ARCHITECT Anti-Tg

REF 2K46-20
REF 2K46-25

en
Anti-Tg
2K46
G1-0384/R06
B2K460

Read Highlighted Changes: Revised February 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 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 iSystem. The ARCHITECT Anti-Tg assay is intended for use as an aid in the diagnosis of autoimmune thyroid disease.

SUMMARY AND EXPLANATION OF THE TEST

Autoimmune thyroiditis was first described by Hashimoto in 1912[1] 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.

1. Sample, assay diluent, and Tg coated paramagnetic microparticles are combined and incubated. Anti-Tg present in the sample binds to the Tg coated microparticles.
2. After washing, anti-human IgG acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another incubation and 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 anti-Tg 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 Anti-Tg 2K46

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

REF	2K46-25	2K46-20
Σ	100	400
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL
ASSAY DILUENT	1 x 10.0 mL	4 x 10.0 mL

MICROPARTICLES Human thyroglobulin coated microparticles in MES buffer with protein (goat) stabilizer. Minimum concentration: 0.10% solids. Preservative: antimicrobial agents.

CONJUGATE Anti-human IgG (mouse, monoclonal) acridinium labeled conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 20.0 ng/mL. Preservative: antimicrobial agents.

ASSAY DILUENT Assay Diluent in MES buffer with protein (goat). Preservative: antimicrobial agents.

Other Reagents

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.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product contains human-sourced and/or potentially infectious components. 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

Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[21-24]

The purified human thyroglobulin used in the microparticles is nonreactive for HBsAg, anti-HCV and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: ASSAY DILUENT	
	
WARNING	
H319	Causes serious eye irritation.
Prevention	
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves / protective clothing / eye protection.
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.

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

When stored and handled as directed, reagents are stable until the expiration date.

	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. Store in upright position.
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.

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 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 Anti-Tg assay file must be installed on the ARCHITECT iSystem 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.

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%.

	Collection Tubes	
Specimen Types	**Glass**	**Plastic**
Serum	Serum No additive (uncoated)	Serum separator tubes
Plasma	Lithium heparin Plasma separator tubes with lithium heparin EDTA	Lithium heparin Plasma separator tubes with lithium heparin Sodium heparin EDTA

- Other specimen collection tube types have not been tested with this assay.
- Follow the manufacturer's processing instructions for serum or plasma collection tubes.
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum/ plasma.
- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.
- 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

- Do not use specimens with the following conditions:
  - heat-inactivated
  - obvious microbial contamination

- 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.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for specimen collection tubes.
- 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.
- 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.
- Patient specimens with a cloudy or turbid appearance must be centrifuged prior to testing.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- 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.
- All samples (patient specimens, controls, and calibrators) should be tested within 3 hours of being placed on board the ARCHITECT iSystem. Refer to the ARCHITECT System Operations Manual, Section 5, for a more detailed discussion of onboard sample storage constraints.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	Room temperature	≤ 8 hours
	2-8°C	≤ 72 hours
	-10°C or colder	≤ 30 days

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. 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.
- It is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- Ship frozen on dry ice.
- Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

2K46 ARCHITECT Anti-Tg Reagent Kit

Materials Required but not Provided

- ARCHITECT Anti-Tg Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 2K46-01 ARCHITECT Anti-Tg Calibrators
- 2K46-10 ARCHITECT Anti-Tg Controls
- 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: 10
  - Priority:

    Sample volume for first test: 75 µL

    Sample volume for each additional test from same sample cup: 25 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 25 µL
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT Anti-Tg 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: 5 drops

    for each control: 5 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 an anti-Tg value exceeding 1000.00 IU/mL are flagged with the code "> 1000.00" and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

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

Suggested dilution: 1:20

1. 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.
2. 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.
3. 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 > 1.00 IU/mL (concentration) before the dilution factor is applied.

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

Calibration

- Test Calibrators A-F 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: 0.0 - 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 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 Anti-Tg assay is that 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 Ant-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.

RESULTS

Calculation

The ARCHITECT Anti-Tg assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) 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 antimouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits that employ mouse monoclonal antibodies. Assay results that are not consistent with other clinical observations may require additional information for diagnosis.[25, 26]
- 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.[27]

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	Within Run %CV	Total SD	Total %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-A[30] 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 ≤ 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 ≤ 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.*

	Comparison Assay	
ARCHITECT Anti-Tg	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.

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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
EC REP	Authorized Representative in the European Community
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF USA	Product of USA
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: EYE IRRITANT	Warning: Causes serious eye irritation.
WASH BUFFER	Wash Buffer


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