TSH using Abbott Architect ci4100

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Applicable Standards	
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Distribution
Christus Spohn Shoreline STAT Lab

TECHNICAL PROCEDURE MANUAL
CHRISTUS Spohn Hospital Corpus Christi Shoreline STAT Lab
TSH Using Abbott Architect ci4100
Proc. #: HSL0350.01

Intended Use
The ARCHITECT TSH assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of human Thyroid Stimulating Hormone (TSH) in human serum and plasma.

Clinical Significance
Human Thyroid Stimulating Hormone (TSH) or thyrotropin is a glycoprotein with a molecular weight of approximately 28,000 daltons, synthesized by the basophilic cells (thyrotropes) of the anterior pituitary.

TSH is composed of two non-covalently linked subunits designated alpha and beta. Although the alpha subunit of TSH is common to the luteinizing hormone (LH), follicle stimulating hormone (FSH) and human chorionic gonadotropin (hCG), the beta subunits of these glycoproteins are hormone specific and confer biological as well as immunological specificity. Both alpha and beta subunits are required for biological activity.

TSH stimulates the production and secretion of the metabolically active thyroid hormones, thyroxine (T4) and triiodothyronine (T3), by interacting with a specific receptor on the thyroid cell surface. T3 and T4 are responsible for regulating diverse biochemical processes throughout the body which are essential for normal development and metabolic and neural activity.

The synthesis and secretion of TSH is stimulated by thyrotropin releasing hormone (TRH), the hypothalamic tripeptide, in response to low levels of circulating thyroid hormones.

Elevated levels of T3 and T4 suppress the production of TSH via a classic negative feedback mechanism.

Other evidence also indicates that somatostatin and dopamine exert inhibitory control over TSH release, suggesting that the hypothalamus may provide both inhibitory and stimulatory influence on pituitary TSH production. Failure at any level of regulation of the hypothalamic-pituitary-thyroid axis will result in either underproduction (hypothyroidism) or overproduction (hyperthyroidism) of T4 and/or T3.

In cases of primary hypothyroidism, T3 and T4 levels are low and TSH levels are significantly elevated. In the case of pituitary dysfunction, either due to intrinsic hypothalamic or pituitary disease; i.e., central hypothyroidism, normal or marginally elevated basal TSH levels are often seen despite significant reduction in T4 and/or T3 levels. These inappropriate TSH values are due to a reduction in TSH bioactivity which is frequently observed in such cases. Routine TRH stimulation is advised to confirm the diagnosis in such cases.

Secondary hypothyroidism typically results in an impaired TSH response to TRH, while in tertiary hypothyroidism the TSH response to TRH may be normal, prolonged or exaggerated.

Primary hyperthyroidism (e.g., Grave's Disease, nodular goiter) is associated with high levels of thyroid hormones and depressed or undetectable levels of TSH. The TRH stimulation test has been used in diagnosis of hyperthyroidism. Hyperthyroid patients show a subnormal response to the TRH test.

In addition, large doses of glucocorticoids, somatostatin, dopamine and replacement doses of thyroid hormones reduce or totally blunt the TSH response to TRH.

Earlier assays for serum TSH lacked the sensitivity to be used as a primary test of thyroid function. Sensitive TSH assays now available, with increased ability to clearly distinguish between euthyroid and hyperthyroid populations, are changing thyroid function testing.

Analytical sensitivity, as a means of assessing low concentration accuracy, is being replaced by functional sensitivity.

The American Thyroid Association has formally recommended the use of functional sensitivity as the means to quantify the sensitivity of TSH assays, although analytical sensitivity is still widely used.

Third generation TSH assays exhibit 20% interassay CVs at < 0.02 µIU/mL and are useful in the discrimination of patients with true hyperthyroidism from those with TSH suppression seen in subclinical hyperthyroidism and some non-thyroidal illnesses.

Other thyroid tests (Free T4 estimate, Total T4, T-Uptake, and Total T3) combined with the ability to accurately measure low levels of TSH, improve the efficiency of thyroid diagnosis.

The ARCHITECT TSH assay is used as an aid in the assessment of thyroid status, diagnosis of thyroid disease, and treatment of thyroid disease.

Principle

The ARCHITECT TSH assay is a two-step immunoassay to determine the presence of Thyroid Stimulating Hormone (TSH) in human serum and plasma using Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample, anti-β TSH antibody coated paramagnetic microparticles and TSH Assay Diluent are combine d. TSH present in the sample binds to the anti-TSH antibody coated microparticles.

After washing, anti-α TSH acridinium labeled conjugate is added in the second step.

Pre-Trigger and Trigger Solutions are then added to the reaction mixture; the resulting chemiluminescent reaction is measured as relative light units (RLUs).

A direct relationship exists between the amount of TSH in the sample and the RLUs detected by the ARCHITECT *i* optical system.
For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

Specimen Collection and Handling
Suitable Specimens

- Human serum (including serum collected in serum separator tubes) or plasma collected in lithium heparin, sodium heparin, or potassium EDTA anticoagulant tubes may be used in the ARCHITECT TSH assay. Other anticoagulants have not been validated for use with the ARCHITECT TSH assay.
- **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 specimens are centrifuged before a complete clot forms, the presence of fibrin or particulate matter may cause erroneous results. Centrifuge specimens containing fibrin, red blood cells, or particulate matter. Note that interfering levels of fibrin may be present in samples that do not have obvious or visible particulate matter.**
- **If proper specimen collection and preparation cannot be verified, or if samples have been disrupted due to transportation or sample handling, an additional centrifugation step is recommended. Centrifugation conditions should be sufficient to remove particulate matter. Aliquots poured versus pipetted from specimen tube types that do not include serum separators are at higher risk of including particulates and generating depressed results.**
- **Failure to follow these instructions may result in depressed specimen results..**

Do not use specimens with the following conditions:

- heat inactivated

Storage
If testing will be delayed more than 24 hours, remove serum or plasma from the clot, serum separator or red blood cells.

Specimens may be stored for up to 7 days at 2-8°C prior to being tested.

If testing will be delayed more than 7 days, specimens should be frozen at -10°C or colder. Specimens stored frozen at -10°C or colder for 6 months showed no performance difference

- Multiple freeze-thaw cycles of specimens should be avoided..

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NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

Materials and Equipment Required

TEST INSTRUMENT: Abbott ARCHITECT System

MATERIALS PROVIDED

7K62 ARCHITECT TSH Reagent Kit

MATERIALS REQUIRED BUT NOT PROVIDED

- ARCHITECT *i* System with *STAT* protocol
- ARCHITECT TSH Assay file, may be obtained from:
- ARCHITECT *i* System e-Assay CD-ROM found on www.abbottdiagnostics.com
- ARCHITECT *i* System Assay CD-ROM
- 7K62-01 ARCHITECT TSH Calibrators
- Biorad Immunoassay Plus Controls (361-362-363)
- 7D82-50 ARCHITECT *i* Multi-Assay Manual Diluent
- ARCHITECT *i* Pretrigger
- ARCHITECT *i* Trigger
- ARCHITECT *i i* Wash Buffer
- ARCHITECT *i* Reaction Vessels
- ARCHITECT *i* Sample Cups
- ARCHITECT *i* Septums
- ARCHITECT *i* Replacement Caps
- Pipettes or pipette tips (optional) to deliver the specified volumes.

Reagent Handling and Storage:

***CAUTION*:**

- For in vitro diagnostic use.
-

CAUTION: This product requires the handling of human specimens.

It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens.

Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.

The following warnings and precautions apply to this component:

- Assay Diluent

WARNING:	Contains Tris Hydroxymethyl Aminomethane and Tromethamine Hydrochloride.
H315	Causes skin irritation.
H319	Causes serious eye irritation.
H335	May cause respiratory irritation.
Prevention	
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves / protective clothing / eye protection.
P261	Avoid breathing mist / vapours / spray.
P271	Use only outdoors or in a well-ventilated area.
Response	
P305+P351 + P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337+P313	If eye irritation persists: Get medical advice / attention.
P302+P352	IF ON SKIN: Wash with plenty of water.
P332+P313	If skin irritation occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
P304+340	IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P312	Call a POISON CENTER or doctor/ physician if you feel unwell.
Storage	
P403 + P233	Store in a well-ventilated place. Keep container tightly closed.
P405	Store locked up.

This material and its container must be disposed of in a safe way.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Before loading the ARCHITECT Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in the package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
- Once a septum has been placed on the reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.

- Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

- The ARCHITECT TSH Reagent Kit must be stored at 2-8°C and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT TSH Reagent Kit may be stored on-board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking on-board time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright.
- For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Reagents

Reagent Kit, 100 Tests/500 Tests

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT *i* Systems. Please contact your local distributor.

ARCHITECT TSH Reagent Kit (7K62)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL/27.0 mL) anti-β TSH (mouse, monoclonal) coated Microparticles in TRIS buffer with protein (bovine) stabilizers. **Minimum concentration: 0.07% solids.** Preservative: antimicrobial agents.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL/26.3 mL) anti-α TSH (mouse, monoclonal) acridinium-labeled Conjugate in MES buffer with protein (bovine) stabilizers. Minimum concentration: 60 ng/mL. Preservative: antimicrobial agent.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (8.0 mL/40.7 mL) TSH Assay Diluent in TRIS buffer. Preservative: antimicrobial agents.

Manual Diluent

ARCHITECT *i* Multi-Assay Manual Diluent (7D82-50)

- **MULTI-ASSAY MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT *i* Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-trigger solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

Calibrator: 7K62-01 ARCHITECT TSH Calibrators

Quality Control: Biorad Immunoassay Plus Controls level 1-2-3. (361-362-363)

Calibration

Frequency:

Recalibration is required with each new reagent lot number.

A new calibration is required:

1. If quality control results do not meet acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary.
2. Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Calibrator Required:

7K62-01 ARCHITECT TSH Calibrators

Reagents:

2 Bottles (4 mL each) of ARCHITECT TSH Calibrators. Calibrator 1 contains TRIS buffer with protein (bovine) stabilizers; Calibrator 2 contains TSH (recombinant) in TRIS buffer with protein (bovine) stabilizers. Preservative: sodium azide.

Calibrator Preparation:

Ready to use.

Calibration Procedure:

To perform an ARCHITECT TSH calibration, test Calibrators 1 and 2 in duplicate.

A single sample of all levels of TSH controls must be tested to evaluate the assay calibration.

Ensure that assay control values are within the concentration ranges specified in the package insert.

Calibrators should be priority loaded.

- Calibrator Range: 0.0000 - 100.0000 µIU/mL.

Troubleshooting and Overall Acceptance Criteria Failure

See ARCHITECT Operations Manual for further calibration troubleshooting.

Quality Control:

Abbott recommends, refer to your laboratory standard operating procedure(s) and/or quality assurance plan for additional quality control requirements and potential corrective actions:

- At a minimum a single level of quality control are to be run every 24 hours
- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory.

Recalibration may be necessary.

- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Instrument Procedure

- The ARCHITECT TSH assay is designed for use on the ARCHITECT *i* System
- The ARCHITECT TSH assay file must be installed on the ARCHITECT *i* System with *STAT* protocol from an ARCHITECT *i* System Assay CD-ROM prior to performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Assay Procedure

For a detailed description of how to run an assay, refer to *Section 5* of the **ARCHITECT System Operations Manual**.

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
  - Priority: 200 µL for the first TSH test plus 150 µL for each additional TSH test from the same sample cup
  - ≤ 3 hours onboard: 200 µL for the first TSH test plus 150 µL for each additional TSH test from the same sample cup
  - > 3 hours onboard: additional sample volume is required. Refer to the ARCHITECT System Operations Manual, Section 5 for information on sample evaporation and volumes.
- If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- ARCHITECT TSH Calibrators and Controls should be mixed by gentle inversion prior to use.

- To obtain the recommended volume requirements for the ARCHITECT TSH Calibrators and Controls, hold the bottles **vertically** and dispense 6 drops of each calibrator or 4 drops of each control into each respective sample cup.
- Load samples
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5
- Press RUN. The ARCHITECT *i* System performs the following function:
  - Moves the sample to the aspiration point
  - Loads a reaction vessel (RV) into the process path
  - Aspirates and transfers sample into the RV
  - Advances the RV one position and transfers microparticles and diluent into the RV
  - Mixes, incubates and washes the reaction mixture
  - Adds conjugate to the RV
  - Mixes, incubates and washes the reaction mixture
  - Adds Pre-Trigger and Trigger Solutions
  - Measures chemiluminescent emission to determine the quantity of TSH in the sample
  - Aspirates contents of RV to liquid waste and unloads RV to solid waste
  - Calculates the result
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Results

The default result unit for the ARCHITECT TSH assay is µIU/ mL.

An alternate result unit, mIU/L, may be selected for reporting results by editing assay parameter "Result concentration units", to mIU/L.

The conversion factor used by the system is 1.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Specific Performance Characteristics

Expected Values

It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics.

Serum/Plasma (Abbott Package Insert)
A normal range of 0.35 µIU/mL to 4.94 µIU/mL (99% confidence interval) was obtained by testing serum specimens from 549 individuals defined as normal by the AxSYM Ultrasensitive hTSH II and AxSYM Free T4 assays.

Serum/Plasma (this facility)

Critical Values *(Refer to Critical value Policy)*

Performance Characteristics

Sensitivity
The ARCHITECT TSH assay is designed to have a functional sensitivity of ≤ 0.01 µlU/mL, which meets the requirements of a third generation TSH assay.

The ARCHITECT TSH assay is designed to have an analytical sensitivity of ≤ 0.0025 µIU/mL.

Linearity
The assay is linear from 0.0025 to 100 µIU/mL
Dilution:
Specimens with a TSH value exceeding 100.0000 µIU/mL, are flagged with the code ">100.0000" and may be diluted with the Automated Dilution Protocol .
- If using the Automated Dilution Protocol, the system performs a 1:5 dilution of the specimen and automatically calculates the concentration of the diluted specimen and reports the result.

Precision:
The ARCHITECT TSH assay is designed to have a precision of ≤ 10% (total CV).

Panel Member	Reagent Lot	Instru-ment	n	Mean Conc. (µIU/mL)	Within Run SD	Within Run %CV	Total SD	Total %CV
1	1	1	80	0.0907	0.00160	1.8	0.00210	2.3
1	1	2	80	0.0879	0.00121	1.4	0.00171	1.9
1	2	1	80	0.0876	0.00135	1.5	0.00225	2.6
1	2	2	80	0.0888	0.00440	5.0	0.00469	5.3
2	1	1	80	5.7062	0.08187	1.4	0.12184	2.1
2	1	2	80	5.4750	0.09116	1.7	0.12761	2.3
2	2	1	80	5.5153	0.08122	1.5	0.11008	2.0
2	2	2	80	5.5320	0.08176	1.5	0.12501	2.3
3	1	1	80	28.4388	0.44471	1.6	0.82863	2.9
3	1	2	80	27.0156	0.76916	2.8	1.03741	3.8
3	2	1	80	27.2486	0.58176	2.1	0.75194	2.8
3	2	2	80	28.0434	0.55278	2.0	0.92480	3.3
4	1	1	80	0.5217	0.00655	1.3	0.00894	1.7
4	1	2	80	0.5024	0.00751	1.5	0.01128	2.2
4	2	1	80	0.4998	0.00653	1.3	0.00973	1.9
4	2	2	80	0.5070	0.00562	1.1	0.01156	2.3
5	1	1	80	2.0057	0.02380	1.2	0.03367	1.7
5	1	2	80	1.9318	0.02679	1.4	0.03842	2.0
5	2	1	80	1.9060	0.03844	2.0	0.04405	2.3
5	2	2	80	1.9369	0.02747	1.4	0.03499	1.8
6	1	1	80	16.5485	0.28856	1.7	0.38175	2.3
6	1	2	80	15.8935	0.27310	1.7	0.41347	2.6
6	2	1	80	15.9947	0.25055	1.6	0.38375	2.4
6	2	2	80	16.3632	0.23302	1.4	0.41631	2.5

Limitations of Procedure

- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies. Additional information may be required for diagnosis.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- Suspected hyperthyroidism based on low or undetectable TSH levels should be confirmed with additional thyroid function testing along with other clinical information.

Specificity

The ARCHITECT TSH assay is designed to have an analytical specificity of < 10% cross reactivity with the following substances, at the concentration levels listed, in human serum samples containing TSH in the normal range.

- FSH - ≤ 500 mIU/mL

- LH - ≤500 mIU/mL
- hCG - ≤ 200,000 mIU/mL.

Interference

The ARCHITECT TSH assay is designed to have a potential interference from hemoglobin, bilirubin, triglycerides and protein of ≤ 10% at the levels indicated below.

- Hemoglobin - ≤ 500 mg/dL
- Bilirubin - ≤ 20 mg/dL
- Triglycerides - ≤ 3000 mg/dL
- Protein - ≤ 2 g/dL and 12 g/dL

References:

1. ABBOTT ARCHITECT TSH package insert
   Abbott Laboratories
   Diagnostics Division
   Abbott Park, IL 60064
   Jan 2014 G4-5947/R05
2. ABBOTT ARCHITECT TSH Calibrator package insert
   Abbott Laboratories
   Diagnostics Division
   Abbott Park, IL 60064
3. Abbott ARCHITECT Operator's Guide

Alternative Method

Sent to Sister facility if unable to perform at this site.

Effective date of this Procedure : 7/25/18

Revised by: Elsa Escobar, MT(ASCP)