ARCHITECT Free T_3

REF 7K63-27
REF 7K63-37
REF 7K63-32

en
Free T3
7K63
G56973R03
B7K6W0

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 Free T_3

INTENDED USE

The ARCHITECT Free T_3 (FT_3) assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of free triiodothyronine (Free T_3) in human serum and plasma.

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]

Free T_3 is typically elevated to a greater degree than free thyroxine (T_4) in Graves' disease.[6, 7]

Occasionally, free T_3 alone is elevated (T_3 thyrotoxicosis) in about 5% of the hyperthyroid population.[8]

In contrast, levels of free T_4 are elevated to a greater degree than free T_3 in toxic multinodular goiter and excessive T_4 therapy.[9]

Serum free T_3 is useful in distinguishing these forms of hyperthyroidism. Free T_3 may also be important in monitoring patients on anti-thyroid therapy where treatment is focused on reducing the T_3 production and the T_4 conversion to T_3. Serum free T_3 may also be useful in assessing the severity of the thyrotoxic state.

The ARCHITECT Free T_3 assay is to be used as an aid in the assessment of thyroid status.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Free T_3 assay is a two-step immunoassay to determine the presence of free (unbound) T_3 in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-T_3 coated paramagnetic microparticles are combined. Free T_3 (unbound) present in the sample binds to the anti-T_3 coated microparticles.
2. After washing, T_3 acridinium-labeled conjugate is added.
3. Pre-Trigger and Trigger Solutions are then 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 Free T_3 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 Free T_3 7K63

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

REF	7K63-27	7K63-37	7K63-32
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_3 (sheep) coated Microparticles in MES buffer with sheep IgG stabilizers. Minimum Concentration: 0.085% solids. Preservative: antimicrobial agent.

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

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 vary 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.[10-13]

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.

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.
On board	System temperature	28 days	Discard after 28 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 Free T_3 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
pg/mL	1.536	pmol/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
	Potassium EDTA

- Other anticoagulants have not been validated for use with this assay.
- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.
- Performance has not been established for the use of neonatal specimens.
- 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
- 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.
- 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.
- Specimens must be mixed THOROUGHLY after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results.
- 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

7K63 ARCHITECT Free T_3 Reagent Kit

Materials Required but not Provided

- ARCHITECT Free T_3 Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K63-02 ARCHITECT Free T_3 Calibrators
- 7K63-12 ARCHITECT Free T_3 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, discard the cap and 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: 72 µL

    Sample volume for each additional test from same sample cup: 22 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 22 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.
- Prepare ARCHITECT Free T_3 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 cannot be diluted for Free T_3 determinations. Specimens which read > 20.00 pg/mL should be reported as such.

Calibration

- Test Calibrators A to 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 - 30.0 pg/mL.
- Once an ARCHITECT Free T_3 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 5.

Quality Control Procedures

The recommended control requirement for the ARCHITECT Free T_3 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.

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 Free T_3 assay belongs to method group 2.

RESULTS

Calculation

The ARCHITECT Free T_3 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.

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.

Measuring Interval

Measuring interval is defined as the range of values in pg/mL which meets the limits of acceptable performance for both imprecision and linearity. The measuring interval for the ARCHITECT Free T_3 assay is 1.5 (Limit of Quantitation - LoQ) to 20 pg/mL.

LIMITATIONS OF THE PROCEDURE

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

EXPECTED VALUES

A normal range of 1.88-3.18 pg/mL (Central 95% interval) was obtained by testing serum specimens from 260 individuals determined as normal by ARCHITECT Anti-Tg, Anti TPO and TSH 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.

Free T_3 is a secondary indicator of thyroid status. Although the majority of patients with hyperthyroidism will have free T_3 values greater than the upper limit of the euthyroid range, some may have free T_3 values which fall within the normal range.[14, 15] Specimens from patients described as "sick euthyroids" generally yield values in the low to normal range.[16, 17]

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Free T_3 assay is designed to have a precision of ≤ 10% (total CV). A study based on guidance from Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) document EP5-A[18] was performed for the ARCHITECT Free T_3 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 summarized in the following table.*

Panel Member	Reagent Lot	Instrument	n	Mean Conc. Value (pg/mL)	Within Run SD	Within Run %CV	Total SD	Total %CV
1	1	1	80	3.22	0.096	3.0	0.115	3.6
1	1	2	80	3.16	0.133	4.2	0.143	4.5
1	2	1	80	3.60	0.108	3.0	0.141	3.9
1	2	2	80	3.35	0.113	3.4	0.131	3.9
2	1	1	80	6.00	0.099	1.7	0.168	2.8
2	1	2	80	5.88	0.166	2.8	0.184	3.1
2	2	1	80	6.28	0.154	2.5	0.176	2.8
2	2	2	80	6.06	0.194	3.2	0.225	3.7
3	1	1	80	10.50	0.252	2.4	0.481	4.6
3	1	2	80	10.01	0.289	2.9	0.496	5.0
3	2	1	80	10.50	0.145	1.4	0.237	2.3
3	2	2	80	10.12	0.217	2.1	0.265	2.6

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

Sensitivity

The ARCHITECT Free T_3 assay is designed to have a Limit of Quantitation (LoQ) of ≤ 1.5 pg/mL. The LoQ is defined as the lowest concentration at which analyte in a sample can be accurately quantified with precision of ≤ 20% CV.

A study was performed based on guidance from the CLSI document EP17-A2[20] with four zero-level samples and 8 samples with T_3 target concentrations ranging from 1.0 to 3.2 pg/mL. The samples were tested over a minimum of 3 days using 2 reagent lots and 6 instruments. In this study, the Limit of Blank (LoB) was 0.94 pg/mL, Limit of Detection (LoD) was 1.07 pg/mL and LoQ was 1.25 pg/mL.*

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

Analytical Specificity

The ARCHITECT Free T_3 assay is designed to have a mean analytical specificity of ≤ 0.001% cross reactivity with thyroxine (T_4) at a concentration of 1,000,000 pg/mL.

Interference

The ARCHITECT Free T_3 assay is designed to have a mean potential interference from hemoglobin, bilirubin, triglycerides, and protein of < 10% at the levels indicated below.

Hemoglobin	≤ 500 mg/dL
Bilirubin	≤ 20 mg/dL
Triglycerides	≤ 2000 mg/dL
Protein	≤ 12 g/dL

Accuracy by Correlation

The ARCHITECT Free T_3 6 point assay is designed to have a slope of 1.00 +/- 0.15 and a correlation coefficient (r) of ≥ 0.90 when compared to the ARCHITECT Free T_3 2 point assay. A study was performed where specimens were tested using the ARCHITECT Free T_3 6 point assay and ARCHITECT Free T_3 2 point assay. Data from this study were analyzed using least squares and Passing Bablok[19] regression methods and are summarized in the following table.*

Abbott ARCHITECT Free T_3 6 point assay vs. Abbott ARCHITECT Free T_3 2 point assay

Method	Number of Specimens	Intercept	Slope	Correlation Coefficient
Least Squares Linear Regression	144	-0.32	1.04	0.99
Passing-Bablok Linear Regression**	144	-0.09	0.97	0.99

In this evaluation, serum specimens tested ranged from 1.50 pg/mL to 17.81 pg/mL with the ARCHITECT Free T_3 6 point assay and from 1.55 pg/mL to 17.66 pg/mL with the ARCHITECT Free T_3 2 point 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.[19]

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
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

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Abbott

ARCHITECT
Free T_3 Controls

REF 7K63-10

en
Free T3
7K63
G5-9120 / R05
C7K630

Read Highlighted Changes: Revised June 2015.

INTENDED USE

The ARCHITECT Free T_3 Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT iSystem (reagents, calibrators and instrument), when used for the quantitative measurement of free triiodothyronine (Free T_3) in human serum and plasma. Refer to the ARCHITECT assay-specific reagent package insert for additional information.

CONTENTS

3 Bottles (8 mL each) of ARCHITECT Free T_3 Controls contain T_3 in human serum. Preservative: Sodium Azide.

The following concentration ranges may be used for individual replicate control specifications on the ARCHITECT iSystem:

Control	Target Concentration (pg/mL)	Range (pg/mL)	Target Concentration (pmol/L)	Range (pmol/L)
CONTROL L	3.1	2.02 - 4.09	4.8	3.1 - 6.29
CONTROL M	6.0	4.20 - 7.80	9.2	6.45 - 11.98
CONTROL H	10.5	7.88 - 14.18	16.1	12.10 - 21.77

Each laboratory should establish its own concentration ranges for new control lots at each control level. This can be accomplished by assaying a minimum of 20 replicates over several (3-5) days. Sources of variation that can be expected should be included in this study in order to be representative of future system performance. These may include:

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

These results should be applied to your laboratory's quality control practices.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** 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.
- The human serum used in the ARCHITECT Free T_3 Controls is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CONTROL L / CONTROL M / CONTROL H	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
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.

STORAGE

- Controls are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

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Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CONC	Concentration
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL L	Control Low, Medium, High (L,M,H)
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
PRODUCT OF IRELAND	Product of Ireland
RANGE	Range
REF	List Number

ARCHITECT is a trademark of Abbott Laboratories in various jurisdictions.

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Revised June 2015.

Abbott

ARCHITECT
Free T_3 Calibrators

REF 7K63-02

en
Free T3
7K63
G6-7702 / R01
S7K6W0

INTENDED USE

The ARCHITECT Free T_3 Calibrators are for the calibration of the ARCHITECT iSystem when used for the quantitative determination of free triiodothyronine (Free T_3) in human serum and plasma. Refer to the ARCHITECT assay-specific reagent package insert for additional information.

CONTENTS

6 Bottles (4 mL each) of ARCHITECT Free T_3 Calibrators prepared in human serum. Preservative: Sodium Azide.

The calibrators yield the following concentrations:

	Free T_3 Concentration	
Calibrator	(pg/mL)	(pmol/L)
CAL A	0.0	0.00
CAL B	1.4	2.15
CAL C	3.5	5.38
CAL D	7.0	10.75
CAL E	17.2	26.42
CAL F	30.0	46.08

STANDARDIZATION

The calibrators are matched to an Abbott internal reference standard. This internal reference standard is manufactured by gravimetric methods based on the Free Triiodothyronine calculation (FT_{3C}) using L-Triiodothyronine (sodium salt, not less than 95% pure by HPLC) and L-Thyroxine (sodium pentahydrate, not less than 95% pure by HPLC) at each concentration level. The FT_{3C} is a calculation of the Free Triiodothyronine hormone concentration, which depends on the amount of Total T_3 and Total T_4 found in the serum as well as the serum's thyroid hormone binding capacity.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- Rx ONLY
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** 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.[1-4]
- The human serum used in the ARCHITECT Free T_3 Calibrators is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CAL A . CAL F	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
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.

STORAGE

- Calibrators are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

PREPARATION FOR USE

Calibrators may be used immediately after removal from 2-8°C storage.

Prior to each use, mix by gentle inversion.

After each use, tightly close the caps and return the calibrators to 2-8°C storage.

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CAL A	Calibrator (A,B,C,D,E or F)
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
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
PRODUCT OF IRELAND	Product of Ireland
REF	List Number
Rx ONLY	For use by or on the order of a physician only (applicable to USA classification only).

ARCHITECT is a trademark of Abbott Laboratories in various jurisdictions.

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Created September 2016.

Abbott

ARCHITECT
Free T_4 Controls

REF 7K65-10

en
Free T4
7K65
G5-9239 / R04
C7K650

Read Highlighted Changes: Revised June 2015.

INTENDED USE

The ARCHITECT Free T_4 Controls are for the verification of the accuracy and precision of the ARCHITECT iSystem when used for the quantitative determination of free thyroxine (Free T_4) in human serum and plasma. Refer to the ARCHITECT assay-specific reagent package insert for additional information.

CONTENTS

3 Bottles (8 mL each) of ARCHITECT Free T_4 Controls contain T_4 prepared in human serum. Preservative: sodium azide.

The following concentration ranges may be used for individual replicate control specifications on the ARCHITECT iSystem:

	Target Concentration	Range	Target Concentration	Range
Control	ng/dL		pmol/L	
CONTROL L	0.65	0.42 - 0.85	8.4	5.41 - 10.94
CONTROL M	1.2	0.86 - 1.62	15.4	11.07 - 20.85
CONTROL H	2.8	1.82 - 3.78	36.0	23.42 - 48.65

Each laboratory should establish its own concentration ranges for new control lots at each control level. This can be accomplished by assaying a minimum of 20 replicates over several (3-5) days. Sources of variation that can be expected should be included in this study in order to be representative of future system performance. These may include:

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

These results should be applied to your laboratory's quality control practices.

STANDARDIZATION

The controls are matched to an Abbott internal reference standard. This internal reference standard is manufactured by gravimetric methods based on the Free Thyroxine calculation (FT_4c) using L-Thyroxine, sodium salt pentahydrate, (HPLC grade), at each concentration level. The FT_4c is a calculation of the free thyroid hormone concentration, which depends on the amount of Total T_4 found in the serum and the serum's T_4 binding capacity.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** 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.[1]
- The human serum used in the ARCHITECT Free T_4 Controls is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CONTROL L / CONTROL M / CONTROL H	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
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.

STORAGE

- Controls are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CONC	Concentration
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL L	Control Low, Medium, High (L,M,H)
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
PRODUCT OF IRELAND	Product of Ireland
RANGE	Range
REF	List Number

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Revised June 2015.

Abbott

ARCHITECT
Free T_4 Calibrators

REF 7K65-02

en
Free T4
7K65
G5-9241 / R02
S7K6U0

Read Highlighted Changes: Revised June 2015.

INTENDED USE

The ARCHITECT Free T_4 Calibrators are for the calibration of the ARCHITECT iSystem when used for the quantitative determination of free thyroxine (Free T_4) in human serum and plasma. Refer to the ARCHITECT assay-specific reagent package insert for additional information.

CONTENTS

6 Bottles (4 mL each) of ARCHITECT Free T_4 Calibrators prepared in human serum. Preservative: sodium azide.

The calibrators yield the following concentrations:

	Free T_4 Concentration	
Calibrators	(ng/dL)	(pmol/L)
CAL A	0.0	0.0
CAL B	0.5	6.4
CAL C	1.0	12.9
CAL D	2.0	25.7
CAL E	3.5	45.0
CAL F	6.0	77.2

STANDARDIZATION

The calibrators are matched to an Abbott internal reference standard. This internal reference standard is manufactured by gravimetric methods based on the Free Thyroxine calculation (FT_4c) using L-Thyroxine, sodium salt pentahydrate (HPLC grade), at each concentration level. The FT_4c is a calculation of the free thyroid hormone concentration, which depends on the amount of Total T_4 found in the serum and the serum's T_4 binding capacity.

PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use
- **CAUTION:** This product contains human-sourced and/or potentially infectious components. Refer to the **CONTENTS** 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.
- The human serum used in the ARCHITECT Free T_4 Calibrators is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HCV and anti-HIV-1/HIV-2.

The following warnings and precautions apply to: CAL A - CAL F	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
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.

STORAGE

- Calibrators are stable until the expiration date when stored and handled as directed.
- Do not use past expiration date.
- 2°C – 8°C

BIBLIOGRAPHY

1. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
2. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; December 2009.
3. World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
4. 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.

Key to Symbols

	Caution
	Consult instructions for use
	Manufacturer
	Temperature limitation
	Use by/Expiration date
CAL A	Calibrator (A,B,C,D,E or F)
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
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
PRODUCT OF IRELAND	Product of Ireland
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Revised June 2015.

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ARCHITECT Free T_4

REF 7K65-29
REF 7K65-24
REF 7K65-39
REF 7K65-34

en
Free T4
7K65
G59250R03
B7K6F0

Read Highlighted Changes: Revised April 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 Free T_4

INTENDED USE

The ARCHITECT Free T_4 (FT4) assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of free thyroxine (Free T_4) in human serum and plasma.

SUMMARY AND EXPLANATION OF THE TEST

Thyroxine (T_4) circulates in the blood as an equilibrium mixture of free and serum protein bound hormone. Thyroxine binding globulin (TBG), albumin and pre-albumin bind approximately 75%, 10% and 15% of the total circulating T_4 respectively.[1-3] The binding of T_4 by these proteins is such that less than 0.03% is present in the circulation as unbound, free T_4.[4] This small percentage of the total T_4 represents the physiologically available hormone which is biologically active. Once the free T_4 is absorbed by the target cells, the equilibrium reestablishes circulating free T_4 levels. The equilibrium results in the maintenance of a constant level of free T_4 when alterations occur in either the concentration or affinity of the serum binding proteins. Therefore, in a variety of normal (pregnancy)[4] and abnormal (Familial Dysalbuminemic Hyperthyroxinemia, FDH)[5-7] states, or as a result of the administration of certain drugs (e.g. furosemide[8, 9] and fenclofenac[10-12]), the target tissues are assured of receiving the required amount of hormone. Free T_4 values may, therefore, provide the best indication of thyroid dysfunction, since free T_4 is less sensitive to changes in the serum binding proteins.

Historically, the diagnosis of thyroid function has involved performing a total T_4 assay[13, 14] in addition[15] to a Thyroxine Uptake (TU) assay of the same sample. The mathematical combination of these two assays produces a Free Thyroxine Index (FTI) which provides an indirect proportional estimate for free T_4.[16]

Alternatively, direct assays have been developed using equilibrium dialysis,[17, 18] ultrafiltration,[19, 20] RIA,[21] and solid-phase EIA technology[22] to measure free T_4. In these methods, separation of free and bound tracer is achieved either with a membrane, or by binding free T_4 to a solid phase antibody. This extraction step removes an amount of T_4 which is proportional to the original amount of free T_4 present in the patient sample. Provided that the extracted T_4 is less than approximately 5% of the T_4 in the sample, a true estimation of the free T_4 content can be obtained.

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

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Free T_4 assay is a two-step immunoassay to determine the presence of free thyroxine (Free 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. Free T_4 (unbound) 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 Free 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 Free T_4 7K65

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

REF	7K65-29	7K65-24	7K65-39	7K65-34
Σ	100	400	500	2000
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL	4 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 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.[23-26]

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.

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.

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 Free 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
ng/dL	12.87	pmol/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 anticoagulants have not been validated for use with this assay.
- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.
- Performance of this test has not been established with neonatal specimens.
- 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
- 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.
- Specimens must be mixed THOROUGHLY after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results.
- 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, plasma separator or red blood cells.

Follow the manufacturer's processing instructions for serum or plasma collection tubes if a removal time of less than 24 hours is specified.

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

7K65 ARCHITECT Free T_4 Reagent Kit

Materials Required but not Provided

- ARCHITECT Free T_4 Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K65-02 ARCHITECT Free T_4 Calibrators
- 7K65-10 ARCHITECT Free 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: 95 µL

    Sample volume for each additional test from same sample cup: 45 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 45 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 probe to ensure sufficient patient specimen is present.

- Prepare ARCHITECT Free 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

Samples cannot be diluted for Free T_4 determinations. Samples which read > 5.00 ng/dL should be reported as such.

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 - 6.0 ng/dL.
- Once an ARCHITECT Free 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 Free T_4 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.

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 Free T_4 assay belongs to method group 6.

RESULTS

Calculation

The ARCHITECT Free 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.

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.

Measuring Interval

Measuring interval is defined as the range of values in ng/dL which meets the limits of acceptable performance for both imprecision and linearity.

The measuring interval for the ARCHITECT Free T4 assay is 0.40 (Limit of Quantitation - LoQ) to 5.00 ng/dL.

LIMITATIONS OF THE PROCEDURE

- Results should be used in conjunction with other data; e.g., symptoms, results of other thyroid tests, clinical impressions, etc.
- If the Free T_4 results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.

EXPECTED VALUES

A normal range of 0.70 ng/dL to 1.48 ng/dL (central 99% interval) was obtained by testing serum specimens from 411 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 Free T_4 assay is designed to have a precision of ≤ 10% (total CV) for concentrations in the range of the low control (0.65 ng/dL), medium control (1.2 ng/dL) and high control (2.8 ng/dL). A study based on guidance from Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) document EP5-A[27] was performed for the ARCHITECT Free 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 summarized in the following table.*

Panel Member	Reagent Lot	Instrument	n	Mean Conc. Value (ng/dL)	Within Run SD	Within Run %CV	Total SD	Total %CV
1	1	1	80	0.69	0.021	3.0	0.032	4.7
1	1	2	80	0.67	0.036	5.3	0.041	6.1
1	2	1	80	0.70	0.021	3.0	0.055	7.8
1	2	2	80	0.72	0.027	3.7	0.043	6.0
2	1	1	80	1.26	0.048	3.8	0.061	4.8
2	1	2	80	1.22	0.029	2.3	0.044	3.5
2	2	1	80	1.25	0.029	2.3	0.066	5.2
2	2	2	80	1.27	0.033	2.6	0.048	3.8
3	1	1	80	2.94	0.084	2.8	0.148	5.1
3	1	2	80	2.87	0.097	3.4	0.151	5.3
3	2	1	80	3.03	0.098	3.3	0.191	6.3
3	2	2	80	3.00	0.088	2.9	0.134	4.5

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

Sensitivity

The ARCHITECT Free T_4 assay is designed to have a Limit of Quantitation (LoQ) of ≤ 0.4 ng/dL. The LoQ is defined as the lowest amount of analyte in a sample that can be accurately quantitated with precision of ≤ 10% CV.

A study was performed based on guidance from the NCCLS document EP17-A[29] with four zero-level samples and 8 samples with Free T_4 concentrations ranging from 0.25 to 1.0 ng/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 0.22 ng/dL, Limit of Detection (LoD) was 0.28 ng/dL and LoQ was 0.40 ng/dL.*

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

Analytical Specificity

The ARCHITECT Free T_4 assay is designed to have a mean analytical specificity of ≤ 0.0035% cross reactivity with triiodothyronine (T_3) at a concentration of 12,000 ng/dL in a sample containing 0.5 ng/dL of Free T_4.

Interference

The ARCHITECT Free T_4 assay is designed to have a mean potential interference from hemoglobin, bilirubin, triglycerides, and protein of < 10% at the levels indicated below.

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

Accuracy by Correlation

The ARCHITECT Free 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 Free T_4 assay.

A study was performed where specimens were tested using the ARCHITECT Free T_4 assay and AxSYM Free T_4 assay. Data from this study were analyzed using least squares and Passing Bablok[28] regression methods and are summarized in the following table.*

Abbott ARCHITECT Free T_4 vs. Abbott AxSYM Free T_4

Method	Number of Specimens	Intercept	Slope	Correlation Coefficient
Least Squares Linear Regression	675	0.03	0.96	0.953
Passing-Bablok Linear Regression**	675	-0.02	1.00	0.953

In this evaluation, serum specimens tested ranged from 0.52 ng/dL to 3.88 ng/dL with the ARCHITECT Free T_4 assay and from 0.46 ng/dL to 4.14 ng/dL with the AxSYM Free 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.[28]

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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

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Abbott

ARCHITECT Total T_3

REF 7K64-25
REF 7K64-20
REF 7K64-35
REF 7K64-30

en
Total T3
7K64
G65478R09
B7K640

Revised April 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_3

INTENDED USE

The ARCHITECT Total T_3 (TT_3) assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of total triiodothyronine (Total T_3) in human serum and plasma.

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, 8-11] 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.[13-15] 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 ARCHITECT Total T_3 assay is to be used as an aid in the assessment of thyroid status.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Total T_3 assay is a two-step immunoassay to determine the presence of Total T_3 in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-T_3 coated paramagnetic microparticles are combined. The T_3 present in the sample binds to the anti-T_3 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_3 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_3 7K64

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

REF	7K64-25	7K64-20	7K64-35	7K64-30
Σ	100	400	500	2000
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL	4 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL	4 x 26.3 mL

MICROPARTICLES Anti-T_3 (sheep) coated microparticles in MES buffer with sheep IgG stabilizers. Minimum Concentration: 0.08% 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.

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 vary 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.[18-21]

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.

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.
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_3 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.

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
ng/mL	1.536	nmol/L
	100.0	ng/dL*

* iSystem Assay CD-ROM version 6.0 and higher will be required to install this alternate result unit (ng/dL).

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
	Potassium EDTA

- Other anticoagulants have not been validated for use with this assay.
- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.
- Performance has not been established for the use of neonatal specimens.
- 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
- 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.
- 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.
- Specimens must be mixed THOROUGHLY after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results.
- 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

7K64 ARCHITECT Total T_3 Reagent Kit

Materials Required but not Provided

- ARCHITECT Total T_3 Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K64-01 ARCHITECT Total T_3 Calibrators
- 7K64-50 ARCHITECT Total T_3 Manual Diluent
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Any commercially available controls
- 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
  - > 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.
- Prepare ARCHITECT Total T_3 Calibrators.
  - Mix calibrator(s) by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 4 drops
  - Follow the manufacturer's instructions for preparation of commercially available control material.
- 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 a Total T_3 value exceeding 8.00 ng/mL are flagged with the code "> 8.00" 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 a minimum of 75 µL of the patient specimen to 75 µL of ARCHITECT Total T_3 Manual Diluent.

   To avoid contamination of Manual Diluent, dispense several drops of Manual Diluent 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 1.0 ng/mL.

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 0.5 ng/mL.

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

Calibration

- Test Calibrators 1 and 2 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 - 8.0 ng/mL.
- Once an ARCHITECT Total T_3 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_3 assay is a single sample of all control levels 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 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_3 assay belongs to method group 2.

RESULTS

Calculation

The ARCHITECT Total T_3 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.

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_3 results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.

EXPECTED VALUES

A normal range of 0.58 ng/mL to 1.59 ng/mL (central 95% interval) was obtained by testing serum specimens from 438 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_3 assay is designed to have a precision of ≤ 10% (total CV). A study based on guidance from Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) document EP5-A[22] was performed for the ARCHITECT Total T_3 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 summarized in the following table.*

Panel Member	Reagent Lot	Instrument	n	Mean Conc. Value (ng/mL)	Within Run SD	Within Run %CV	Total SD	Total %CV
1	1	1	80	0.75	0.021	2.7	0.027	3.6
1	1	2	80	0.73	0.023	3.1	0.030	4.1
1	2	1	80	0.79	0.036	4.6	0.043	5.4
1	2	2	80	0.81	0.047	5.8	0.057	7.0
2	1	1	80	1.50	0.029	1.9	0.110	7.3
2	1	2	80	1.49	0.040	2.7	0.053	3.6
2	2	1	80	1.53	0.031	2.0	0.035	2.3
2	2	2	80	1.54	0.040	2.6	0.049	3.2
3	1	1	80	3.27	0.062	1.9	0.128	3.9
3	1	2	80	3.29	0.107	3.3	0.140	4.2
3	2	1	80	3.55	0.054	1.5	0.071	2.0
3	2	2	80	3.54	0.066	1.9	0.077	2.2

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

Recovery

The ARCHITECT Total T_3 assay is designed to have a mean recovery of 100 ± 10% when analyzing samples spiked with known amounts of T_3. T_3 was added to nine normal human serum samples. The concentration of T_3 was determined using the ARCHITECT Total T_3 assay and the resulting percent recovery was calculated.*

Sample	Endogenous T_3 Concentration (ng/mL)	T_3 Added (ng/mL)	Observed Total T_3 Concentration (ng/mL)	% Recovery**
1	2.01	0.77	2.74	94.8
2	0.97	0.78	1.64	85.9
3	1.13	0.79	1.95	103.8
4	0.99	1.54	2.43	93.5
5	0.88	1.53	2.41	100.0
6	0.90	1.54	2.54	106.5
7	1.07	3.03	4.28	105.9
8	1.23	3.04	4.21	98.0
9	0.90	3.03	3.89	98.7

Average Recovery: 98.6%

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

$$** \% \text{ Recovery} = \frac{\text{Observed Total } T_3 \text{ Conc. (ng/mL)} - \text{Endogenous Total } T_3 \text{ Conc. (ng/mL)}}{T_3 \text{ Added (ng/mL)}} \times 100$$

Analytical Sensitivity

The ARCHITECT Total T_3 assay is designed to have an analytical sensitivity of ≤ 0.25 ng/mL.

Analytical sensitivity is defined as the concentration calculated as the mean plus two standard deviations of replicates of the ARCHITECT Total T_3 MasterCheck Level 0 (0.0 ng/mL). The analytical sensitivity (low-linearity) is defined in the ARCHITECT Total T_3 assay parameters as 0.25 ng/mL.

Analytical Specificity

The ARCHITECT Total T_3 assay is designed to have a mean analytical specificity of ≤ 0.1% cross reactivity with thyroxine (T_4) at a concentration of 1,100 ng/mL.

Interference

The ARCHITECT Total T_3 assay is designed to have a mean potential interference from hemoglobin, bilirubin, triglycerides, and protein of ≤ 10% at the levels indicated below.

Hemoglobin	≤ 500 mg/dL
Bilirubin	≤ 20 mg/dL
Triglycerides	≤ 2000 mg/dL
Protein	≤ 12 g/dL

Accuracy by Correlation

The ARCHITECT Total T_3 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_3 assay.

A study was performed where specimens were tested using the ARCHITECT Total T_3 assay and AxSYM Total T_3 assay. Data from this study were analyzed using Least Squares and Passing-Bablok[23] regression methods and are summarized in the following table.*

Abbott ARCHITECT Total T_3 vs. Abbott AxSYM Total T_3				
Method	Number of Specimens	Intercept	Slope	Correlation Coefficient
Least Squares				
Linear Regression	1440	0.02	1.04	0.954
Passing-Bablok				
Linear Regression**	1440	-0.08	1.13	0.964

In this evaluation, serum specimens tested ranged from 0.25 ng/mL to 5.83 ng/mL with the ARCHITECT Total T_3 assay and from 0.34 ng/mL to 5.19 ng/mL with the AxSYM Total T_3 assay.

* Representative data; variables such as differences in sampling size and sample population may impact 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.[23]

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
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

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