ARCHITECT TSH

REF 7K62-25
REF 7K62-20
REF 7K62-35
REF 7K62-30

en

TSH
7K62
G6-2729/R06
B7K620

Read Highlighted Changes: Revised November 2015.

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

NAME

ARCHITECT TSH

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.

SUMMARY AND EXPLANATION OF THE TEST

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.[1] 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.[1] TSH stimulates the production and secretion of the metabolically active thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3), by interacting with a specific receptor on the thyroid cell surface.[2] T_3 and T_4 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.[3, 4] Elevated levels of T_3 and T_4 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.[5] Failure at any level of regulation of the hypothalamic-pituitary-thyroid axis will result in either underproduction (hypothyroidism) or overproduction (hyperthyroidism) of T_4 and/or T_3.

In cases of primary hypothyroidism, T_3 and T_4 levels are low and TSH levels are significantly elevated.[6] 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 T_4 and/or T_3 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.[7-9]

Primary hyperthyroidism (e.g., Grave's Disease, nodular goiter) is associated with high levels of thyroid hormones and depressed or undetectable levels of TSH.[10] The TRH stimulation test has been used in diagnosis of hyperthyroidism. Hyperthyroid patients show a subnormal response to the TRH test.[11] In addition, large doses of glucocorticoids, somatostatin, dopamine and replacement doses of thyroid hormones reduce or totally blunt the TSH response to TRH.[11, 12]

Earlier assays for serum TSH lacked the sensitivity to be used as a primary test of thyroid function.[13] 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.[14] The American Thyroid Association has formally recommended the use of functional sensitivity as the means to quantify the sensitivity of TSH assays,[15] 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.[16] Other thyroid tests (Free T_4 estimate, Total T_4, T-Uptake, and Total T_3) combined with the ability to accurately measure low levels of TSH, improve the efficiency of thyroid diagnosis.[17]

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

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

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

1. 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.
2. After washing, anti-α TSH acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of TSH in the sample and the RLUs detected by the ARCHITECT iSystem optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

ARCHITECT TSH 7K62

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

REF	7K62-25	7K62-20	7K62-35	7K62-30
Σ	100	400	500	2000
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL	4 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL	4 x 26.3 mL
ASSAY DILUENT	1 x 8.0 mL	4 x 8.0 mL	1 x 40.7 mL	4 x 40.7 mL

MICROPARTICLES Anti-β TSH (mouse, monoclonal) coated Microparticles in TRIS buffer with protein (bovine) stabilizers. Minimum concentration: 0.07% solids. Preservative: antimicrobial agents.

REF	7K62-25	7K62-20	7K62-35	7K62-30
Σ	100	400	500	2000

CONJUGATE 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 TSH Assay Diluent in TRIS buffer. Preservative: antimicrobial agents.

Other Reagents

MULTI-ASSAY MANUAL DILUENT 1 x 100 mL ARCHITECT Multi-Assay Manual Diluent, **REF** 7D82-50, containing phosphate buffered saline solution. Preservative: antimicrobial agent.

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

NOTE: Bottle and volume varies based on order.

Warnings and Precautions

- **IVD**
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and 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.[18-21]

The following warnings and precautions apply to: **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 / vapors / 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+P340	IF INHALED: Remove person to fresh air and keep 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.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- 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. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **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 this package insert.**
  - To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on an open 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

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. 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. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT TSH assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to performing the assay.

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.

Alternate Result Units

Edit assay parameter "Result concentration units" to select an alternate unit.

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) = (Concentration in Alternate result unit)

Default result unit	Conversion factor	Alternate result unit
µIU/ mL	1	mIU/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Validated specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human serum	Serum
	Serum separator tubes (SST)
Human plasma	Lithium heparin
	Sodium heparin
	Potassium EDTA

- Other anticoagulants have not been validated for use with the ARCHITECT TSH assay.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- **For optimal results, serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter. Centrifuge specimens containing fibrin, red blood cells, or particulate matter prior to use to ensure consistency in the results.**
- **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.**
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- **Follow these package insert instructions as well as the specimen collection tube manufacturer's instructions for specimen collection and preparation for analysis. Refer to the specimen collection tube manufacturer's instructions for centrifugation time and speed.**
- **Insufficient processing of sample, or disruption of the sample during transportation may cause depressed results.**
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- Prepare frozen specimens as follows:
  - Frozen specimens must be completely thawed before mixing.
  - Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous. If samples are not mixed thoroughly, inconsistent results may be obtained.
  - Centrifuge mixed specimens as described below.
- To ensure consistency in results, centrifuge specimens before testing if
  - they contain fibrin, red blood cells, or other particulate matter or
  - they were frozen and thawed.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	2-8°C	≤ 7 days

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

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.

Specimens must be mixed thoroughly after thawing to ensure consistency of the results.

Avoid multiple freeze/thaw cycles.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

7K62 ARCHITECT TSH Reagent Kit

Materials Required but not Provided

- ARCHITECT TSH Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K62-01 ARCHITECT TSH Calibrators
- 7K62-10 ARCHITECT TSH Controls
- 7D82-50 ARCHITECT Multi-Assay Manual Diluent
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- 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.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 9
  - Priority:

    Sample volume for first test: 200 µL

    Sample volume for each additional test from same sample cup: 150 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 200 µL

    Sample volume for each additional test from same sample cup: 150 µL
  - > 3 hours on board: 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.
- Prepare ARCHITECT TSH Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 6 drops

    for each control: 4 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
  - 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.

Specimen Dilution Procedures

Specimens with a TSH value exceeding 100.0000 µIU/mL are flagged with the code ">100.0000" and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

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.

Manual Dilution Procedure

Suggested dilution: 1:10

It is recommended that dilutions not exceed 1:10.

1. Add 30 µL of the patient specimen to 270 µL of ARCHITECT Multi-Assay Manual Diluent.
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result should be > 0.0100 µIU/mL before the dilution factor is applied.
3. If the operator does not enter the dilution factor, the reported result will be that of the diluted sample. This result should be > 0.0100 µIU/mL before the dilution factor is applied.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- Test Calibrators 1 and 2 in duplicate. The calibrators should be priority loaded.

  A single sample of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Calibration Range: 0.0000 - 100.0000 µIU/mL.
- Once an ARCHITECT TSH calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT TSH assay is that a single replicate of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

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

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT TSH assay belongs to method group 1.

The lower limit of the dynamic range is defined as the functional sensitivity of the assay.

RESULTS

Calculation

The ARCHITECT TSH assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

For information on alternate result units, refer to the **INSTRUMENT PROCEDURE, Alternate Result Units** section of this package insert.

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.

LIMITATIONS OF THE PROCEDURE

- 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.
- Results should be used in conjunction with other data; e.g., symptoms, results of other tests, and clinical impressions.
- If the TSH results are inconsistent with clinical evidence, additional testing is recommended to confirm the result.
- Suspected hyperthyroidism based on low or undetectable TSH levels should be confirmed with additional thyroid function testing along with other clinical information.
- 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 such as ARCHITECT TSH that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.[22, 23]
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed. Additional information may be required for diagnosis.[24]

EXPECTED VALUES

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 T_4 assays. It is recommended that each laboratory establish its own normal range which may be unique to the population it serves depending upon geographical, patient, dietary, or environmental factors.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT TSH assay is designed to have a precision of ≤ 10% (total CV). A study based on guidance from Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) document EP5-A[25] was performed for the ARCHITECT TSH assay. Three buffer based panel members (1, 2 and 3) and three processed human serum based panel members (4, 5 and 6) were assayed, using two lots of reagents, in replicates of two at two separate times per day for 20 testing days. Data from this study are summarized in the following table.*

Panel Member	Reagent Lot	Instrument	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

* Representative data; results in individual laboratories may vary from these data.

Recovery

The ARCHITECT TSH assay is designed to have a mean recovery of 100 +/- 10% when analyzing samples spiked with known amounts of TSH. TSH (spanning the dynamic range) was added to 10 aliquots of human serum. The concentration of TSH was determined using the ARCHITECT TSH assay and the resulting percent recovery was calculated.* The percent recovery of the ARCHITECT TSH assay ranged from 91.8% to 104.3% with an average of 99.4%.

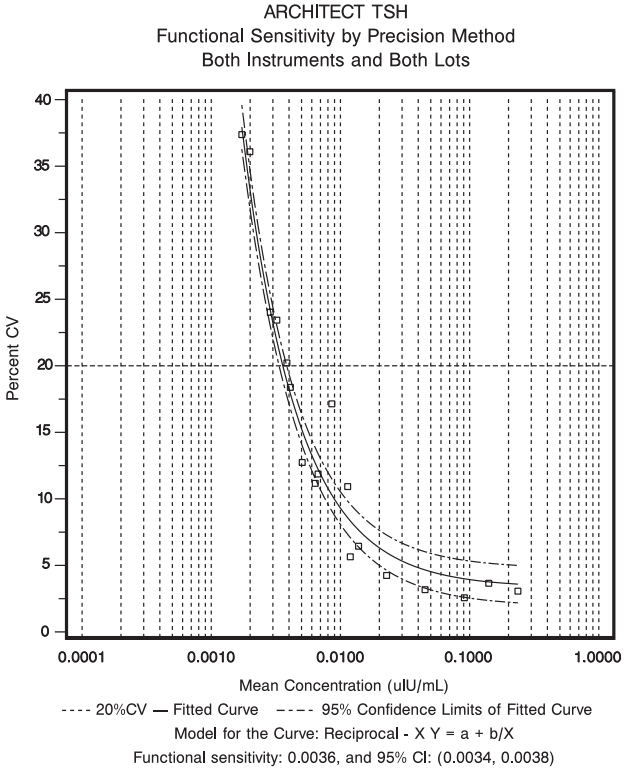
* Representative data; results in individual laboratories may vary from these data.

Sensitivity

Functional

Functional sensitivity is defined as the concentration of TSH that can be measured with an interassay CV of 20%.[6] The ARCHITECT TSH assay is designed to have a functional sensitivity of ≤ 0.01 µIU/mL, which meets the requirements of a third generation TSH assay.

In a representative study, the functional sensitivity was calculated to be ≤ 0.0038 µIU/mL (upper 95% confidence limit of 0.0042 µIU/mL). In addition, a total %CV was calculated from the pooled data generated using two lots of reagents and two instruments. The data exhibited a functional sensitivity of ≤ 0.0036 µIU/mL (upper 95% confidence limit of 0.0038 µIU/mL). This was determined by testing human serum and processed human serum samples ranging from 0.0007 µIU/mL to 0.2365 µIU/mL. Each sample was tested over 35 to 42 days on each of two ARCHITECT iSystems using two reagent lots with at least 10 replicates per lot per instrument. The total and interassay %CVs were calculated and plotted against the mean concentration. A reciprocal curve was fitted through the data and the functional sensitivity was estimated as the concentration corresponding to the 20% CV on the fitted curve.



Analytical

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

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 µIU/mL). The analytical sensitivity (low-linearity) is defined in the ARCHITECT TSH assay parameters as 0.0025 µIU/mL.

Analytical 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

Accuracy by Correlation

The ARCHITECT TSH assay is designed to have a slope of 1.0 +/- 0.2 and a correlation coefficient (r) of ≥ 0.95 when compared to the AxSYM Ultrasensitive hTSH II assay.

A study was performed where specimens were tested using the ARCHITECT TSH assay and AxSYM Ultrasensitive hTSH II assay. Data from this study were analyzed using least squares and Passing-Bablok[26] regression methods and are summarized in the following table.*

Abbott ARCHITECT TSH vs. Abbott AxSYM Ultrasensitive hTSH II

Method	Number of Specimens	Intercept	Slope	Correlation Coefficient
Least Squares Linear Regression	534	-0.7135	0.96	0.987
Passing-Bablok Linear Regression**	534	0.0098	0.91	0.987

In this evaluation, serum specimens tested ranged from 0.0109 µIU/mL to 127.9816 µIU/mL with the ARCHITECT TSH assay.

* Representative data; variables such as differences in sampling size and sample population may impact the correlation of the assay; therefore, results in individual laboratories may vary from these data.

** A linear regression method with no special assumptions regarding the distribution of the samples and the measurement errors.[26]

BIBLIOGRAPHY

1. Pierce JG. The Subunits of Pituitary Thyrotropin. Their Relationship to other Glycoprotein Hormones. *Endocrinology* 1971; 89:1331-1344.
2. Rees Smith B, Pyle GA, Petersen VB, Hall R. Interaction of Thyrotropin with the Human Thyrotropin Receptor. *J Endocrinol* 1977; 75:391-400.
3. Sterling K, Lazarus JH. The Thyroid and Its Control. *Annu Rev Physiol* 1977; 39:349-371.
4. Patel YC, Alford FP, Burger HG. The 24-Hour Plasma Thyrotropin Profile. *Clin Sci* 1972; 43:71-77.
5. Morley JE. Neuroendocrine Control of Thyrotropin Secretion. *Endocr Rev* 1981; 2:396-436.
6. Burger HG, Patel YC. The Value of Serum Thyrotropin Measurement in the Diagnosis and Management of Hypothyroidism. *Med J Aust* 1972; 2:293-297.
7. Petersen VB, McGregor AM, Belchetz PE, Elkeles RS, Hall R. The Secretion of Thyrotropin with Impaired Biological Activity in Patients with Hypothalimic-Pituitary Disease. *Clin Endocrinol* 1978; 8:397-402.
8. Faglia G, Bitensky L, Pinchera A, Ferrari C, Paracchi A, Beck-Pecooz P, et al. Thyrotropin Secretion in Patients with Central Hypothyroidism: Evidence for Reduced Biological Activity of Immunoreactive Thyrotropin. *J Clin Endocrinol Metab* 1979; 48:989-998.
9. Beck-Peccoz P, Amr S, Menezes-Ferreira MM, Faglia G, Weintraub BD. Decreased Receptor Binding of Biologically Inactive Thyrotropin in Central Hypothyroidism. *N Engl J Med* 1985; 312:1085-1090.
10. Wehmann RE, Rubenstein HA, Pugeat MM, Nisula BC, Extended Clinical Utility of a Sensitive and Reliable Radioimmunoassay of Thyroid-Stimulating Hormone. *South Med J* 1983; 76:969-976.
11. Lauridsen UB, Deckert T, Friis TH, Kirkegaard C, Hansen JM, Siersbaek-Nielsen K. Estimation of Serum Thyrotropin (TSH) and Stimulation with Thyrotropin-Releasing Hormone (TRH) in Thyroid Diseases. *Acta Med Scand* 1974; 196:171-176.
12. Jackson IMD. Thyrotropin-Releasing Hormone. *N Engl J Med* 1982; 306:145-155.
13. Spencer CA. Clinical Uses and Limitations of Rapid TSH Assays. *Medical Laboratory Products* 1988; 17-19.
14. Bayer MF. Performance Criteria for Appropriate Characterization of "(Highly) Sensitive" Thyrotropin Assays. *Clin Chem* 1987; 33:630-631.
15. Hay ID, Bayer MF, Kaplan MM, Klee GG, Larsen PR, and Spencer CA. American Thyroid Association Assessment of Current Free Thyroid Hormone and Thyrotropin Measurements and Guidelines for Future Clinical Assays. *Clin Chem* 1991; 37:2002-2008.
16. The National Academy of Clinical Biochemistry: Standards of Laboratory Practice. *Laboratory Support for the Diagnosis & Monitoring of Thyroid Disease*. NACB, 1996.
17. Hay ID, Klee GG. Linking Medical Needs and Performance Goals: Clinical and Laboratory Perspectives on Thyroid Disease. *Clin Chem* 1993; 39:1519-1524.
18. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
19. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
20. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.

21. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition.* CLSI Document M29-A4. Wayne, PA: CLSI; 2014.
22. Primus FJ, Kelley EA, Hansen HJ, et al. "Sandwich"-type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34(2):261-264.
23. Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45(2):879-885.
24. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
25. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline.* NCCLS Document EP5-A. Wayne, PA: NCCLS; 1999.
26. Passing H, Bablok W. A new biometrical procedure for testing the equality of measurements from two different analytical methods. Application of linear regression procedures for method comparison studies in clinical chemistry, Part I. *J Clin Chem Clin Biochem* 1983;21(11):709–720.

Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTROL NO.	Control Number
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCT OF IRELAND	Product of Ireland
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SEVERE IRRITANT	Warning: Severe Irritant
WASH BUFFER	Wash Buffer

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