ARCHITECT Total T_4

REF 7K66-27
REF 7K66-37
REF 7K66-32

en
Total T4
7K66
G65409R02
B7K6T0

Read Highlighted Changes: Revised May 2017.

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 Total T_4

INTENDED USE

The ARCHITECT Total T_4 (TT_4) assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of thyroxine (Total T_4) in human serum and plasma on the ARCHITECT iSystem.

SUMMARY AND EXPLANATION OF THE TEST

Thyroxine (T_4) is an iodine-containing hormone which has a molecular weight of approximately 777 daltons and is secreted by the thyroid gland. T_4 and its associate thyroid hormone T_3 are responsible for regulating diverse biochemical processes throughout the body which are essential for normal metabolic and neural activity.[1]

Although T_3 has greater biologic potency[2], T_4 is normally present in human serum in approximately 50-fold excess of circulating T_3 and accounts for more than 90% of the circulating protein-bound iodine. T_4 is 99.9% bound to serum thyroxine binding proteins (TBP). The hormone is transported bound primarily to thyroxine binding globulin (TBG) and secondarily by thyroxine binding prealbumin (TBPA) and albumin.[3] Less than 0.05% of the total circulating T_4 is unbound and therefore biologically active.[4, 5] Clinically, T_4 measurements have long been recognized as an aid in the assessment and diagnosis of thyroid status. Elevated T_4 values are characteristically seen in patients with overt hyperthyroidism, while T_4 levels are generally depressed in patients with overt hypothyroidism. Normal T_4 levels accompanied by high T_3 values are seen in patients with T_3-thyrotoxicosis.[6] T_4 levels are altered by physiological or pathological changes in TBP capacity.[3, 4] Thyroxine binding globulin (TBG) capacity has a pronounced effect on the concentration of thyroid hormones. Consequently, T_4 levels may be elevated with increased concentrations of TBG, such as in pregnancy, administration of oral contraceptives or estrogen, infectious and chronic active hepatitis, biliary cirrhosis or congenital increase in TBG levels.[7-9] Conversely, when TBG levels are decreased, such as in nephrotic syndrome, androgen therapy, glucocorticoid therapy, major systemic illness or congenital decrease of TBG, T_4 may be reduced.

Drugs which compete for protein binding sites, such as phenylbutazone, diphenylhydantoin or salicylates, can result in a depressed T_4 measurement.[7-9] Serum T_4 levels in neonates and infants are higher than values in the normal adult, due to the increased concentration of TBG in neonate serum.[10]

While in many cases T_4 values give good indications of thyroid status, T_4 values should be normalized for individual variations in thyroxine binding protein (TBP) capacity. The Free Thyroxine Index (FTI) is conventionally used to achieve this measurement.[11, 12]

To ensure maximum diagnostic accuracy, the final definition of thyroid status should be determined in conjunction with other thyroid function tests such as TSH, Free T_4, Total T_3, FTI and clinical evaluation by the physician.

The ARCHITECT Total T_4 assay is to be used as an aid in the assessment of thyroid status.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Total T_4 assay is a two-step immunoassay to determine the presence of thyroxine (Total T_4) in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-T_4 coated paramagnetic microparticles are combined. Bound T_4 is removed from the binding sites on thyroxine binding globulin, prealbumin and albumin. The T_4 present in the sample binds to the anti-T_4 coated microparticles.
2. After washing, T_3 acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is an inverse relationship between the amount of Total T_4 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 Total T_4 7K66

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

REF	7K66-27	7K66-37	7K66-32
Σ	100	500	2000
MICROPARTICLES	1 x 6.6 mL	1 x 27.0 mL	4 x 27.0 mL
CONJUGATE	1 x 5.9 mL	1 x 26.3 mL	4 x 26.3 mL

MICROPARTICLES Anti-T_4 (sheep) coated Microparticles in TRIS buffer with sheep IgG stabilizers. Minimum concentration: 0.05% solids. Preservative: Sodium Azide.

CONJUGATE T_3 acridinium-labeled Conjugate in MES buffer with NaCl and Triton X-100 stabilizers. Minimum concentration: 0.2 ng/mL. Preservative: ProClin.

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.

NOTE: Bottle and volume varies based on order.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[13-16]

The following warnings and precautions apply to: MICROPARTICLES	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: 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.

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.

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 Total T_4 assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Alternate Result Units

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

Conversion formula:

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

Default result unit	Conversion factor	Alternate result unit
µg/dL	12.87	nmol/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Validated specimen types to be used with this assay:

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

- Other specimen collection tube types have not been validated with this assay.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.
- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.
- **For optimal results, 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

- 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.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	2-8°C	≤ 6 days

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

If testing will be delayed more than 6 days, specimens should be frozen at -10°C or colder.

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.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

7K66 ARCHITECT Total T_4 Reagent Kit

Materials Required but not Provided

- ARCHITECT Total T_4 Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K66-02 ARCHITECT Total T_4 Calibrators
- 7K66-12 ARCHITECT Total T_4 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 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: 74 µL

    Sample volume for each additional test from same sample cup: 24 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 24 µL
  - > 3 hours on board: Additional sample volume is required. Refer to the ARCHITECT System Operations Manual, Section 5 for information on sample evaporation and volumes.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.

- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Prepare ARCHITECT Total T_4 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: 4 drops

    for each control: 4 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens with a Total T_4 value exceeding 24.00 µg/dL are flagged with the code ">24.00" and may be diluted using the Manual Dilution Procedure.

Manual Dilution Procedure

Suggested dilution: 1:2

It is recommended that dilutions not exceed 1:2.

1. Add 75 µL of the patient specimen to 75 µL of ARCHITECT Total T_4 Calibrator A.

   To avoid contamination of Calibrator A, dispense several drops of Calibrator A into a clean test tube prior to pipetting.
2. The operator must enter the dilution factor (2) 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 reported result reads greater than 6.0 µg/dL.

   If the operator does not enter the dilution factor, the reported result will be that of the diluted sample. This result (before dilution factor is applied) should be greater than 3.00 µg/dL.

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 replicate 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 - 24.0 µg/dL.
- Once an ARCHITECT Total T_4 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 Total T_4 assay is that a single replicate of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

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

Verification of Assay Claims

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

The ARCHITECT Total T_4 assay belongs to method group 1.

RESULTS

Calculation

The ARCHITECT Total T_4 assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

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

Measuring Interval

Measuring interval is defined as the range of values in µg/dL which meets the limits of acceptable performance for both imprecision and linearity. The measuring interval for the ARCHITECT Total T_4 assay is 3.00 µg/dL (Limit of Quantitation - LoQ) to 24.00 µg/dL.

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

- 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_4 results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Performance of this test has not been established with neonatal specimens.

EXPECTED VALUES

A normal range of 4.87 µg/dL to 11.72 µg/dL (central 95% interval) was obtained by testing serum specimens from 437 individuals determined as normal by AxSYM Ultrasensitive hTSH II and AxSYM Free T_4 assays. It is recommended that each laboratory establish its own normal range, which may be unique to the population it serves depending upon geographical, patient, dietary, or environmental factors.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Total T_4 assay is designed to have a precision of ≤ 10% (total CV) for concentrations in the range of the low control (4.2 µg/dL), medium control (7.4 µg/dL), and high control (14.6 µg/dL). A study based on guidance from Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) document EP5-A[17] was performed for the ARCHITECT Total T_4 assay. A three member processed human serum based panel was assayed, using two lots of reagents, in replicates of two at two separate times per day for 20 testing days. Data from this study are shown in the following table.*

Panel Member	Reagent Lot	Instrument	n	Mean Conc. Value (µg/dL)	Within Run SD	Within Run %CV	Total SD	Total %CV
1	1	1	80	4.20	0.155	3.7	0.188	4.5
1	2	1	80	4.32	0.176	4.1	0.196	4.5
1	1	2	80	4.45	0.133	3.0	0.167	3.8
1	2	2	80	4.30	0.136	3.2	0.151	3.5
2	1	1	80	7.46	0.251	3.4	0.300	4.0
2	2	1	80	7.35	0.222	3.0	0.268	3.6
2	1	2	80	7.90	0.234	3.0	0.301	3.8
2	2	2	80	7.32	0.210	2.9	0.224	3.1
3	1	1	80	14.87	0.896	6.0	1.084	7.3
3	2	1	80	14.94	0.521	3.5	0.655	4.4
3	1	2	80	16.22	0.616	3.8	0.738	4.5
3	2	2	80	15.13	0.595	3.9	0.703	4.6

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

Recovery

The ARCHITECT Total T_4 assay is designed to have a mean recovery of 100 ± 10% when analyzing samples spiked with known amounts of T_4.

T_4 was added to five normal human serum samples. The concentration of Total T_4 was determined using the ARCHITECT Total T_4 assay and the resulting percent recovery was calculated.*

Sample	Endogenous T_4 Concentration (µg/dL)	T_4 Added (µg/dL)	Observed Total T_4 Concentration (µg/dL)	%Recovery*
1	7.472	1.20	8.825	112.7
2	7.301	1.20	8.487	98.9
3	7.574	1.20	8.631	88.2
4	6.760	1.20	7.911	95.9
5	8.547	1.20	10.015	122.3

Mean Recovery 103.6%

$$* \% \text{ Recovery} = \frac{\text{Observed Total } T_4 \text{ Conc. (µg/dL)} - \text{Endogenous Total } T_4 \text{ Conc. (µg/dL)}}{T_4 \text{ Added (µg/dL)}} \times 100$$

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

Sensitivity

The ARCHITECT Total T_4 assay is designed to have a Limit of Quantitation (LoQ) of ≤ 3.0 µg/dL. The LoQ is defined as the lowest concentration at which analyte in a sample can be accurately quantitated with precision of ≤ 10% CV.

A study was performed based on guidance from the CLSI document EP17-A2[18] with four zero-level samples and 8 samples with T_4 concentrations ranging from 2.0 to 3.5 µg/dL. The samples were tested in at least 5 separate runs over a minimum of 3 days using 2 reagent lots and 6 instruments. In this study, the Limit of Blank (LoB) was 0.70 µg/dL, Limit of Detection (LoD) was 0.91 µg/dL and LoQ was 2.0 µg/dL.*

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

Analytical Specificity

The ARCHITECT Total T_4 assay is designed to have a mean analytical specificity of ≤ 3.2% cross reactivity with triiodothyronine (T_3) at a concentration of 100 µg/dL in a sample containing approximately 3 µg/dL of Total T_4 as confirmed by a study based on guidance from CLSI document EP7-A.[19]

Interference

The ARCHITECT Total T_4 assay is designed to have a mean potential interference from hemoglobin, bilirubin, triglycerides, and protein of < 10% at the levels indicated below as confirmed by a study based on guidance from CLSI document EP7-A.[19]

Hemoglobin	≤ 500 mg/dL
Bilirubin	≤ 20 mg/dL
Triglycerides	≤ 3000 mg/dL
Protein	≥ 4.5 and ≤ 12 g/dL

Accuracy by Correlation

The ARCHITECT Total T_4 assay is designed to have a slope of 1.00 ± 0.20 and a correlation coefficient (r) of ≥ 0.90 when compared to the AxSYM Total T_4 assay.

A study was performed where specimens were tested using ARCHITECT Total T_4 assay and AxSYM Total T_4 assay. Data from this study were analyzed using least squares and Passing Bablok[20] regression methods and are summarized in the following table.*

Abbott ARCHITECT Total T_4 vs. Abbott AxSYM Total T_4

Method	Number of Specimens	Intercept	Slope	Correlation Coefficient
Least Squares Linear Regression	656	-0.26	0.96	0.97
Passing-Bablok Linear Regression**	656	-0.20	0.94	0.97

In this evaluation, serum specimens tested ranged from 1.03 to 20.55 µg/dL with the ARCHITECT Total T_4 assay and from 1.12 to 22.46 µg/dL with the AxSYM Total T_4 assay.

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

** A linear regression method with no special assumptions regarding the distribution of the samples and the measurement errors.[20]

BIBLIOGRAPHY

1. Felig P, Baxter JD, Broadus AE, Frohman LA, editors. *Endocrinology and Metabolism* (2nd Ed.). New York: McGaw-Hill Book Co., 1987;389-409.
2. Lerman J. The Physiologic Activity of L-Triiodothyronine. *J Clin Endocrinol Metab* 1953;13:1341-1346.
3. Oppenheimer JH. Role of Plasma Proteins in the Binding, Distribution and Metabolism of the Thyroid Hormones. *N Engl J Med* 1968; 278:1153-1162.
4. Robbins J, Rall JE. Thyroxine-Binding Proteins. In: Gray CH, Bacharach AL, editors. *Hormones in Blood* (2nd Ed.). London: Academic Press, 1967;1:427-440.
5. Ekins RP, editor. *Methods for the Measurement of Free Thyroid Hormones.* Amsterdam: Excerpta Medica Foundation. 1979;72-92.
6. Sterling K, Refetoff S, Selenkow HA. T_3 Thyrotoxicosis: Thyrotoxicosis Due to Elevated Serum Triiodothyronine Levels. *JAMA* 1970;213: 571-575.
7. Witherspoon LR, Shuler SE. Estimation of Free Thyroxine Concentration: Clinical Methods and Pitfalls. *J Clin Immunoassay.* 1984;7:192-205.
8. Bermudez F, Surks MI, Oppenheimer JH. High Incidence of Decreased Serum Triiodothyronine Concentration in Patients with Nonthyroid Disease. *J Clin Endocrinol Metab.* 1975;41:27-40.
9. Larsen PR. Triiodothyronine: Review of Recent Studies of Its Physiology and Pathophysiology in Man. *Metabolism* 1972;21:1073-1092.
10. Abuid J, Klein AH, Foley Jr TP, Larsen TP. Total and Free Triiodothyronine and Thyroxine in Early Infancy. *J Clin Endocrinol Metab* 1974;39: 263-268.
11. Szpunar WE, Stoffer SS, Bednarz MN. Clinical Evaluation of a Thyroxine-Binding Globulin Assay in Calculating a Free-Thyroxine Index. *J Nucl Med* 1981;22:793-795.

12. Nusynowitz L. Free Thyroxine Index. *JAMA* 1975;232:1050.
13. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
14. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
15. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
16. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition.* CLSI Document M29-A4. Wayne, PA: CLSI; 2014.
17. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline.* NCCLS Document EP5-A. Wayne, PA: NCCLS; 1999.
18. Clinical and Laboratory Standards Institute (CLSI). *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition.* CLSI Document EP17-A2. Wayne, PA: CLSI; 2012.
19. National Committee for Clinical Laboratory Standards (NCCLS). *Interference Testing in Clinical Chemistry; Approved Guideline.* NCCLS Document EP7-A. Wayne, PA: NCCLS; 2002.
20. Passing H, Bablok W. A new biometrical procedure for testing the equality of measurements from two different analytical methods. Application of linear regression procedures for method comparison studies in clinical chemistry, Part I. *J Clin Chem Clin Biochem* 1983;21(11):709–720.

Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL NO.	Control Number
DISTRIBUTED IN THE USA BY	Distributed in the USA by
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
PRODUCT OF IRELAND	Product of Ireland
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WARNING: SENSITIZER	Warning: May cause an allergic reaction.
WASH BUFFER	Wash Buffer


Abbott Ireland
Diagnostics Division
Lisnamuck, Longford
Co. Longford
Ireland
+353-43-3331000

DISTRIBUTED IN THE USA BY

Abbott Laboratories
Abbott Park, IL 60064 USA

Customer Service: Contact your local representative or find country-specific contact information on www.abbottdiagnostics.com

Revised May 2017.