Alinity i Total T_3-23

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INTENDED USE

The Alinity i Total T_3 (TT3) assay is a chemiluminescent microparticle immunoassay (CMIA) used for the quantitative determination of total triiodothyronine (Total T_3) in human serum and plasma on the Alinity i analyzer.

SUMMARY AND EXPLANATION OF THE TEST

3,5,3' Triiodothyronine (T_3) is a thyroid hormone with a molecular weight of 651 daltons[1] and a half-life in serum of 1.5 days.[2] T_3 circulates in the blood as an equilibrium mixture of free and protein bound hormone.[3] T_3 is bound to thyroxine binding globulin (TBG), prealbumin, and albumin. The actual distribution of T_3 among these binding proteins is controversial as estimates range from 38-80% for TBG, 9-27% for prealbumin, and 11-35% for albumin.[4] The binding of these proteins is such that only 0.2-0.4% of the total T_3 is

present in solution as unbound or free T_3.[5] This free fraction represents the physiologically active thyroid hormone.[3]

It has become apparent in recent years that T_3 plays an important role in the maintenance of the euthyroid state. Serum T_3 measurements can be a valuable component of a thyroid screening panel in diagnosing certain disorders of thyroid function as well as conditions caused by iodine deficiency. Clinically, measurements of serum T_3 concentration are especially valuable in diagnosing hyperthyroidism and in following the course of therapy for this disorder.[2, 6, 7] Under conditions of strong thyroid stimulation, the T_3 measurement provides a good estimation of thyroid reserve.[2] Recognition of a thyroid dysfunction called T_3-thyrotoxicosis, associated with an increased serum T_3 level but normal thyroxine (T_4), free T_4, and *in vitro* Uptake results have further highlighted the importance of serum T_3 measurements.[2, 8, 9, 10, 11] Dietary iodine deficiency results in inadequate production of thyroid hormones despite the presence of normal thyroid tissue. In these cases, the serum T_4 concentration is often low while the Thyroid Stimulating Hormone (TSH) concentration is elevated. Elevated TSH associated with low T_4 is normally indicative of hypothyroidism. However, in iodine deficiency, these results together with normal or slightly elevated serum T_3 are indicative of euthyroid status in most individuals.[12]

T_3 levels are also affected by conditions which affect TBG concentration.[13, 14, 15] Slightly elevated T_3 levels may occur in pregnancy or during estrogen therapy, while depressed levels may occur during severe illness, malnutrition, in renal failure and during therapy with anti-thyroid drugs, propranolol and propylthiouracil and salicylates.[2, 16, 17] In patients with severe or chronic illnesses, many abnormalities of thyroid hormone balance occur. T_4 production and the extent of serum thyroid hormone binding may be independently abnormal, resulting in a low, normal or high free T_4 estimate. Serum T_3 concentrations are often low; TSH levels may be normal or slightly elevated. Total T_3 measurements may be valuable when hyperthyroidism is suspected and the free T_4 estimate is normal.[13] The Alinity i Total T_3 assay is to be used as an aid in the assessment of thyroid status.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

This assay is a two-step immunoassay for the quantitative determination of total triiodothyronine (Total T_3) in human serum and plasma using **chemiluminescent microparticle immunoassay (CMIA) technology.**

Sample and anti-T_3 coated paramagnetic microparticles are combined and incubated. The T_3 present in the sample binds to the anti-T_3 coated microparticles. The mixture is washed. T_3 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 an inverse relationship between the amount of Total T_3 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 Total T_3 Reagent Kit 07P94

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

REF	07P9420	07P9430
Tests per cartridge	100	600
Number of cartridges per kit	2	2
Tests per kit	200	1200
MICROPARTICLES	6.6 mL	32.1 mL
CONJUGATE	4.2 mL	16.3 mL

MICROPARTICLES Anti-T_3 (sheep) coated microparticles in MES buffer with sheep IgG stabilizers. Minimum concentration: 0.05% solids. Preservative: ProClin 300.

CONJUGATE T_3 acridinium-labeled conjugate in citrate buffer with NaCl and Triton X-100 stabilizers. Minimum concentration: 0.33 ng/mL. Preservative: ProClin 300.

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.[18, 19, 20, 21]

The following warnings and precautions apply to: MICROPARTICLES / CONJUGATE	
	
WARNING	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.

P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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.abbottdiagnostics.com or/and SDS folder.

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 2 hours 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 2 hours 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
- 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 Total T_3 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.**

Alternate Result Units

Edit assay parameter "Result Units" to select an alternate unit.

Conversion formula:

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

Default Result Unit	Conversion Factor	Alternate Result Unit
ng/mL	1.536	nmol/L
	100.0	ng/dL

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

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

Specimen Types	Collection Tubes
Serum	Serum
	Serum separator
Plasma	Sodium heparin
	Lithium heparin
	Potassium EDTA

- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.

Specimen Conditions

Do not use:

- heat-inactivated specimens

- 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.
- 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 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.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low speed vortex or by inverting 10 times 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 inverting 10 times.
- 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	2 to 8°C	6 days	If testing will be delayed more than 6 days, specimens should be frozen at -10°C or colder.

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

Specimens stored frozen at -10°C or colder for 6 days showed no performance difference.

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.

PROCEDURE

Materials Provided

07P94 Alinity i Total T_3 Reagent Kit

Materials Required but not Provided

- Alinity i Total T_3 assay file
- 07P9401 Alinity i Total T_3 Calibrators
- Commercially available controls containing Total T_3
- 07P9440 Alinity i Total T_3 Manual Diluent
- 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: 70 µL
- Sample volume for each additional test from same sample cup: 20 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: 20 µL

> 3 hours on the reagent and sample manager:

- Replace with a fresh aliquot of sample.

- Refer to the Alinity i Total T_3 calibrator package insert and the commercially available 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 a Total T_3 value exceeding 6.00 ng/mL (9.22 nmol/L) are flagged with the code "> 6.00 ng/mL" (>9.22 nmol/L) and may be diluted with the Manual Dilution Procedure.

Manual Dilution Procedure

Suggested dilution: 1:2

It is recommended that dilutions not exceed 1:2.

Add a minimum of 75 µL of the sample to 75 µL of Alinity i Total T_3 Manual Diluent.

To avoid contamination of Alinity i Total T_3 Manual Diluent, dispense several drops of the diluent into a clean test tube prior to pipetting.

The operator must enter the dilution factor (2) 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 dilution should be performed so that the reported result reads greater than 1.0 ng/mL (1.5 nmol/L).

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 ≤ 0.5 ng/mL (0.8 nmol/L), 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 Total T_3 assay is that a single sample of each control level be tested once every day testing performed.

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.[22]

- If quality control results do not meet the acceptance criteria defined by laboratory QC procedure, sample results may be suspect. Follow the established quality control procedures to troubleshoot. 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.[23]

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 Total T_3 assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration and results.

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

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the Alinity ci-series Operations Manual, Section 5.

Measuring Interval

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

The measuring interval of the Alinity i Total T_3 assay is **0.40 to 6.00 ng/mL** (0.61 to 9.22 nmol/L).

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other thyroid tests, clinical impressions, etc.
- If the Total T_3 results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.

EXPECTED VALUES

This study was performed on the ARCHITECT i System.

A normal range of **0.35 - 1.93 ng/mL** (Central 99% interval) was obtained by testing serum specimens from 379 individuals determined as normal by ARCHITECT TSH and Free T_4 assays. The minimum concentration obtained was 0.30 ng/mL and the maximum concentration obtained was 2.02 ng/mL.

Manufacturers provided reference range adopted, effort made to verify locally.

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. Testing was conducted using 1 lot of the Alinity i Total T_3 Reagent Kit, 1 lot of the Alinity i Total T_3 Calibrator Kit, and 1 lot of commercially available controls and 1 instrument. Three serum panels were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.[24]

Sample	n	Mean (ng/mL)	Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
			SD	%CV	SD	%CV
Panel 1	120	0.36	0.018	5.0	0.018	5.1
Panel 2	120	1.01	0.023	2.2	0.023	2.3
Panel 3	120	5.67	0.500	8.8	0.550	9.7

Sample	n	Mean (nmol/L)	Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
			SD	%CV	SD	%CV
Panel 1	120	0.55	0.027	4.9	0.028	5.0
Panel 2	120	1.56	0.035	2.2	0.036	2.3
Panel 3	120	8.72	0.768	8.8	0.845	9.7

[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. Testing was conducted using 3 lots of the Alinity i Total T_3 Reagent Kit on each of 2 instruments over a minimum of 3 days. The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) values are summarized below. These representative data support the lower limit of the measuring interval.[25]

	ng/mL	nmol/L
LoB[a]	0.00	0.00
LoD[b]	0.05	0.08
LoQ[c,d]	0.30	0.50

[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 is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met.

[d]This value represents the observed LoQ on the ARCHITECT System. The LoQ observed on the Alinity i analyzer supports this LoQ.

Linearity

A study was performed based on guidance from CLSI EP06-A.[26]

This assay is linear across the measuring interval of **0.40 to 6.00** ng/mL (0.61 to 9.22 nmol/L).

Analytical Specificity

This study was performed on the ARCHITECT i System.

Analytical specificity was evaluated with the ARCHITECT Total T_3 assay and determined to have a mean analytical specificity of ≤ 0.1% cross reactivity with thyroxine (T_4) at a concentration of 1100 ng/mL.

Interference

This study was performed on the ARCHITECT i System.

Potentially Interfering Endogenous Substances

The testing demonstrated ≤ 10% mean interference at the levels indicated below.

Potentially Interfering Substance	Interferent Level
Hemoglobin	≤ 500 mg/dL
Bilirubin	≤ 20 mg/dL
Triglycerides	≤ 2000 mg/dL
Protein	≤ 12 g/dL

Method Comparison

A study was performed based on guidance from CLSI EP09-A3 using the Passing-Bablok regression method.[27]

Assay	Sample Type	Units	n	Correlation Coefficient	Intercept	Slope	Concentration Range
Alinity i Total T_3 vs ARCHITECT Total T_3	Serum	ng/mL	123	1.00	0.06	0.90	0.46-5.44
	Serum	nmol/L	123	1.00	0.09	0.90	0.70-8.36

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