Hormone

AFIAS TSH

INTENDED USE

AFIAS TSH is a fluorescence immunoassay (FIA) for the quantitative determination of Thyroid stimulating hormone (TSH) in human whole blood/serum/plasma. It is useful as an aid in management and monitoring of thyroid disorders.

For *in vitro* diagnostic use only.

INTRODUCTION

The determination of blood 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 metabolism3. 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 AFIAS tests to show TSH concentration in the sample.

COMPONENTS

AFIAS TSH consists of 'cartridges'

- Each sealed aluminum pouch contains two cartridges.
- Each cartridge packaged in an aluminum pouch has three components including a cartridge part, a detector part and a diluent part.
- The cartridge part contains the membrane called a test strip which has streptavidin at the test line, and chicken IgY at the control line.
- The detector part has a granule containing anti human TSH-fluorescence conjugate, anti-Human beta-TSH biotin conjugator, anti-chicken IgY-fluorescence conjugator, bovine serum albumin (BSA) as a stabilizer and sodium azide as a preservative in Tris-HCl.
- The diluent part contains sodium chloride as a stabilizer and sodium azide as a preservative in Tris-HCl.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow 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 and ID chip) must match each other.
- Do not interchange 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. A cartridge should be used for testing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use a cartridge, if 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 and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for AFIAS tests may generate slight vibration during use.
- Used cartridges, C-tips and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The cartridge contains sodium azide (NaN_3), and they may cause certain health issues like convulsions, low blood pressure and 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 **AFIAS 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.
- **AFIAS TSH** will provide accurate and reliable results subject to the below conditions.
  - **AFIAS TSH** should be used only in conjunction with the instrument for AFIAS tests.
  - Have to use recommended anticoagulant sample.

Recommended anticoagulant
Sodium heparin

- **C-tip should be used when the following conditions are met.**
  - C-tip provided with the kit is recommended to obtain correct test result.
  - Whole blood should be immediately tested after collection.
  - Do not perform a test with C-tip on General Mode. It might cause an erroneous result.
  - Excess whole blood around the C-tip should be wiped off.
  - In order to avoid cross-contamination, please do not re-use C-tip for multiple samples.
  - AFIAS cartridge should be inserted and positioned in the cartridge holder prior to the blood sample collection.
  - While collecting blood, be careful not to create air bubbles in the C-tip.

LIMITATIONS 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 antigen 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 antigen with time and/or temperature may also cause false negative result as it makes the antigen 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	Unopened
		1 month	Resealed

- Return an unused cartridge to the spare cartridge zipper bag containing the desiccant pack. Reseal along entire edge of zip-seal.

MATERIALS SUPPLIED

REF SMFP-20

Components of **AFIAS TSH**

- Cartridge box:
  - Cartridge 24
  - Pipette tip (Zipper bag) 24
  - ID chip 1
  - Instructions for use 1
  - Spare cartridge zipperbag 1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **AFIAS TSH**. Please contact our sales division for more information.

- **AFIAS-1** REF FPRR019
- **AFIAS-3** REF FPRR040
- **AFIAS-6** REF FPRR020
- **AFIAS-10** REF FPRR038
- **Boditech TSH Control** REF CFPO-228
- **Boditech TSH Calibrator** REF CFPO-254
- **Boditech Hormone Control** REF CFPO-95
- **Boditech Hormone Calibrator** REF CFPO-107
- **C-tip (30 µL)** REF CFPO-199

SAMPLE COLLECTION AND PROCESSING

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

- It is recommended to test the sample within 24 hours after collection.
- 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 week at 2-8 °C prior to being tested. If testing will be delayed more than 2 week, samples (serum, plasma) should be frozen at -70 ~ -20 °C.
- The samples (serum, plasma) stored frozen at -70 ~ -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 the test result, do not refreeze previously frozen samples.
- Collection of whole blood sample using C-tip
  (1) Hold the C-tip horizontally and touch the surface of the blood with the tip of the C-tip.
  (2) Capillary action will automatically draw the blood sample to C-tip and stop.
  (3) Wipe off any excess blood around the tip.
  (4) Double-check if whole blood is filled accurately in the C-tip and AFIAS reader is ready for a test on the 'C-tip mode'.

TEST SETUP

- Check the components of the **AFIAS TSH** as described below. : Cartridges, pipette tips, C-tips, an ID chip, a spare cartridge zipper bag and an instructions for use
- Ensure that the lot number of the cartridge matches that of the ID chip.
- If the sealed cartridge has 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 AFIAS tests.
- Empty the tip box.
- Insert the ID chip into the 'ID chip port'.
- **Please refer to the instrument for AFIAS tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

▶ **AFIAS-1, AFIAS-3, AFIAS-6**

General mode

1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Select the 'General mode' in the instrument for AFIAS tests.
4) Take 100 µL of the sample (whole blood/serum/plasma/control) using a pipette and dispense it into the sample well of the cartridge.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 12 minutes.

C-tip mode

1) Insert a cartridge into the cartridge holder.
2) Take 30 µL of whole blood using a C-tip.
3) Insert the whole blood-filled C-tip into the tip hole of

the cartridge.
4) Select the 'C-tip mode' in the instrument for AFIAS tests.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 12 minutes.

▶ **AFIAS-10**

Normal mode
1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Tap the 'Load' button of the bay that holds the cartridge with the tip to read the barcode of the cartridge and please confirm the item name written on the cartridge.
4) Insert the sample tube into the tube rack.
5) Insert the tube rack into the loading part of the sampling station.
6) Tap the 'Start' button on the screen.
7) The test result will be displayed on the screen after 12 minutes.

Emergency mode – General tip
1) The test procedure is same with the 'Normal mode 1) – 3)'.
2) Convert the 'Emergency mode' in AFIAS-10.
3) Select the tip type (general tip) on the screen.
4) Select the sample type (whole blood/serum/plasma) on the screen.
5) Take 100 µL of the sample (whole blood/serum/plasma/ control) using a pipette and dispense it into the sample well of the cartridge.
6) Tap the 'Start' button on the screen.
7) The test result will be displayed on the screen after 12 minutes.

Emergency mode – C-tip
1) Insert a cartridge into the cartridge holder.
2) Take 30 µL of whole blood using a C-tip.
3) Insert the C-tip with sample into the tip hole of the cartridge.
4) Tap the 'Load' button of the bay that holds the cartridge with a tip to read the barcode of the cartridge and please confirm the item name written on the cartridge.
5) Convert the 'Emergency mode' in AFIAS-10.
6) Select the tip type (C-tip) on the screen.
7) Tap the 'Start' button on the screen.
8) The test result will be displayed on the screen after 12 minutes.

INTERPRETATION OF TEST RESULT

- The instrument for AFIAS 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 **AFIAS TSH**. For more information regarding obtaining the control materials, contact Boditech Med Inc.'s Sales Division for assistance.
  (Please refer to the instructions 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. **AFIAS TSH** test results did not show any significant cross-reactivity with these biomolecules.

Cross reactivity materials	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. K_2 EDTA and sodium citrate have effects on **AFIAS TSH** test in the procedure. So, K_2 EDTA and sodium citrate as an anticoagulant are not recommended on AFIAS TSH tests.

Interference materials	Concentration
D-glucose	1000mg/dL
L-Ascorbic acid	5.25mg/dL
Bilirubin (Conjugated)	40mg/dL
Hemoglobin	1000mg/dL
Cholesterol	400mg/dL
Triglyceride	1500mg/dL
K_2 EDTA	9.9mg/ml
Sodium Heparin	330U/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 **AFIAS TSH** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.

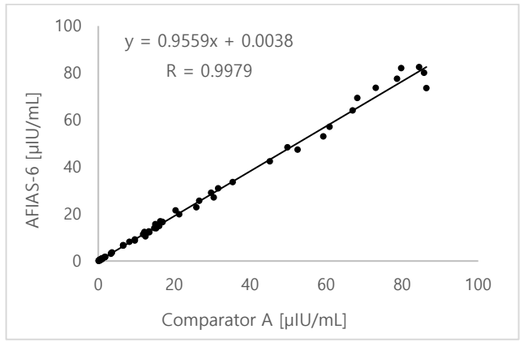
- Multi-site study
Reproducibility
1 Lot of **AFIAS TSH** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

Conc. [uIU/ml]	Repeatability		Total precision	
	AVG	CV (%)	AVG	CV (%)
0.5	0.51	5.50	0.51	6.06
5.0	5.06	5.14	5.05	6.32
50.0	49.54	6.56	49.57	6.02
Conc. [uIU/ml]	Lot to lot precision		Reproducibility	
	AVG	CV (%)	AVG	CV (%)
0.5	0.50	6.37	0.50	6.33
5.0	5.03	6.20	5.00	6.14
50.0	49.83	6.59	49.90	6.11

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

TSH Conc. (µIU/mL)	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
50.00	49.85	49.05	49.15	49.35	98.7
25.25	25.64	24.33	24.33	24.77	98.1
5.45	5.21	5.31	5.45	5.32	97.7
2.48	2.50	2.43	2.37	2.44	98.2
1.19	1.16	1.18	1.14	1.16	97.3
0.50	0.50	0.50	0.49	0.50	99.1

- **Comparability**
Cortisol concentrations of 100 clinical samples were quantified independently with **AFIAS TSH (AFIAS-6)** 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.

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

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