Alinity i Anti-TPO-27

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BIENNIAL REVIEW:

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SUPERSEDES: Procedure titled _____

The Alinity i Anti-TPO assay is a chemiluminescent microparticle immunoassay (CMIA) used for the quantitative determination of the IgG class of thyroid peroxidase autoantibodies (anti-TPO) in human serum and plasma (EDTA and Heparin) on the Alinity i analyzer.

The Alinity i Anti-TPO assay is to be used as an aid in the diagnosis of autoimmune thyroid disease.

SUMMARY AND EXPLANATION OF THE TEST

It was first demonstrated by Trotter et al. in 1957[1] and subsequently by Roitt and Doniach in

1958[2] that many patients with Hashimoto's thyroiditis had detectable autoantibodies in their blood directed at a thyroid antigen distinct from thyroglobulin. This antigen was termed thyroid microsomal and it has since been demonstrated that most if not all anti-thyroid microsomal autoantibodies recognize thyroid peroxidase (TPO).[3]

TPO is a membrane-bound glycoprotein enzyme with an approximate mass of 107kD. The *in vivo* function is the iodination of tyrosine in the synthesis of T_3 and T_4.[4] Autoimmune reactivity to TPO is believed to be polyclonal and heterogeneous in nature with a minimum of six antigenic determinants being recognized, comprising both conformational and linear epitopes.[5, 6] In addition, the proportion of each immunoglobulin class (G or M) or subclass (G1 – G4) as well as their affinity varies widely from patient to patient.[7, 8] Unlike autoantibodies to thyroglobulin (anti-Tg), autoantibodies to TPO fix complement,[9] are potentially deleterious and may have a pathogenic role in (destructive) autoimmune thyroid disease.[10, 11] Anti-TPO antibodies are found often in conjunction with anti-Tg in the majority of cases of Hashimoto's thyroiditis, Primary Myxedema, and Graves' disease. The relationship of autoimmune thyroid disease to pregnancy has been the subject of considerable interest with the recognition of the postpartum thyroid disease syndromes.[12] Anti-TPO antibodies are demonstrable in most cases of postpartum thyroiditis and it has been found that the presence of autoantibody in early pregnancy was associated with a high risk of asymptomatic postpartum hypothyroidism.[13, 14, 15, 16, 17]

It is common to find anti-TPO antibodies in the absence of autoantibodies to thyroglobulin, particularly in patients with small goitres and up to 64% of cases of autoimmune hypothyroidism have been reported to be associated with anti-TPO antibodies alone.[18] In addition, anti-TPO antibodies are frequently found in patients with other autoimmune diseases such as Rheumatoid Arthritis, Addison's Disease and Type I Diabetes.[19, 20, 21] They are also detectable at low levels in up to 20% of asymptomatic individuals,[22] particularly the elderly[23] and more often in women than in men, although the clinical significance of these autoantibodies is unclear.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

This assay is a two-step immunoassay for the quantitative determination of anti-TPO in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Sample, TPO coated paramagnetic microparticles, and assay diluent are combined and incubated. The anti-TPO present in the sample binds to the TPO coated microparticles. The mixture is washed. Anti-human IgG acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of anti-TPO in the sample and the RLUs detected by the system optics.

For additional information on system and assay technology, refer to the Alinity ci-series Operations Manual, Section 3.

REAGENTS

Kit Contents

Alinity i Anti-TPO Reagent Kit 09P35

Volumes (mL) listed in the table below indicate the volume per cartridge.

REF	09P3521
Tests per cartridge	100
Number of cartridges per kit	2
Tests per kit	200
MICROPARTICLES	6.6 mL
CONJUGATE	6.1 mL
ASSAY DILUENT	10.4 mL

MICROPARTICLES Thyroid peroxidase (recombinant) coated microparticles in MES buffer with protein (bovine) 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: 80.0 ng/mL. Preservative: antimicrobial agents.

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

Warnings and Precautions

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

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials and all consumables contaminated with potentially infectious materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate regional, national, and institutional biosafety practices should be used for materials that contain, are suspected of containing, or are contaminated with infectious agents.[24, 25, 26, 27]

The following warnings and precautions apply to: MICROPARTICLES


WARNING	Contains potassium ferricyanide.
H361	Suspected of damaging fertility or the unborn child.
Prevention	
P201	Obtain special instructions before use.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P308+P313	IF exposed or concerned: Get medical advice / attention.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: CONJUGATE	
Contains polyethylene glycol octylphenyl ether	
H402*	Harmful to aquatic life.
H412	Harmful to aquatic life with long lasting effects.
Prevention	
P273	Avoid release to the environment.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EC 1272/2008 (CLP) has been implemented.

The following warnings and precautions apply to: ASSAY DILUENT	
	
WARNING	Contains polyethylene glycol octylphenyl ether
H319	Causes serious eye irritation.
H401*	Toxic to aquatic life.
H411	Toxic to aquatic life with long lasting effects.
Prevention	

P264	Wash hands thoroughly after handling.
P273	Avoid release to the environment.
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.
P391	Collect spillage.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EC 1272/2008 (CLP) has been implemented.

Follow local chemical disposal regulations based on your location along with recommendations and content in the Safety Data Sheet to determine the safe disposal of this product.

For the most current hazard information, see the product Safety Data Sheet.

Safety Data Sheets are available at www.corelaboratory.abbott or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 8.

Reagent Handling

- Upon receipt, gently invert the unopened reagent kit by rotating it over and back for a full 180 degrees, 5 times with green label stripe facing up and then 5 times with green label stripe facing down. This ensures that liquid covers all sides of the bottles within the cartridges. During reagent shipment, microparticles can settle on the reagent septum.
    - Place a check in the square on the reagent kit to indicate to others that the inversions have been completed.
- After mixing, place reagent cartridges in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- If a reagent cartridge is dropped, place in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.

- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.

For a detailed discussion of reagent handling precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 7.

Reagent Storage

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright, gently invert the cartridge 10 times and place in an upright position for 1 hour before use.
Onboard	System Temperature	30 days	
Opened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright during storage, discard the cartridge. Do not reuse original reagent caps or replacement caps due to the risk of contamination and the potential to compromise reagent performance.

Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 2 to 8°C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.

For information on unloading reagents, refer to the Alinity ci-series Operations Manual, Section 5.

Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when a calibration error occurs or a control value is out of the specified range. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, refer to the Alinity ci-series Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The Alinity i Anti-TPO assay file must be installed on the Alinity i analyzer prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the Alinity ci-series Operations Manual, Section 2.

For information on printing assay parameters, refer to the Alinity ci-series Operations Manual, Section 5.

For a detailed description of system procedures, refer to the Alinity ci-series Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below were verified for use with this assay.

Other specimen types and collection tube types have not been verified with this assay.

Specimen Types	Collection Tubes
Serum	Serum
	Serum separator
Plasma	Lithium heparin
	Plasma separator with lithium heparin
	Sodium heparin
	EDTA

- Performance has not been established for the use of cadaveric specimens or the use of bodily fluids other than human serum or 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 types. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use:

- heat-inactivated specimens
- specimens with obvious microbial contamination

- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

To ensure consistency in results, recentrifuge specimens prior to testing if

- they contain fibrin, red blood cells, or other particulate matter.
- they have a cloudy or turbid appearance.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low speed vortex or by gently inverting prior to recentrifugation.

Prepare frozen specimens as follows:

- Frozen specimens must be completely thawed before mixing.
- Mix thawed specimens thoroughly by low speed vortex or by gently inverting.
- Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous.
- If specimens are not mixed thoroughly, inconsistent results may be obtained.
- Recentrifuge specimens.

Recentrifugation of Specimens

- Transfer specimens to a centrifuge tube and centrifuge.
- 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.

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Serum/Plasma	Room temperature	8 hours	Specimens may be stored on or off the clot, red blood cells, or separator gel.
	2 to 8°C	72 hours	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.
	-10°C or colder	30 days	Remove serum or plasma from the serum or plasma separator, red blood cells, or clot.

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

09P35 Alinity i Anti-TPO Reagent Kit

Materials Required but not Provided

- Alinity i Anti-TPO assay file
- 09P3501 Alinity i Anti-TPO Calibrators
- 09P3510 Alinity i Anti-TPO Controls or other commercially available controls
- Alinity Trigger Solution
- Alinity Pre-Trigger Solution
- Alinity i-series Concentrated Wash Buffer

For information on materials required for operation of the instrument, refer to the Alinity ci-series Operations Manual, Section 1.

For information on materials required for maintenance procedures, refer to the Alinity ci-series Operations Manual, Section 9.

Assay Procedure

For a detailed description of how to run an assay, refer to the Alinity ci-series Operations Manual, Section 5.

- If using primary or aliquot tubes, refer to the Alinity ci-series Operations Manual, Section 4 to ensure sufficient specimen is present.
- 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: 60 µL
    - Sample volume for each additional test from same sample cup: 10 µL
  - ≤ 3 hours on the reagent and sample manager:
    - Sample volume for first test: 150 µL
    - Sample volume for each additional test from same sample cup: 10 µL
  - > 3 hours on the reagent and sample manager:
    - Replace with a fresh aliquot of sample.
- Refer to the Alinity i Anti-TPO calibrator package insert and/or Alinity i Anti-TPO control package insert for preparation and usage.
- For general operating procedures, refer to the Alinity ci-series Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the Alinity ci-series Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Sample Dilution Procedures

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

Automated Dilution Protocol

The system performs a 1:2 dilution of the sample and automatically calculates the concentration by multiplying the result by the dilution factor.

After the automatic dilution is performed, if the sample concentration is > 2000.00 IU/mL, dilute the sample 1:4 and run using the Manual Dilution Procedure.

Manual Dilution Procedure

Suggested dilution: 1:4

Add 50 µL of the sample to 150 µL of the Alinity i Anti-TPO Calibrator A.

The operator must enter the dilution factor in the Specimen or Control tab of the Create Order screen. The system will use this dilution factor to automatically calculate the concentration of the sample and report the result. The result should be > 5.61 IU/mL before the dilution factor is applied.

If the operator does not enter the dilution factor, the result must be manually multiplied by the appropriate dilution factor before reporting the result. If a diluted sample result is less than or equal to 5.61 IU/mL, do not report the result. Rerun using an appropriate dilution.

For detailed information on ordering dilutions, refer to the Alinity ci-series Operations Manual, Section 5.

Calibration

For instructions on performing a calibration, refer to the Alinity ci-series Operations Manual, Section 5.

Each assay control must be tested to evaluate the assay calibration.

Once a 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.
- Daily quality control results are outside of statistically-based quality control limits used to monitor and control system performance, as described in the Quality Control Procedures section of this package insert.
    - If statistically-based quality control limits are not available, then the calibration should not exceed a 30-day limit for recalibration frequency.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

Quality Control Procedures

The recommended control requirement for the Alinity i Anti-TPO assay is that a single sample of each control level be tested once every 24 hours each day of use.

Additional controls may be tested in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory’s quality control policy.

To establish statistically-based control limits, each laboratory should establish its own concentration target and ranges for new control lots at each clinically relevant control level. This can be accomplished by assaying a minimum of 20 replicates over several (3-5) days and using the reported results to establish the expected average (target) and variability about this average (range) for the laboratory. Sources of variation that should be included in this study in order to be representative of future system performance include:

- Multiple stored calibrations
- Multiple reagent lots
- Multiple calibrator lots
- Multiple processing modules (if applicable)
- Data points collected at different times of the day

Refer to published guidelines for information or general control recommendation, for example Clinical and Laboratory Standards Institute (CLSI) Document C24-A3 or other published guidelines, for general quality control recommendations.[28]

- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, sample results may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary. For troubleshooting information, refer to the Alinity ci-series Operations Manual, Section 10.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Commercial controls should be used according to the guidelines and recommendations of the control manufacturer. Concentration ranges provided in the control package insert should be used only for guidance.

For any control material in use, the laboratory should ensure that the matrix of the control material is suitable for use in the assay per the assay package insert.

Quality Control Guidance

Refer to “Basic QC Practices” by James O Westgard, Ph.D. for guidance on laboratory quality control practices.[29]

Verification of Assay Claims

For protocols to verify package insert claims, refer to Verification of Assay Claims in the Alinity ci-series Operations Manual.

RESULTS

Calculation

The Alinity i Anti-TPO assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration and results.

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 Alinity ci-series Operations Manual, Section 5.

Measuring Interval

Measuring interval is defined as the range of values in IU/mL which meets the limits of acceptable performance for linearity, imprecision, and bias.

The measuring interval of the Alinity i Anti-TPO assay is 3.00 to 1000.00 IU/mL.

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-TPO autoantibodies reflecting the prevalence in apparently healthy populations. The prevalence of anti-TPO 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). 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.*30*, *31*
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. The presence of heterophilic antibodies in a patient specimen may cause anomalous values to be observed. Additional information may be required for diagnosis.*32*

EXPECTED VALUES

This study was performed on the ARCHITECT i System.

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

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

In a study, human serum specimens were collected from a population of 236 apparently healthy individuals. All specimens delivered TSH values within the normal reference range. Of this study population, 9 specimens delivered positive results on a commercially available anti-TPO assay device and were excluded from further normal range analysis. The 97.5 percentile concentration of the remaining population was 5.61 IU/mL. In this study population, the normal range is < 5.61 IU/mL. A total of 97.8% (222/227) of the population gave values within this normal range.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

The Alinity i analyzer and the ARCHITECT i System utilize the same reagents and sample/reagent ratios.

Unless otherwise specified, all studies were performed on the Alinity i analyzer.

Precision

Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A2.[33] Testing was conducted using 1 lot of the Alinity i Anti-TPO Reagent Kit, 1 lot of the Alinity i Anti-TPO Calibrators, and 1 lot of the Alinity i Anti-TPO Controls and 1 instrument. One control and 3 human plasma panels were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.

Sample	n	Mean (IU/mL)	Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
			SD	%CV	SD	%CV
Positive Control	120	75.60	1.740	2.3	2.450	3.2
Panel 1	120	1.71	0.136	8.0	0.168	9.8
Panel 2	120	19.85	0.599	3.0	0.761	3.8
Panel 3	120	209.43	4.076	1.9	6.540	3.1

[a] Includes within-run, between-run, and between-day variability.

Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.[34] Testing was conducted using 3 lots of the Alinity i Anti-TPO Reagent Kit on each of 2 instruments over a minimum of 3 days. The maximum observed Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) values are summarized below.

	IU/mL
LoB[a]	0.00
LoD[b]	0.03
LoQ[c]	0.21

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low-analyte level samples.

[c] The LoQ was determined from n ≥ 60 replicates of low-analyte level samples and is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met.

Linearity

A study was performed based on guidance from CLSI EP06-A.[35]

This assay is linear across the measuring interval of 3.00 to 1000.00 IU/mL.

Clinical Sensitivity

This study was performed on the ARCHITECT i System.

In two studies, clinical sensitivity was evaluated by testing 139 clinically defined Hashimoto's thyroiditis specimens and 125 Graves' disease specimens. The clinical diagnosis was based on the criteria of the respective laboratory and the presence of autoantibodies against thyroglobulin and/or TPO was not necessarily a diagnostic criterion. Anti-TPO concentrations ≥ 5.61 IU/mL were considered positive for ARCHITECT Anti-TPO. Data from these studies are summarized in the following table.

ARCHITECT Anti-TPO						
	Hashimoto's Thyroiditis			Graves' Disease		
Study	n	Number of Positives	% Pos (95% CI)	n	Number of Positives	% Pos (95% CI)
1	89	57	64.0 (53.2 to 73.9)	75	69	92.0 (83.4 to 97.0)
2	50	37	74.0 (59.7 to 85.4)	50	50	100.0 (92.9 to 100.0)
Total	139	94	67.6 (59.2 to 75.3)	125	119	95.2 (89.8 to 98.2)

Percent Agreement

A study was performed based on guidance from CLSI EP12-A2.[36]

The performance of the Alinity i Anti-TPO and ARCHITECT Anti-TPO assays was compared for the determination of anti-TPO. A total of 250 specimens were tested in singlicate using 3 lots of the Alinity i Anti-TPO Reagent Kit on 1 Alinity i analyzer and 1 lot of the ARCHITECT Anti-TPO Reagent Kit on 1 ARCHITECT i2000SR instrument.

		ARCHITECT Anti-TPO Assay	
		Positive (≥ 5.61 IU/mL)	Negative (< 5.61 IU/mL)
Alinity i Anti-TPO Assay	**Positive (≥ 5.61 IU/mL)**	137	0
	Negative (< 5.61 IU/mL)	0	113

Positive % Agreement = 100.00% (137/137) with 95% CI: 97.34% to 100.00%

Negative % Agreement = 100.00% (113/113) with 95% CI: 96.79% to 100.00%

Overall % Agreement = 100.00% (250/250) with 95% CI: 98.54% to 100.00%

Sample Range (Alinity i Anti-TPO Assay) = < 3.00 to > 1000.00 IU/mL

Sample Range (ARCHITECT Anti-TPO Assay) = < 3.00 to > 1000.00 IU/mL

Interference

These studies were performed on the ARCHITECT i System.

Potentially Interfering Endogenous Substances

A study was performed based on guidance from NCCLS Protocol EP7-A.37 Specimens with anti-TPO levels between 45.07 and 361.64 IU/mL were supplemented with the following potentially interfering compounds. The average amount of interference observed during the study ranged from -3.6% to +3.7%.

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

Note: As the Alinity i Anti-TPO assay does not utilize a biotinylated antibody complex, there is no risk of potential interference to Anti-TPO values reported by the assay when analyzing samples containing Biotin.

Potentially Interfering Autoimmune Disease Specimens and High Titer IgG Samples

In a study, the ARCHITECT Anti-TPO assay was evaluated by testing specimens with known autoimmune diseases and elevated IgG. Specimens were evaluated with anti-TPO levels spiked between 131.44 and 568.78 IU/mL. Mean absolute % interference is summarized in the following table.

Clinical Condition	Mean Absolute % Interference
Anti-Nuclear Antibody (ANA)	1.6
Rheumatoid Arthritis (RA)	1.6
Systemic Lupus Erythematosus (SLE)	1.1
Insulin Dependent Diabetes Mellitus (IDDM)	1.0
Crohn’s Disease	2.4
Multiple Sclerosis	1.7
Ulcerative Colitis	1.5
Hyperglobulinemia (high IgG)	0.9

Potentially Interfering Other Conditions

In a study, the ARCHITECT Anti-TPO assay was evaluated by testing specimens with HAMA and rheumatoid factor (RF) to further assess the clinical specificity. Specimens positive for HAMA and specimens positive for RF were evaluated for % interference with anti-TPO levels spiked between 163.0 and 184.3 IU/mL. Mean absolute % interference is summarized in the following table.

Clinical Condition	n	Mean Absolute % Interference
RF Positive	10	1.6
HAMA Positive	10	2.1

High Dose Hook

This study was performed on the ARCHITECT i System.

High dose hook is a phenomenon whereby very high level specimens may falsely read within the dynamic range of the assay. For ARCHITECT Anti-TPO, no high dose hook effect was observed when samples containing up to approximately 17 000 IU/mL of Anti-TPO antibody were assayed.

Method Comparison

A study was performed based on guidance from CLSI EP09-A3 using the Passing-Bablok regression method.*38*

	Sample Type	Units	n	Correlation Coefficient	Intercept	Slope	Concentration Range
Alinity i Anti-TPO vs ARCHITECT Anti-TPO	Serum	IU/mL	135	1.00	-0.12	1.01	4.33 - 959.91

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Note for number formatting:

- A space is used as thousands separator (example: 10 000 specimens).
- A period is used to separate the integer part from the fractional part of a number written in decimal form (example: 3.12%).

Key to Symbols

ISO 15223 Symbols	
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
REF	List Number
SN	Serial number

Other Symbols	
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
DISTRIBUTED IN THE USA BY	Distributed in the USA by
INFORMATION FOR USA ONLY	Information needed for United States of America only
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MICROPARTICLES	Microparticles
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