instruction for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**
  - Limit of Blank (LoB) 0.03 µIU/mL
  - Limit of Detection (LoD) 0.07 µIU/mL
  - Limit of Quantitation (LoQ) 0.09 µIU/mL

- **Analytical specificity**
  - Cross reactivity
    Biomolecules such as below the ones in the table were added to the test sample(s) at concentrations much higher than their normal physiological levels in the blood. **ichroma™ TSH** test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactants	Concentration
hCG	10,000 mIU/mL
LH	100 mIU/mL
FSH	100 mIU/mL

  - Interference
    Interferents listed in the following table were added to the test sample at the concentrations mentioned below. EDTA_K2 and sodium citrate have effects on **ichroma™ TSH** test in the procedure. So, K_2 EDTA and sodium citrate as an anticoagulant are not recommended on ichroma™ TSH test.

Interferents	Concentration
D-glucose	1000 mg/dL
L-Ascorbic acid	5.25 mg/dL
Bilirubin (Unconjugated)	40 mg/dL
Hemoglobin	1000 mg/dL
Cholesterol	400 mg/dL
Triglyceride	1500 mg/mL
K_2 EDTA	9.9 mg/mL
Sodium heparin	330 U/L
Sodium citrate	40 mg/mL

■ **Precision**

- Single-site study

Repeatability (within-run precision)
within-laboratory precision (Total precision)
Lot to lot precision

3 Lots of **ichroma™ TSH** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

Single-site study						
TSH [μIU/mL]	Repeatability		within-laboratory precision		Lot to lot precision	
	AVG [μIU/mL]	CV (%)	AVG [μIU/mL]	CV (%)	AVG [μIU/mL]	CV (%)
0.5	0.50	7.28	0.5	6.95	0.51	6.62
5.0	5.00	5.58	5.02	6.28	4.99	6.07
50.0	49.93	7.21	49.72	6.84	49.88	6.53

- Multi-site study

Reproducibility

1 Lot of **ichroma™ TSH** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

Multi-site study		
TSH [μIU/mL]	Reproducibility	
	AVG [μIU/mL]	CV (%)
0.5	0.5	5.54
5.0	5.0	6.18
50.0	49.74	5.85

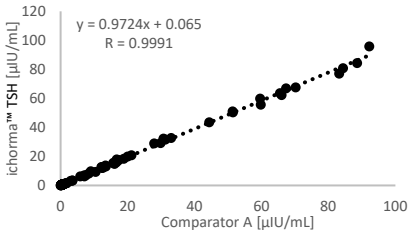
■ **Accuracy**

The accuracy was confirmed by testing with 3 different lots of **ichroma™ TSH.** The tests are repeated 10 times at each concentration of the control standard.

TSH [μIU/mL]	Lot 1	Lot 2	Lot 3	AVG [μIU/mL]	Recovery (%)
50	47.43	48.93	48.69	48.35	96.7
25.25	24.31	24.45	23.8	24.19	95.8
5.45	5.39	5.31	5.23	5.31	97.4
2.48	2.49	2.46	2.41	2.45	98.9
1.19	1.15	1.16	1.14	1.15	96.2
0.5	0.48	0.49	0.52	0.49	98.9

■ **Comparability**

TSH concentrations of 100 clinical samples were quantified independently with **ichroma™ TSH (ichroma™ II)** and **comparator A** as per prescribed test procedures. Test results were compared, and their comparability was investigated with linear regression and correlation coefficient (R). The regression equation and correlation coefficient are as follows.



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Note: Please refer to the table below to identify various symbols.

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
	Batch code
	Catalog number
	Caution
	Manufacturer
	Authorized representative of the European Community
	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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