




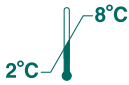


Anti-Tg

Customer Service
United States: 1-877-4ABBOTT
International: Call your Abbott Representative

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

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 May 2006

Key to symbols used

REF	List Number	LOT	Lot Number
IVD	For <i>In Vitro</i> Diagnostic Use		Expiration Date
	Store at 2-8°C	REACTION VESSELS	Reaction Vessels
	Consult instructions for use	SAMPLE CUPS	Sample Cups
SN	Serial Number	SEPTUM	Septum
EC REP	Authorized Representative	REPLACEMENT CAPS	Replacement Caps
	Legal Manufacturer	REAGENT LOT	Reagent Lot
		ASSAY CD-ROM	Assay CD-ROM
		CONTROL NO.	Control Number



Produced by
 Fisher Scientific, 8365 Valley Pike,
 Middletown, VA 22645, USA
 for Abbott Laboratories,
 Abbott Park, IL 60064, USA

EC REP ABBOTT
 Max-Planck-Ring 2
 65205 Wiesbaden
 Germany
 +49-6122-580

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NAME

ARCHITECT® Anti-Tg

INTENDED USE

ARCHITECT Anti-Tg is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of the IgG class of thyroglobulin autoantibodies (anti-Tg) in human serum and plasma on the ARCHITECT *i* System. The ARCHITECT Anti-Tg assay is intended for use as an aid in the diagnosis of autoimmune thyroid disease.

SUMMARY AND EXPLANATION OF TEST

Autoimmune thyroiditis was first described by Hashimoto in 1912¹ and autoimmune thyroid disease with associated goitre is termed Hashimoto's thyroiditis. The presence of anti-Tg in patients with this disease was first demonstrated in 1956 by Roitt, *et al*² using a precipitin reaction. Unlike autoantibodies to thyroid peroxidase (anti-TPO), autoantibodies to thyroglobulin do not appear to be pathogenic and may simply be indicators of disease.³ They have been found to be polyclonal in nature and are also heterogeneous with respect to heavy chain subclass.⁴⁻⁹

Thyroglobulin is a glycoprotein of 670,000 daltons, which is comprised of two identical subunits and represents the major protein found in the thyroid. This protein provides 40 tyrosine residues, of the 140 in the molecule, used for iodination during the biosynthesis of thyroxine (T4) and triiodothyronine (T3) and, therefore, is responsible for the accumulation of iodine by the thyroid gland.¹⁰

Although anti-Tg are found in conjunction with anti-TPO in the majority of cases of Hashimoto's thyroiditis, Primary Myxedema and Graves' disease,^{11,12} up to 1% of cases of hypothyroidism are associated with anti-Tg alone.¹³ Anti-Tg are associated with cases of mild hypothyroidism or hyperthyroidism, and are frequently found in patients with other autoimmune diseases such as Rheumatoid Arthritis, Pernicious Anaemia and Type I Diabetes.¹⁴⁻¹⁶ Anti-Tg are detected in 30-60% of cases of thyroid carcinoma patients. In such patients, measurement of Tg antigen must take into account the likelihood of the presence of significant levels of anti-Tg, since measurement and detection of Tg antigen may be influenced by the presence of anti-Tg.^{17,18}

Furthermore, low levels of anti-Tg are also found in up to 20% of asymptomatic individuals, particularly the elderly and more often in women than men, although the clinical significance of these autoantibodies is unclear.^{19,20}

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Anti-Tg assay is a two-step immunoassay for the quantitative determination of the IgG class of thyroglobulin autoantibodies (anti-Tg) in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex®.

In the first step, sample, assay diluent and Tg coated paramagnetic microparticles are combined and incubated. Anti-Tg present in the sample binds to the Tg coated microparticles. After washing, anti-human IgG acridinium labeled conjugate is added in the second step. Following another incubation and wash, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-Tg in the sample and the RLUs detected by the ARCHITECT *i** system optics.

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

* *i* = immunoassay

REAGENTS

Reagent Kit, 100 Tests

NOTE: Some kit sizes are not available in all countries; please contact your local distributor.

ARCHITECT Anti-Tg Reagent Kit (2K46)

- **MICROPARTICLES** 1 or 4 Bottles (6.6 mL) Human thyroglobulin (tested and found to be nonreactive to HBsAg, anti-HCV and anti-HIV-1/HIV-2) coated microparticles in MES buffer with protein (goat) stabilizer. Preservative: antimicrobial agents.
- **CONJUGATE** 1 or 4 Bottles (5.9 mL) Anti-human IgG (mouse, monoclonal) acridinium labeled conjugate in MES buffer with protein (bovine) stabilizer. Preservative: antimicrobial agents.
- **ASSAY DILUENT** 1 or 4 Bottles (10.0 mL) Assay Diluent in MES buffer with protein (goat). Preservative: antimicrobial agents.

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 0.35N sodium hydroxide.


ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: antimicrobial agent.

WARNINGS AND PRECAUTIONS

IVD For In Vitro Diagnostic Use.

Safety Precautions

-  **CAUTION:** This product contains human sourced and/or potentially infectious components. For a specific listing, refer to the REAGENTS section of this package insert. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens²¹. Biosafety Level 2²² or other appropriate biosafety practices^{23,24} should be used for materials that contain or are suspected of containing infectious agents.

- The ARCHITECT *i* Trigger Solution contains sodium hydroxide (NaOH) and is classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.



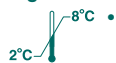
R41	Risk of serious damage to eyes.
S25	Avoid contact with eyes.
S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S35	This material and its container must be disposed of in a safe way.
S36/39	Wear suitable protective clothing and eye/face protection.
S46	If swallowed, seek medical advice immediately and show this container or label.

- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Prior to loading the ARCHITECT Anti-Tg Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septa MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septa 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.**
- Prior to placing the septum on an uncapped reagent bottle, squeeze the septum in half to confirm that the slits are open. If the slits appear sealed, continue to gently squeeze the septum to open the slits.
- 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 which 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.

Storage Instructions



- The ARCHITECT Anti-Tg Reagent Kit must be stored at 2-8°C in an upright position 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 Anti-Tg 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. Recalibration may be required to obtain maximum onboard reagent stability. For information on tracking onboard 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 septa 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.** After reagents are removed from the system, one must initiate a scan to update the onboard stability timer.

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 must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT Anti-Tg assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM Addition B 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 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.
- The default result unit for the ARCHITECT Anti-Tg assay is IU/mL.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

- The following specimen collection tubes may be used in the ARCHITECT Anti-Tg assay. Interference from all tube types listed below, when compared with serum in uncoated glass (no additive), was less than 10%.

	Glass	Plastic
Serum	<ul style="list-style-type: none">• No additive (uncoated)	<ul style="list-style-type: none">• Serum separator tubes
Plasma	<ul style="list-style-type: none">• Lithium heparin	<ul style="list-style-type: none">• Lithium heparin
	<ul style="list-style-type: none">• Plasma separator tubes with lithium heparin	<ul style="list-style-type: none">• Plasma separator tubes with lithium heparin
	<ul style="list-style-type: none">• EDTA	<ul style="list-style-type: none">• Sodium heparin• EDTA

Other anticoagulants have not been validated for use with the ARCHITECT Anti-Tg assay. Follow the manufacturer's processing instructions for serum or plasma collection tubes.

- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify the correct specimen types are used in the ARCHITECT Anti-Tg assay.

Specimen Conditions

- Do not use specimens with the following conditions:
 - heat-inactivated specimens
 - cadaver specimens or body fluids other than human serum or plasma
 - obvious microbial contamination
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- Serum and plasma specimens should be free of fibrin, red blood cells or other particulate matter.
- 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 the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.

Preparation for Analysis

- Patient specimens with a cloudy or turbid appearance must be centrifuged prior to testing. Following centrifugation, avoid the lipid layer (if present) when pipetting the specimen into a sample cup or secondary tube.
- Specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results. Multiple freeze-thaw cycles of specimens should be avoided.
- All samples (patient specimens, controls, and calibrators) should be tested within 3 hours of being placed on board the ARCHITECT *i* System. Refer to the ARCHITECT System Operations Manual, Section 5, for a more detailed discussion of onboard sample storage constraints.

Storage

- If testing will be delayed for more than 8 hours, remove serum or plasma from the serum or plasma separator, red blood cells or clot. Specimens removed from the separator gel, cells or clot may be stored up to 72 hours at 2-8°C.
- Specimens can be stored up to 30 days frozen at -10°C or colder.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the serum or plasma separator, red blood cells or clot. When shipped, specimens must be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens must be shipped frozen (dry ice). Do not exceed the storage time limitations identified in this section of the package insert.

PROCEDURE

Materials Provided:

- 2K46 ARCHITECT Anti-Tg Reagent Kit

Materials Required but not Provided:

- ARCHITECT *i* System
- 3K51 ARCHITECT *i* **ASSAY CD-ROM** - US - Addition B
- 3K53 ARCHITECT *i* **ASSAY CD-ROM** WW (excluding US) Addition B
- 2K46-01 ARCHITECT Anti-Tg Calibrators
- 2K46-10 ARCHITECT Anti-Tg Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional)

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

Assay Procedure

- Before loading the ARCHITECT Anti-Tg Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment.
 - Invert the microparticle bottle 30 times.
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain 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 Laboratories representative.**
- Once the microparticles have been resuspended, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Squeeze the septum in half to confirm that the slits are open. Carefully snap the septum onto the top of the bottle.
- 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, refer to the ARCHITECT System Operations Manual, Section 5.
- Load the ARCHITECT Anti-Tg Reagent Kit on the ARCHITECT *i* System.
 - Verify that all necessary assay reagents are present. Ensure that septa are present on all reagent bottles.

- The minimum sample 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. Verify adequate sample cup volume is present prior to running the test.
 - Priority: 75 µL for the first ARCHITECT Anti-Tg test plus 25 µL for each additional ARCHITECT Anti-Tg test from the same sample cup.
 - ≤ 3 hours on board: 150 µL for the first ARCHITECT Anti-Tg test plus 25 µL for each additional ARCHITECT Anti-Tg test from the same sample cup.
 - To minimize the effects of evaporation, all samples (patient specimens, calibrators and controls) must be tested within 3 hours of being placed on board the ARCHITECT *i* System.
 - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare Calibrators and Controls.
 - ARCHITECT Anti-Tg Calibrators and Controls should be prepared according to their respective package inserts.
 - To obtain the recommended volume requirements for the ARCHITECT Anti-Tg Calibrators and Controls, hold the bottles **vertically** and dispense 5 drops of each calibrator or 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 system performs the following functions:
 - 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 assay diluent and microparticles 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 anti-Tg in the sample.
 - Aspirates contents of RV to liquid waste and unloads RV to solid waste.
 - Calculates the result.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with an anti-Tg value exceeding 1000.00 IU/mL are flagged with the code ">1000.00" and may be diluted with the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

- If using the Automated Dilution Protocol, the system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.
- Specimens with an anti-Tg value exceeding 10000.00 IU/mL are flagged with the code ">10000.00" when run using the Automated Dilution Protocol. These specimens may be diluted by following the Manual Dilution Procedure.

Manual Dilution Procedure

- Manual dilutions should be performed as follows:
 - The suggested dilution for an anti-Tg test is 1:20.
 - Prior to diluting the specimen, dispense approximately 10 drops of ARCHITECT Anti-Tg Calibrator A into a clean test tube for use in the next step.
 - Transfer 190 µL of ARCHITECT Anti-Tg Calibrator A from the test tube prepared in the prior step into another clean test tube and add 10 µL of the patient specimen.
 - 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. This will be the reported result. The dilution should be performed so that the diluted result (before the dilution factor is applied) reads greater than 1.00 IU/mL.
 - For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- To perform an ARCHITECT Anti-Tg calibration, test Calibrators A, B, C, D, E, and F in duplicate. A single sample of each ARCHITECT Anti-Tg Control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the control package insert. Calibrators should be priority loaded.
- Calibration Range: 0.0 - 1000.0 IU/mL.
- Once an ARCHITECT Anti-Tg 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.
 - 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 Anti-Tg assay is a single sample 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.

The ARCHITECT Anti-Tg Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT Anti-Tg assay belongs to method group 1. Use ARCHITECT Anti-Tg Calibrators in place of MasterCheck® as described in the ARCHITECT System Operations Manual, Appendix B.

RESULTS

Calculation

The ARCHITECT Anti-Tg assay uses a 4 Parameter Logistic Curve Fit (4PLC, Y-weighted) data reduction method to generate a calibration curve.

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

- Antibody measurement represents one parameter in a multi-criteria diagnostic process. When making a diagnosis of thyroid disease, a combination of test methods should be used in conjunction with clinical symptoms.
- About 20% of asymptomatic specimens may present with anti-Tg autoantibodies reflecting the prevalence in apparently healthy populations. The prevalence of anti-Tg may also depend on age, gender, and geographic region of the selected population.
- Some specimens may not dilute linearly because of the heterogeneity of the autoantibodies with respect to physiochemical properties.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).²⁵ Such specimens may show either falsely elevated or depressed values when tested with assay kits that employ mouse monoclonal antibodies.^{25,26} Assay results that are not consistent with other clinical observations may require additional information for diagnosis.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.²⁷ The presence of heterophilic antibodies in a patient specimen may cause anomalous values to be observed.²⁷ Additional information may be required for diagnosis.

EXPECTED VALUES

Human serum specimens were collected from a population of 234 apparently healthy individuals. All specimens delivered TSH values within the normal reference range. Of this study population, 6 specimens delivered positive results on a commercially available anti-Tg assay device and were excluded from further analysis. The 97.5 percentile concentration of the remaining population was 4.11 IU/mL. On the basis of this study population, the expected normal range is < 4.11 IU/mL. A total of 97.8% (223/228) of the population gave values within this expected normal range.* This normal range is suggested as a guideline and each laboratory should establish a normal range appropriate to their patient populations, giving due consideration to age, gender, geographical location and their clinical practice.

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

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Anti-Tg assay is designed to have an assay precision of ≤ 10% total CV for samples ≥ 4.0 IU/mL.

A study was performed with guidance from the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A.²⁸ ARCHITECT Anti-Tg Positive Control and four human panels were assayed using three lots of reagents in replicates of two at two separate times per day for 20 days on three instruments. Each reagent lot used a single calibration curve throughout the study. Data from this study are summarized in the following table.*

Sample	Instrument	Reagent Lot	n	Mean Conc. (IU/mL)	Within Run SD	% CV	Total SD	% CV	
Positive Control	1	A	80	146.83	2.94	2.0	4.69	3.2	
		B	80	150.99	3.13	2.1	4.53	3.0	
		C	80	149.35	3.41	2.3	4.10	2.7	
	2	A	80	151.19	3.81	2.5	4.22	2.8	
		B	80	153.22	2.71	1.8	3.47	2.3	
		C	80	145.63	3.46	2.4	3.90	2.7	
	3	A	80	146.23	2.85	2.0	4.76	3.3	
		B	80	149.41	3.14	2.1	4.15	2.8	
		C	80	146.82	3.51	2.4	4.70	3.2	
	Panel 1	1	A	80	4.16	0.15	3.6	0.21	5.0
			B	80	4.12	0.11	2.7	0.13	3.1
			C	80	3.84	0.11	3.0	0.16	4.3
2		A	80	4.08	0.18	4.4	0.25	6.2	
		B	80	3.78	0.11	2.9	0.14	3.7	
		C	80	3.88	0.13	3.5	0.17	4.5	
3		A	80	4.26	0.17	4.0	0.27	6.2	
		B	80	4.26	0.11	2.7	0.20	4.8	
		C	80	3.73	0.11	3.0	0.21	5.7	
Panel 2		1	A	80	17.27	0.45	2.6	0.62	3.6
			B	80	17.38	0.80	4.6	0.85	4.9
			C	80	16.99	0.38	2.3	0.50	3.0
	2	A	80	17.46	0.49	2.8	0.66	3.8	
		B	80	17.32	0.40	2.3	0.53	3.1	
		C	80	17.16	0.41	2.4	0.56	3.3	
	3	A	80	17.61	0.46	2.6	0.79	4.5	
		B	80	17.80	0.44	2.5	0.67	3.7	
		C	80	16.68	0.48	2.9	0.94	5.6	
	Panel 5	1	A	80	368.42	6.17	1.7	12.25	3.3
			B	80	422.83	11.28	2.7	11.66	2.8
			C	80	421.51	13.64	3.2	17.14	4.1
2		A	80	383.97	9.74	2.5	14.30	3.7	
		B	80	441.17	12.54	2.8	21.81	4.9	
		C	80	406.97	12.36	3.0	19.00	4.7	
3		A	80	391.42	13.69	3.5	16.96	4.3	
		B	80	449.02	12.38	2.8	22.10	4.9	
		C	80	429.86	13.35	3.1	21.25	4.9	
Panel 6		1	A	80	739.28	21.82	3.0	28.40	3.8
			B	80	757.48	25.09	3.3	28.03	3.7
			C	80	753.34	33.05	4.4	35.69	4.7
	2	A	80	759.26	23.19	3.1	25.63	3.4	
		B	80	794.80	27.45	3.5	29.58	3.7	
		C	80	737.07	23.92	3.2	28.95	3.9	
	3	A	80	827.71	55.03	6.6	68.26	8.2	
		B	80	842.48	30.16	3.6	51.23	6.1	
		C	80	765.29	37.90	5.0	45.10	5.9	

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

Functional Sensitivity

In a study, human panels ranging in concentration from 0.07-1.38 IU/mL were tested in replicates of 2 over 10 days on one instrument using two reagent lots and three calibrations for a total of 40 replicates per panel. The total %CVs (combining variance components for replicate, run, day and reagent lot) were calculated and plotted against the mean concentration. A reciprocal curve was fitted through the data and the functional sensitivity value was calculated as the concentration corresponding to the 20% CV level of the fitted curve. The lowest ARCHITECT Anti-Tg assay value exhibiting a 20% CV is 0.31 IU/mL.*

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

Sensitivity

The ARCHITECT Anti-Tg assay is designed to have a limit of detection of ≤ 1.0 IU/mL. The limit of detection of the ARCHITECT Anti-Tg assay, defined as the concentration at two standard deviations above the ARCHITECT Anti-Tg Calibrator A (0.0 IU/mL) was calculated to be 0.07 IU/mL* at the 95% level of confidence (based upon one study with n=48 runs, 10 replicates of Calibrator A and 4 replicates of Calibrator B per run).

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

Linearity

The ARCHITECT Anti-Tg assay is linear between 3.0 and 1000.0 IU/mL based on a study performed with guidance from NCCLS protocol EP6-A.²⁹ Three high sample pools (1000, 300, and 30 IU/mL) were each combined with a low pool (ARCHITECT Anti-Tg Calibrator A) to prepare nine sets of test dilutions extending to 1/10th of the starting concentration. All of these dilutions were analyzed with the ARCHITECT Anti-Tg assay using a single reagent lot.

Autodilution Verification

The ARCHITECT Anti-Tg automated dilution protocol is designed to recover within 20% of manually diluted specimens.

In a study, the automated dilution protocol (1:10) was compared to a manual 1:10 dilution procedure using 6 human specimens with anti-Tg levels that were greater than Calibrator E (500 IU/mL). The manual dilution was performed with ARCHITECT Anti-Tg Calibrator A. The observed percent recovery results are summarized in the following table.*

Sample ID	Automated Dilution (IU/mL)	Manual Dilution (IU/mL)	% Recovery**
1	2103.48	2132.50	98.6
2	1656.16	1649.87	100.4
3	732.79	621.43	117.9
4	557.55	561.10	99.4
5	994.66	973.70	102.2
6	526.18	562.63	93.5

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

$$** \% \text{ Recovery} = \frac{\text{Automated Dilution (IU/mL)}}{\text{Manual Dilution (IU/mL)}} \times 100$$

Interference

Interference from elevated levels of bilirubin, hemoglobin, triglycerides, and total protein in the ARCHITECT Anti-Tg assay is designed to be ≤ 15% at the levels indicated.

A study based on guidance from the NCCLS Protocol EP7-A³⁰ was performed for the ARCHITECT Anti-Tg assay. Specimens with anti-Tg levels between 53.41 and 320.25 IU/mL were supplemented with the following potentially interfering compounds. The average amount of interference observed during the study ranged from -3.8% to +1.7%.*

Potentially Interfering Substance	Potentially Interfering Substance Concentration
Bilirubin	20 mg/dL
Hemoglobin	1000 mg/dL
Total Protein (Low)	4 g/dL
Total Protein (High)	10 g/dL
Triglycerides	2000 mg/dL

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

Evaluation of Autoimmune Disease Specimens and High Titer IgG Samples
Potential interference from autoimmune disease specimens and high titer IgG samples in the ARCHITECT Anti-Tg assay is designed to be $\leq 20\%$. In a study, the ARCHITECT Anti-Tg assay was evaluated by testing specimens with known autoimmune diseases and elevated IgG. Specimens were evaluated with anti-Tg levels spiked between 175.58 and 235.86 IU/mL. Mean absolute % interference is summarized in the following table.*

Clinical Condition	Mean Absolute % Interference
Anti-Nuclear Antibody (ANA)	1.2
Rheumatoid Arthritis (RA)	1.8
Systemic Lupus Erythematosus (SLE)	2.1
Insulin Dependent Diabetes Mellitus (IDDM)	3.0
Crohn's Disease	2.5
Multiple Sclerosis	3.6
Ulcerative Colitis	2.6
Hyperglobulinemia (high IgG)	4.5

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

Evaluation of Other Potential Interferents

Potential interference from HAMA and rheumatoid factor (RF) in the ARCHITECT Anti-Tg assay is designed to be $\leq 20\%$. In a study, the ARCHITECT Anti-Tg assay was evaluated by testing specimens with HAMA and RF to further assess the clinical specificity. Specimens positive for HAMA and specimens positive for RF were evaluated for % interference with anti-Tg levels spiked between 218.05 and 235.86 IU/mL. Mean absolute % interference is summarized in the following table.*

Other Potential Interferents	Number of Specimens	Mean Absolute % Interference
HAMA Positive	10	1.3
RF Positive	10	1.8

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

Clinical Sensitivity

In a study, clinical sensitivity was evaluated by testing 68 clinically defined Hashimoto's thyroiditis specimens and 85 Graves' disease specimens. The clinical diagnosis was based on the criteria of the respective laboratory. The presence of autoantibodies against thyroglobulin and/or TPO was not necessarily a diagnostic criterion of these Graves' disease and Hashimoto's thyroiditis specimens. Data from this study are summarized in the following table.*

Hashimoto's Thyroiditis		Graves' Disease	
n	% Positive	n	% Positive
68	75.0	85	75.3

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

High Dose Hook

High dose hook is a phenomenon whereby very high level specimens may falsely read within the dynamic range of the assay. For the ARCHITECT Anti-Tg, no high dose hook effect was observed when samples containing up to approximately 100,000 IU/mL of Anti-Tg antibody were assayed.

Concordance

The performance of the ARCHITECT Anti-Tg was compared to a commercially available immunoassay for the determination of anti-Tg. A total of 234 specimens were evaluated in a study, encompassing a population of apparently healthy individuals and patients with autoimmune thyroid disease (Graves' disease and Hashimoto's thyroiditis). Specimens were tested in replicates of one using the ARCHITECT Anti-Tg assay with three reagent lots on three instruments and compared with a commercially available immunoassay (Comparison Assay). Data from this study are summarized in the following table.*

ARCHITECT Anti-Tg	Comparison Assay	
	Negative	Positive
Negative	111	6
Positive	11	106

Concordance = 92.7%

Sample Range (ARCHITECT) = 0.2 to 7350.6 IU/mL

Sample Range (Competitor Assay) = <1.0 to 13484.0 IU/mL

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

BIBLIOGRAPHY

1. Hashimoto H. Zur Kenntniss der lymphomatösen Veränderung der Schilddrüse (Struma lymphomatosa). *Arch Klin Chir* 1912;97:219-48.
2. Roitt IM, Doniach D, Campbell PN, *et al*. Auto-antibodies in Hashimoto's Disease (Lymphadenoid Goitre). *Lancet* 1956;6947:820-1.
3. Tomer Y. Anti-thyroglobulin autoantibodies in autoimmune thyroid diseases: cross-reactive or pathogenic? *Clin Immunol Immunopath* 1997;82:3-11.
4. Laing P. Both K and λ light chain types are present in thyroid microsomal and thyroglobulin autoantibodies. *Proc Univ Otago Me. Sch.* 1983;61:75-7.
5. Nye L, Decarvalho LP, Roitt IM. An investigation of the clonality of human autoimmune thyroglobulin antibodies and their light chains. *Clin Exp Immunol* 1981;46:161-70.
6. Weetman AP, Black CM, Cohen SB, *et al*. Affinity purification of IgG subclasses and the distribution of thyroid auto-antibody reactivity in Hashimoto's thyroiditis. *Scan J Immunol* 1989;30:73-82.
7. Weetman AP, Yateman ME, Ealey PA, *et al*. Thyroid-stimulating antibody activity between different immunoglobulin G subclasses. *J Clin Invest* 1990;86:723-7.
8. Shimojo N, Saito K, Kohno Y, *et al*. Antigenic determinants on thyroglobulin: comparison of the reactivities of different thyroglobulin preparations with serum antibodies and T cells of patients with chronic thyroiditis. *J Clin Endocrinol Metab* 1988;66(4):689-95.
9. McIntosh RS, Asghar MS, Weetman AP. The antibody response in human autoimmune thyroid disease. *Clinical Science* 1997;92:529-41.
10. DeGroot LJ, Larsen PR, Hennemann G, editors. Thyroid hormone synthesis and secretion. In: *The Thyroid and its Diseases 6th edition*. New York: Churchill Livingstone; 1996:45-8.
11. Rosenbaum D, Davies TF. The clinical use of thyroid autoantibodies. *The Endocrinologist* 1992;2(1):55-62.
12. Burek CL, Rose NR. Thyroglobulin autoantibodies. In: Peter JB and Shoenfeld Y, editors. *Autoantibodies*. Amsterdam: Elsevier Science B.V.; 1996:810-5.
13. Nordyke RA, Gilbert FI Jr, Miyamoto LA, *et al*. The superiority of antimicrosomal over antithyroglobulin antibodies for detecting Hashimoto's thyroiditis. *Arch Intern Med* 1993;153:862-5.
14. Ruf J, Feldt-Rasmussen U, Hegedüs L, *et al*. Bispecific thyroglobulin and thyroperoxidase autoantibodies in patients with various thyroid and autoimmune diseases. *J Clin Endocrinol Metab* 1994;79(5):1404-9.
15. Scherbaum WA. On the clinical importance of thyroid microsomal and thyroglobulin antibody determination. *Acta Endocrinol (Copenh)* 1987;S281:325-9.
16. Walker DJ, Griffiths M, Griffiths ID. Occurrence of autoimmune diseases and autoantibodies in multicase rheumatoid arthritis families. *Ann Rheum Dis* 1986;45:323-6.
17. Feldt-Rasmussen U, Rasmussen ÅK. Serum thyroglobulin (Tg) in presence of thyroglobulin autoantibodies (TgAb). Clinical and methodological relevance of the interaction between Tg and TgAb *in vitro* and *in vivo*. *J Endocrinol Invest* 1985;8:571-6.
18. Schaadt B, Feldt-Rasmussen U, Rasmussen B, *et al*. Assessment of the influence of thyroglobulin (Tg) autoantibodies and other interfering factors on the use of serum Tg as tumor marker in differentiated thyroid carcinoma. *Thyroid* 1995;5(3):165-70.
19. Ericsson U-B, Christensen SB, Thorell JI. A high prevalence of thyroglobulin autoantibodies in adults with and without thyroid disease as measured with a sensitive solid-phase immunosorbent radioassay. *Clin Immunol Immunopathol* 1985;37:154-62.
20. Weetman AP and McGregor AM. Autoimmune thyroid disease: further developments in our understanding. *Endocrine Reviews* 1994;15(6): 788-830.
21. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Occupational Exposure to Bloodborne Pathogens.
22. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*, Fourth Edition. Washington, DC: US Government Printing Office, May 1999.
23. World Health Organization. *Laboratory Biosafety Manual*. Geneva: World Health Organization; 2004.
24. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline – Third Edition*. CLSI Document M29-A3. Wayne, PA: Clinical and Laboratory Standards Institute, 2005.
25. Schroff RW, Foon KA, Beatty SM, *et al*. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45:879-85.
26. 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):261-4.

27. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.
28. National Committee for Clinical Laboratory Standards. *Evaluation of Precision Performance of Clinical Chemistry Devices – Approved Guideline*. NCCLS document EP5-A. Wayne, PA: NCCLS, 1999.
29. National Committee for Clinical Laboratory Standards. *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. NCCLS document EP6-A. Wayne, PA: NCCLS, 2003.
30. National Committee for Clinical Laboratory Standards. *Interference Testing in Clinical Chemistry: Approved Guideline*. NCCLS document EP7-A. Wayne, PA: NCCLS, 2002.

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Abbott Laboratories,
Abbott Park, IL 60064, USA

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