ARCHITECT

SYSTEM

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Free T_4

REF 7K65

48-9249/R3

B7K650

Read Highlighted Changes
Revised January, 2010

Free T_4

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

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.

Key to symbols used

REF	List Number	CAL 1	Calibrator (1, 2)
IVD	*In Vitro* Diagnostic Medical Device	SEPTUM	Septum
		SN	Serial Number
LOT	Lot Number	CONTROL L	Control Low, Medium, High (L, M, H)
	Expiration Date	SAMPLE CUPS	Sample Cups
2°C 8°C	Store at 2-8˚C	REAGENT LOT	Reagent Lot
		ASSAY CD-ROM	Assay CD-ROM
	Caution	REACTION VESSELS	Reaction Vessels
		REPLACEMENT CAPS	Replacement Caps
	Consult instructions for use	WARNING: SENSITIZER	Warning: May cause an allergic reaction
	Manufacturer	CONTAINS: AZIDE	Contains sodium azide. Contact with acids liberates very toxic gas.

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

Abbott

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 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 Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

In the first step, 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. After washing, T_3 acridinium labeled conjugate is added in the second step.

Pre-Trigger and Trigger Solutions are then added to the reaction mixture; the resulting chemiluminescent reaction is measured as relative light units (RLUs). An inverse relationship exists between the amount of Free T_4 in the sample and the RLUs detected by the ARCHITECT *i* optical system.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100 Tests/500 Tests

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

ARCHITECT Free T_4 Reagent Kit (7K65)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL/27.0 mL) anti-T_4 (sheep) coated Microparticles in TRIS buffer with sheep IgG stabilizers. Minimum Concentration: 0.08% solids. Preservative: antimicrobial agent.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL/26.3 mL) 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

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

NOTE: Bottle and volume varies based on order.

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

WARNINGS AND PRECAUTIONS

- **IVD**
- For *In Vitro* Diagnostic Use.
- 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.

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[23]. Biosafety Level 2[24] or other appropriate biosafety practices[25,26] should be used for materials that contain or are suspected of containing infectious agents.

The following warnings and precautions apply to this component:

- Conjugate

WARNING:	Contains methylisothiazolones.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapours / 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 soap and water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P363	Wash contaminated clothing before use.

This material and its container must be disposed of in a safe way.

- This product (the microparticles) contain sodium azide. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not mix reagents from different reagent kits.**
- Prior to loading the ARCHITECT Free T_4 Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that 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 which 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.

Storage Instructions

- The ARCHITECT Free T_4 Reagent Kit must be stored at 2-8°C and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT Free T_4 Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. 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.** After reagents are removed from the system, you must initiate a scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results may be invalid and may require retesting. 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 *i* System from the ARCHITECT *i* Assay CD-ROM prior to performing the assay. For detailed instructions on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.
- The default result unit for the ARCHITECT Free T_4 assay is ng/dL. An alternate result unit, pmol/L, may be selected for reporting results by editing assay parameter "Result concentration units", to pmol/L. The conversion factor used by the system is 12.87.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Human serum (including serum collected in serum separator tubes) or plasma collected in sodium heparin, lithium heparin (including lithium heparin plasma separator tubes), or potassium EDTA anticoagulant tubes may be used in the ARCHITECT Free T_4 assay. Other anticoagulants have not been validated for use with the ARCHITECT Free T_4 assay. Follow the manufacturer's processing instructions for serum or plasma collection tubes.
- When serial specimens are being evaluated, the same type of specimen should be used throughout the study.
- The ARCHITECT *i* System does not provide the capability to verify the specimen type. It is the responsibility of the operator to verify the correct specimen types are used in the ARCHITECT Free T_4 assay.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Do not use heat-inactivated specimens.
- For optimal results, inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- 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.
- 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. Specimens may be stored for up to 6 days at 2-8°C prior to being tested. 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.
- Multiple freeze-thaw cycles of specimens should be avoided. 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.
- When shipped, specimens must be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Prior to shipment, it is recommended that specimens be removed from the clot, serum separator or red blood cells.

PROCEDURE

Materials Provided:

- 7K65 ARCHITECT Free T_4 Reagent Kit

Materials Required but not Provided:

- ARCHITECT *i* System
- ARCHITECT *i* **ASSAY CD-ROM**
- 7K65-01 ARCHITECT Free T_4 Calibrators
- 7K65-10 ARCHITECT Free T_4 Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

Assay Procedure

- Before loading the ARCHITECT Free T_4 Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment:
  - 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.
  - Once the microparticles have been resuspended, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Carefully snap the septum onto the top of the bottle.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
- Order tests.
- Load the ARCHITECT Free T_4 Reagent Kit on the ARCHITECT *i* System. Verify that all necessary assay reagents are present. Ensure that septums are present on all reagent bottles.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation verify adequate sample cup volume is present prior to running the test.
  - Priority: 95 µL for the first Free T_4 test plus 45 µL for each additional Free T_4 test from the same sample cup.
  - ≤ 3 hours on board: 150 µL for the first Free T_4 test plus 45 µL for each additional Free T_4 test from the same sample cup.
  - > 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.
- ARCHITECT Free T_4 Calibrators and Controls should be mixed by gentle inversion prior to use.
- To obtain the recommended 150 µL volume requirements for the ARCHITECT Free T_4 Calibrators and Controls, hold the bottles **vertically** and dispense 4 drops of each calibrator or 4 drops of each control into each respective sample cup.
- Load samples
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN. The ARCHITECT *i* System performs the following function:
  - Moves the sample to the aspiration point
  - Loads a reaction vessel (RV) into the process path
  - Aspirates and transfers sample into the RV
  - Advances the RV one position and transfers microparticles into the RV
  - Mixes, incubates and washes the reaction mixture
  - Adds conjugate to the RV
  - Mixes, incubates and washes the reaction mixture
  - Adds Pre-Trigger and Trigger Solutions
  - Measures chemiluminescent emission to determine the quantity of Free T_4 in the sample
  - Aspirates contents of RV to liquid waste and unloads RV to solid waste
  - Calculates the result
- For information on ordering patient specimens and controls and general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Samples cannot be diluted for Free T_4 determinations. Samples which read > 6.00 ng/dL should be reported as such.

Calibration

- To perform an ARCHITECT Free T_4 calibration, test Calibrators 1 and 2 in duplicate. A single sample of all levels of Free T_4 controls must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the package insert. Calibrators should be priority loaded.
- Calibrator 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
  - 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 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 Free T_4 assay belongs to method group 6.

RESULTS

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

Alternate Result Units

- The default result unit for the ARCHITECT Free T_4 assay is ng/dL. When the alternate result unit, pmol/L, is selected, the conversion factor used by the system is 12.87.
- Conversion Formula:

  (Concentration in ng/dL) x (12.87) = Concentration in pmol/L.

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 Free 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 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	3.6
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.

Analytical Sensitivity

The ARCHITECT Free T_4 assay is designed to have an analytical sensitivity of ≤ 0.4 ng/dL.

Analytical sensitivity is defined as the concentration calculated as the mean plus two standard deviations of replicates of the ARCHITECT Free T_4 MasterCheck Level 0 (0.0 ng/dL). The analytical sensitivity (low-linearity) is defined in the ARCHITECT Free T_4 assay parameters as 0.4 ng/dL.

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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