Thyroid Stimulating Hormone on Architect i2000

In-Use Date: May 1, 2016

I. 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 the 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 combined. 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.

II. POLICY/SCOPE

This is intended for the China Basin Chemistry section of the Clinical Laboratories and intended for testing by licensed Clinical Laboratory Scientists and Clinical Laboratory staff.

III. SPECIMEN REQUIRMENTS

a. Serum or plasma from SST, red, or green top tubes (sodium/lithium heparin). Any other tube type is NOT acceptable.
b. Allow complete clot formation to take place in serum samples prior to centrifugation.
c. Samples should be free of fibrin, red blood cells, or other particulate matter. Centrifuge samples containing fibrin, red blood cells, or particulate matter.
d. Samples should be free of bubbles.
e. Specimen storage and stability:
    i. If testing will be delayed more than 24 hours, remove serum or plasma from the clot, serum separator or red blood cells.
    ii. Serum or plasma may be stored for up to 7 days at 2-8°C.
    iii. Serum or plasma stored at -10°C or colder is stable for 6 months.
    iv. Multiple freeze-thaw cycles of samples should be avoided. Samples must be mixed thoroughly after thawing by low speed vortexing or by gentle inversion and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results.

IV. EQUIPMENT, REAGENTS, AND SUPPLIES

a. ARCHITECT TSH Reagent Kit (500 tests), Catalog # 07K6235
    i. Storage and Stability:
        1. Store reagents at 2-8°C.
        2. Unopened: Stable until the expiration date on the carton.
        3. On-board: Stable for a maximum of 30 days.
    ii. Preparation:
        1. Before loading the reagent kit on the system for the first time, gently invert the microparticle bottle 30 times or until all microparticles have been resuspended. *NOTE: If the microparticles do not resuspend, DO NOT USE.*
        2. Once the microparticles are resuspended, remove caps from all reagent bottles and discard. Wearing clean gloves remove septums from the bag, squeeze to check the each opening, and then carefully snap the septum onto the top of the each reagent bottle.

b. ARCHITECT *i* Multi-Assay Manual Diluent (100 mL), Catalog # 7D82-50
    i. Storage and Stability:
        1. Store the reagent at room temperature until expiration date on bottle.

V. WARNINGS AND PRECAUTIONS

Caution: This product requires the handling of human specimens. It is recommended that all human sourced materials are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens. Appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.

VI. CALIBRATION

a. ARCHITECT TSH Calibrators, Catalog # 07K6201
    i. To obtain the recommended volume requirements for the ARCHITECT TSH Calibrators, hold the bottles vertically and dispense 6 drops of each calibrator into each respective sample cup.
b. Two-point calibration is performed:
    i. Every 60 days
    ii. When changing lot numbers of primary reagent packs.
    iii. When quality control results are repeatedly out of range.
c. Refer to "Architect i2000 Operating Procedure" for instructions on checking calibration status, performing calibration, and reviewing calibration data.

VII. QUALITY CONTROL

a. BioRad Immunoassay Plus Controls Level 1, Level 2 and Level 3.
    i. Preparation: Reconstitute with 5.0 mL of Type 1 deionized water.
    ii. Stability: 7 days when stored at 2-8°C.
b. See posted QC chart for acceptability limits.
c. Frequency:
    i. Analyze all levels of QC on each day that samples are analyzed.
    ii. Analyze all levels of QC every time a two-point calibration is performed.
    iii. Analyze all levels of QC on every primary reagent pack used for sample analysis.
d. Refer to "Architect i2000 Operating Procedure" for instructions on programming QC on the instrument.

VIII. PROCEDURE

Refer to "Architect i2000 Operating Procedure" for instructions on scheduling and loading patient samples.

IX. RESULTING/REPORTABLE RANGE

a. Analytical Measuring Range (AMR)
    i. The AMR for Abbott Architect TSH assay is 0.01 to 80.00 mIU/L.
b. Reportable Range
    i. The reportable range for Abbott Architect TSH assay is 0.01 mIU/L to 800.00 mIU/L.
    ii. Values below 0.01 mIU/L are reported as "<0.01 mIU/L".
    iii. Values greater than 800.00 mIU/L are reported as ">800.00 mIU/L".
    iv. Results are reported with two decimal points.
c. Dilutions
    i. Samples with TSH levels greater than 80.00 mIU/L should be programmed to run an onboard 1:5 dilution that will automatically calculate the concentrations of the diluted sample.
    ii. A manual 1:10 dilution may be performed for samples with TSH levels >400.00 mIU/L. For example, to perform a 1:10 dilution, add 30 µL of the patient sample to 270 µL of ARCHITECT *i* Multi-Assay Manual Diluent.
    iii. **It is recommended that dilutions do not exceed 1:10**.
    iv. Ensure that results are mathematically corrected for dilution.
    v. Refer to "Architect i2000 Operating Procedure" for instructions on ordering dilutions.

X. EXPECTED VALUES

a. Reference Range

Age	Reference range (mIU/L)
<2 months	1.12-6.31
2 months to <6 months	0.73-4.77
6 months to <14 years	0.70-4.17
14 years to <18 years	0.47-3.41
18 years and above	0.45-4.12

Reference ranges apply to non-pregnant individuals. In pregnant subjects, TSH levels decline in the first trimester and then rise after 10 -12 weeks gestation. The upper reference limit is 2.5 mIU/L in the first trimester, 3.0 in the second trimester, and 3.5 mIU/L in the third trimester. The lower reference limit for TSH in pregnancy is 0.1 – 0.2 mIU/L lower than the range limit in non-pregnant subjects (Garber JR et al. Clinical Practice Guidelines for Hypothyroidism in Adults: American Association of Clinical Endocrinologists and the American Thyroid Association, Thyroid 12:1200-1235, 2012).

Pediatric reference ranges adopted from Pediatric Reference Intervals seventh edition (Soldin, Steven J. et al) and the Canadian Laboratory Initiative on Reference Interval Database (CALIPER) study, Clinical Chemistry September 2013 vol. 59 no. 9 1393-1405.

Neonatal and cord blood levels are 2-4x higher than levels at ≥ 2 weeks of age through adult life. Neonatal levels are also screened by the State program.

Adult reference ranges were adopted from NHANES III and verified in 63 adult blood donors (Hollowell JG et al. Serum TSH, T4, and thyroid antibodies in the United States population ,1988 to 1994: National Health and Nutrition Examination Survey , NHANES III. J Clin Endocrinol Metab 87:489–499, 2002. Garber JR et al. Clinical Practice Guidelines for Hypothyroidism in Adults: American Association of Clinical Endocrinologists and the American Thyroid Association, Thyroid 12:1200-1235, 2012).

XI. LIMITATIONS OF PROCEDURE

a. Specimens run on the ARCHITECT TSH assay MUST be processed according to the specimen test tube manufacturer's instruction. Insufficient processing including deviations from recommended clotting times, centrifugation times, centrifugation speed and sample preparation techniques may cause inaccurate results.
b. For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other thyroid tests, clinical impressions, etc.
c. If the TSH results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
d. Suspected hyperthyroidism based on low or undetectable TSH levels should be confirmed with additional thyroid function testing along with other clinical information.
e. 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.
f. 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.

XII. PERFORMANCE CHARACTERISTICS

a. SPECIFICITY

i. 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 the human serum samples containing TSH in the normal range.

FSH	≤ 500 mIU/mL
LH	≤ 500 mIU/mL
hCG	≤ 200,000 mIU/mL

b. SENSITIVITY

i. The ARCHITECT TSH assay has a functional sensitivity of <0.01 mIU/L, which meets the requirements of a third generation TSH assay. Functional sensitivity is defined as the concentration of TSH that can be measured with an interassay CV of 20%
ii. The ARCHITECT TSH assay has an analytical sensitivity of <0.0025 mIU/L. The analytical sensitivity is defined as the concentration calculated as the mean plus two standard deviations of replicates of the ARCHITECT TSH MasterCheck Level 0 (0.0 mIU/L). The analytical sensitivity (low-linearity) is defined in the ARCHITECT TSH assay parameters as 0.0025 mIU/L.

c. PRECISION

i. Intra-Precision study performed with BioRad Immunoassay Plus Controls Lot 40311, 40312, 40313.

	%CV	%CV	%CV
Control	CL1	CL2	CL3
Criteria	<10%	<10%	<10%
Results	**3.0%**	**1.4%**	**2.1%**

ii. Inter-Precision study performed with BioRad Immunoassay Plus Controls Lot 40311, 40312, 40313.

	%CV	%CV	%CV
Control	CL1	CL2	CL3
Criteria	<10%	<10%	<10%
Results	**2.5%**	**2.7%**	**2.6%**

d. METHOD COMPARISON

i. Laboratory performed study using 101 patient samples comparing Beckman DXI results to the Architect i2000 results.

	Slope	**R value**	**Mean Bias**
Criteria	0.9-1.1	> 0.95	10%
Subrange Results (<5.19 mIU/L)	0.884	0.9412	-14.524%
Results	0.738	0.9674	-23.800%

e. INTERFERENCES

i. 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	≤ 200 mg/dL
Triglycerides	≤ 3,000 mg/dL
Protein	≤ 2 g/dL and 12 g/dL

XIII. TECHNICAL NOTES (N/A)

XIV. ALTERNATE METHODS – Immunology Architect i2000

XV. REFERENCES

a. Abbott ARCHITECT System TSH Package Insert, B7K620, G4-5947/R05

b. Hollowell JG et al. Serum TSH, T4, and thyroid antibodies in the United States population ,1988 to 1994:

c. National Health and Nutrition Examination Survey , NHANES III. J Clin Endocrinol Metab 87:489–499, 2002.

d. Garber JR et al. Clinical Practice Guidelines for Hypothyroidism in Adults: American Association of Clinical Endocrinologists and the American Thyroid Association, Thyroid 12:1200-1235, 2012).