ichroma™ TSH

INTENDED USE
ichroma™ TSH is a lateral flow chromatography, Fluorescence Immunoassay (FIA) for the quantitative determination of Thyroid Stimulating Hormone (TSH) level in serum or plasma.

INTRODUCTION
The determination of serum or plasma levels of thyroid stimulating hormone (TSH or thyrotropin) is recognized as an important measurement in the assessment of thyroid function1,2. Thyroid stimulating hormone is secreted by the anterior lobe of the pituitary gland, and induces the production and release of thyroxine (T4) and triiodothyronine (T3) from the thyroid gland3. It is a glycoprotein with a molecular weight of approximately 28,000 daltons, consisting of two chemically different subunits, alpha and beta4,5. Although the concentration of TSH in the bloodstream is extremely low, it is essential in the maintenance of normal thyroid function. The release of TSH is regulated by a TSH-releasing hormone (TRH) produced by the hypothalamus. The levels of TSH and TRH are inversely related to the level of thyroid hormone. When there is a high level of thyroid hormone in the blood, less TRH is released by the hypothalamus, so less TSH is secreted by the pituitary. 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 hormones6,7,8.

PRINCIPLE
The test uses a sandwich immunodetection method, such that the detector antibody in buffer binds to TSH in sample and antigen-antibody complexes are captured to another TSH antibody that has been immobilized on test strip as sample mixture migrates nitrocellulose matrix. Thus the more TSH antigen in sample, the more antigen-antibody complexes accumulated on the test strip. Signal intensity of fluorescence on detector antibody reflects the amount of antigen captured and is processed by ichroma™ Reader to show TSH concentration in specimen.

Reference Value9

<table>
<thead>
<tr>
<th>TSH(μIU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation and Childhood</td>
</tr>
<tr>
<td>0 day</td>
</tr>
<tr>
<td>5 days</td>
</tr>
<tr>
<td>1 year</td>
</tr>
<tr>
<td>2 years</td>
</tr>
<tr>
<td>3 years</td>
</tr>
<tr>
<td>4-19 years</td>
</tr>
<tr>
<td>Adults</td>
</tr>
<tr>
<td>20-54 years</td>
</tr>
<tr>
<td>55-87 years</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>1st Trimester</td>
</tr>
<tr>
<td>2nd Trimester</td>
</tr>
<tr>
<td>3rd Trimester</td>
</tr>
</tbody>
</table>

- It is recommended that each laboratory establish its own reference range for population of interest.

COMPONENTS AND REAGENTS
ichroma™ TSH consists of a ‘Test cartridge’, an ‘ID chip’, a Sample mixing tube, and a ‘Detection buffer vial’
- The test cartridge contains a test strip; on the membrane of which, mouse antibodies against TSH and streptavidin have been immobilized at the test line and the control line respectively.
- Each test cartridge is individually sealed in an aluminum foil pouch containing a desiccant. 25 sealed test cartridges are packed in a box which also contains an ID chip.
- The detection buffer pre-dispensed in a tube contains fluorochrome-labeled anti-TSH antibodies, fluorescent-labeled biotin-BSA, bovine serum albumin (BSA) as a stabilizer and sodium azide in phosphate buffered saline (PBS) as a preservative.
- The detection buffer is dispensed in each detection buffer vial. Detection buffer are packed in a separate zipper bag which is further packed in a Styrofoam box provided with ice packs for the purpose of shipment.

WARNINGS AND PRECAUTIONS
- For in vitro diagnostic use only.
- Carefully follow the instructions and procedures described in this insert.
- Lot numbers of all the test components (test cartridge, ID chip and detection buffer) must match with each other.
- Do not interchange the test components from different lots or use the test components beyond the expiration date.
- Test performed by using any test component with mismatching lot number or that beyond the expiration date may yield misleading test result(s).
- The test cartridge should remain sealed in its original pouch until use. Do not use the test cartridge that is damaged or already opened.
- Allow a minimum of 30 minutes for the test cartridge to attain room temperature, which has been stored in a refrigerator.
- The detection buffer should attain room temperature prior to performing the test.
- ichroma™ TSH as well as the ichroma™ Reader should be used away from vibration and/or magnetic field. During normal usage, ichroma™ Reader may produce minor vibrations which should be regarded as normal.
- A detection buffer tube should be used for processing one sample only. Similarly a test cartridge should be used for testing one processed sample only. Both the detection buffer tube as well as the test cartridge should be discarded after single use.
- Used detection buffer tubes, pipette tips and test cartridges should be handled carefully and disposed of by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.

STORAGE AND STABILITY
- The test cartridge is stable for 20 months (while sealed in an aluminum foil pouch) if stored at 4 - 30°C.
- The detection buffer dispensed in a tube is stable for 20 months if stored at 2 - 8°C.
- After the test cartridge pouch is opened, the test should be performed immediately.
LIMITATIONS OF THE TEST SYSTEM
ichroma™ TSH provides accurate and reliable results subject to the following constraints:
- Use ichroma™ TSH should be used only in conjunction with ichroma™ Reader.
- The test should always be performed on freshly collected sample(s).
- Anticoagulants other than heparin sodium have not been evaluated for obtaining the sample(s) for the purpose of this test. Hence their use should be avoided.
- The test sample must be at room temperature prior to testing. If the test samples are to be shipped for the purpose of this test, appropriate precautions must be exercised.
- Effectiveness of the test is highly dependent on storage of test components and test samples at prescribed optimal conditions.
- The test may yield false positive result(s) due to cross-reactions of some components of serum with the capture/detector antibodies and/or non-specific adhesion of certain components having similar epitopes to bind with these antibodies.
- The test may also yield false negative results; the most common factor being non-responsiveness of the antigen to the antibodies due to its epitopes being masked by some unknown components such that the antigen cannot be detected or captured by the antibodies. False negative results may also be obtained due to instability or degradation of the TSH antigen with time and/or temperature making it unrecognizable by the antibodies.
- Other factors interfering with the test and causing erroneous results include technical/procedural errors, degradation of the test components/reagents as well as 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 including clinical symptoms and other relevant test results.

SAMPLE COLLECTION AND PROCESSING
The test can be performed on either serum/plasma.
- It is recommended to test the sample within 24 hours after collection.
- The serum and plasma should be prepared by centrifugation within 3 hours after the collection of whole blood.
- If the test could not be performed within 24 hours after the preparation of test samples, they should be immediately frozen below -10 degrees, and it’s allowed to keep them in a freezer for 3 months only.
- In case of the whole blood sample, it should not be kept in a freezer in any case, but it can be centrifuged into serum and plasma within 3 hours after collection for the freezing storage.
- Once the sample was frozen, it should be used one time only for test, because repeated freezing and thawing can result in the decrease in test values.

MATERIALS SUPPLIED
 ichroma™ Reader
 Components of ichroma™ TSH

- Test Cartridge Box:
  - Sealed Test Cartridges: 25
  - ID Chip: 1
  - Package Insert: 1

- Box containing Detection Buffer Vial: 1

TEST SETUP
1. Check the contents of ichroma™ TSH: Sealed Test Cartridge, ID Chip, Sample Mixing Tube, and Detection Buffer Tube.
2. Ensure that the lot number of the test cartridge matches with that of the ID chip as well as the detection buffer tube.
3. Keep the sealed test cartridge (if stored in refrigerator) and the detection buffer tube at room temperature for at least 30 minutes just prior to the test. Place the test cartridge on a clean, dust-free and flat surface.
4. Turn on the ichroma™ Reader.
5. Insert the ID Chip into the ID chip port of the ichroma™ Reader.
6. Press the ‘Select’ button on the ichroma™ Reader. (Please refer to the ‘ichroma™ Reader Operation Manual’ for complete information and operating instructions.)

TEST PROCEDURE
1. Transfer 150 µL of serum/plasma/control sample using a transfer pipette to a tube containing the sample mixing buffer.
2. Add 75 µL detection buffer to the sample mixing tube containing serum/plasma/control.
3. Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
4. Pipette out 75 µL of a sample mixture and dispense it into the sample well on the test cartridge.
5. Leave the sample-loaded test cartridge at room temperature for 12 minutes.
6. To scan the sample-loaded test cartridge, insert it into the test cartridge holder of the ichroma™ Reader. Ensure proper orientation of the test cartridge before pushing it all the way inside the test cartridge holder. An arrow has been marked on the test cartridge especially for this purpose.
7. Press ‘Select’ button on the ichroma™ Reader to start the scanning process.
8. ichroma™ Reader will start scanning the sample-loaded test cartridge immediately.
9. Read the test result on the display screen of the ichroma™ Reader.

INTERPRETATION OF TEST RESULT
- ichroma™ Reader calculates the test result automatically and displays TSH concentration of the test sample in terms of µIU/mL.
- Working range of ichroma™ TSH is 0.1 - 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.
- Before testing a clinical sample using a new test lot, control reagents should be tested to confirm the test procedure, and to verify whether the test produces the expected results.
Quality control tests should also be performed whenever there is any question concerning the validity of the test results.

Control reagents are not provided with ichroma™ TSH. For more information regarding obtaining the control reagents, contact Boditech Med Inc.’s Sales Division for assistance.

ichroma™ TSH test has a built-in internal control that satisfies the routine quality control requirements. This internal control test is performed automatically each time a clinical sample is tested. An invalid result from the internal control leads to display an error message on the ichroma™ Reader indicating that the test should be repeated.

PERFORMANCE CHARACTERISTICS

1. **Interference:** Other bio-molecules, such as LH (300mIU/mL), FSH (200mIU/mL), and hCG (200,000 mIU/mL) were added to test specimen with much higher level than their physiological level in normal blood. There was no significant interference with the TSH measurement, nor was there any significant assay cross-reactivity with those bio-molecules tested.

2. **Hook Effect:** No high dose hook effect is observed in this assay at TSH concentrations up to 500µIU/mL.

3. **Imprecision:** For the intra-assay imprecision, 10 replicates were tested at each control sample. For the imprecision evaluation, tests were conducted on 10 sequential days with 5 replicates and for 3 persons at each TSH concentration.

<table>
<thead>
<tr>
<th>TSH (µIU/mL)</th>
<th>Intra-assay Mean</th>
<th>CV%</th>
<th>Inter-assay Mean</th>
<th>CV%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>0.24</td>
<td>16.35</td>
<td>0.23</td>
<td>17.40</td>
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<tr>
<td>0.5</td>
<td>0.50</td>
<td>11.50</td>
<td>0.51</td>
<td>12.17</td>
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<tr>
<td>2</td>
<td>2.02</td>
<td>6.10</td>
<td>2.07</td>
<td>4.87</td>
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<tr>
<td>5</td>
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<td>4.61</td>
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<td>4.10</td>
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<tr>
<td>20</td>
<td>20.58</td>
<td>5.87</td>
<td>20.28</td>
<td>6.01</td>
</tr>
<tr>
<td>50</td>
<td>50.44</td>
<td>3.84</td>
<td>50.50</td>
<td>5.60</td>
</tr>
</tbody>
</table>

4. **Comparability:** TSH concentrations of 125 serum samples were quantified independently with ichroma™ TSH and Beckman Coulter Access 2 Automatic analyzer as per prescribed test procedures. Test results were compared and their compatibility was investigated with linear regression and coefficient of correlation (R). Linear regression and coefficient of correlation between the two tests were

\[
y = 0.9903x + 0.1506
\]

and

\[
R = 0.992
\]

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

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read instructions for use</td>
<td></td>
</tr>
<tr>
<td>Use by</td>
<td></td>
</tr>
<tr>
<td>Batch code</td>
<td></td>
</tr>
<tr>
<td>Catalog number</td>
<td></td>
</tr>
<tr>
<td>Caution</td>
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</tr>
<tr>
<td>Authorized representative of the European Community</td>
<td></td>
</tr>
<tr>
<td>In vitro diagnostic medical device</td>
<td></td>
</tr>
<tr>
<td>Temperature limit</td>
<td></td>
</tr>
<tr>
<td>Do not reuse</td>
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</tbody>
</table>

This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices.

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**REFERENCES**