Abbott AXSYM® SYSTEM

E

T-Uptake
REF 7A56
34-2990/R9

T-Uptake

Customer Service
United States: 1-877-4ABBOTT
International: Call your Abbott Representative

This package insert must be read carefully prior to product use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Note Changes Highlighted

Key to symbols used

- **REF** List Number
- **LOT** Lot Number
- **IVD** For *In Vitro* Diagnostic Use
- Expiration Date
- 2°C–8°C Store at 2-8°C
- **STANDARD CAL A** Standard Calibrator (A-F)
- **CONTROL L** Control Low, Medium, High (L, M, H)
- 15°C–30°C Store at 15-30°C
- **REAGENT PACK** Reagent Pack
- Consult instructions for use
- **CHECKSUM** Checksum
- **MASTER CAL 1** Master Calibrator (1, 2)
- **MASTER CALIBRATION BARCODE** Master Calibration Barcode
- **REACTION VESSELS** Reaction Vessels
- **EC REP** Authorized Representative
- **SAMPLE CUPS** Sample Cups
- **ASSAY NO.** Assay Number
- CE ABBOTT LABORATORIES Abbott Park, IL 60064 USA Legal Manufacturer

CE ABBOTT LABORATORIES Abbott Park, IL 60064 USA

EC REP ABBOTT
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580

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

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Diagnostics Division
Abbott Park, IL 60064 USA

Printed in USA

File: In Alms
Specific Plates: PMS 222 CVC
PMS 3165
Black
Editor: Linda
DTP: Robert, Brandon

NAME
T-Uptake

INTENDED USE
AxSYM T-Uptake is a Fluorescence Polarization Immunoassay (FPIA) for the quantitative determination of the total Thyroxine binding capacity in human serum or plasma. This assay is used in conjunction with Total T_4 to yield the Free Thyroxine Index (FTI), an indicator of thyroid function.

SUMMARY AND EXPLANATION OF THE TEST
The classical *in vitro* thyroid hormone "Uptake" assays measure the unsaturated thyroxine binding sites of serum proteins. The AxSYM T-Uptake assay measures the total binding capacity, that is, the total amount of binding proteins present in a sample. The thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3), are transported in serum bound to the thyroxine binding proteins, thyroxine binding globulin (TBG), thyroxine binding prealbumin (TBPA) and albumin. TBG, TBPA and albumin bind approximately 75%, 15% and 10% of the total circulating T_4 respectively, and bind 38%, 27% and 35% of T_3 respectively.[1] In a euthyroid patient, T_4 occupies approximately one-third of the binding sites.[2] Free, or unbound fractions of the thyroid hormones are thought to be responsible for biologic activity.[3,4] The Free Thyroxine Index (FTI) has been the most widely used method to estimate free T_4. Uptake assays are of greatest value when used in conjunction with a serum Total T_4 assay to provide the FTI.[5]

The Uptake assays are used to normalize the Total T_4 levels for variations in serum thyroxine binding protein (TBP) concentrations. Performing an Uptake assay and subsequent calculation of the FTI is important since certain conditions such as pregnancy, estrogen therapy, infectious and chronic active hepatitis, biliary cirrhosis or congenital disorders alter the number of T_4 binding sites.[6-8] These variations can produce abnormal T_4 values in an individual with no thyroid disease. Since the T_4 values or the T-Uptake value alone may give misleading information, an FTI can be calculated to provide a clinically useful and accurate estimate of circulating free thyroxine.[9-11] The FTI in conjunction with other thyroid function tests such as hTSH, and clinical evaluation by the physician should be determined to ensure maximum diagnostic accuracy of the thyroid status.

Since the AxSYM T-Uptake assay is a direct measurement of the total binding capacity in the human serum or plasma, a linear relationship is displayed which provides for both low and high end accuracy. This is not observed with the traditional T_3 Uptake assays, since they are non-linear relative to the TBP concentration.

AxSYM T-Uptake and $\%T_3$ Uptake both respond to variations in TBG concentration. Thus, the T-Uptake values can be mathematically converted to transformed %Uptake which show a general positive correlation with $\%T_3$ Uptake. However, since T-Uptake and $\%T_3$ Uptake do not measure the same exact phenomena, a direct conversion of units to transformed % is not possible and this % transformed value should be viewed as an approximation only.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE
AxSYM T-Uptake is based on Fluorescence Polarization Immunoassay (FPIA) technology.

The AxSYM T-Uptake Reagents and sample are pipetted in the following sequence:

SAMPLING CENTER
- Sample and all AxSYM T-Uptake reagents required for one test are pipetted by the Sampling Probe into various wells of a reaction vessel (RV).
- Sample and Line Diluent (Solution 4) are pipetted into one well of the RV.
- Aliquots of the predilution mixture and Pretreatment Solution are transferred to the cuvette of the RV.

The RV is immediately transferred into the Processing Center. Further pipetting is done in the Processing Center with the Processing Probe.

PROCESSING CENTER
- Additional aliquots of the predilution mixture and Pretreatment Solution are transferred to the cuvette along with the T_4 Fluorescein Tracer.
- T_4 Fluorescein Tracer binds to the sites on the thyroxine binding proteins.
- The intensity of polarized fluorescent light is measured by the FPIA optical assembly.

For further information, refer to the AxSYM System Operations Manual, Section 3.

REAGENTS
REAGENT PACK, 100 TESTS

AxSYM T-Uptake Reagent Pack (7A56-20)*

- 1 Bottle (9.4 mL) T_4 Fluorescein Tracer (<0.01%) in phosphate buffer containing surfactant and stabilizer. Preservative: Sodium Azide. (Reagent Bottle 1)
- 1 Bottle (14.1 mL) T-Uptake Pretreatment Solution. Surfactant in water containing an organic base. Preservative: Sodium Azide. (Reagent Bottle 3)

*7A56-99 includes an AxSYM T-Uptake Reagent Pack (100 Tests) and reaction vessels (100 each). 7A56-20 includes these items for International shipments.

CALIBRATORS
AxSYM T-Uptake Master Calibrators (7A56-30)

2 Bottles (4 mL each) of AxSYM T-Uptake Master Calibrators. Master Calibrator 1 contains phosphate buffer. Master Calibrator 2 contains sheep thyroxine antibody prepared in a phosphate buffered protein matrix (human, donor units nonreactive for HBsAg, HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2) at the following T-Uptake values:

Bottle	T-Uptake Unit
MASTER CAL 1	0.0
MASTER CAL 2	1.2

Preservative: Sodium Azide

AxSYM T-Uptake Standard Calibrators (7A56-01)

6 Bottles (4 mL each) of AxSYM T-Uptake Standard Calibrators. Standard Calibrator A contains phosphate buffer. Standard Calibrators B-F contain sheep thyroxine antibody prepared in a phosphate buffered protein matrix (human, donor units nonreactive for HBsAg, HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2) at the following T-Uptake values:

Bottle	T-Uptake Unit
STANDARD CAL A	0.0
STANDARD CAL B	0.4
STANDARD CAL C	0.8
STANDARD CAL D	1.2
STANDARD CAL E	1.6
STANDARD CAL F	2.0

Preservative: Sodium Azide

There is no internationally recognized standard for thyroxine binding capacity assays. Abbott has developed an internal reference method that generates a calibration curve designed to measure the binding capacity of serum for T_4. The linear response is based upon the millipolarization (mP) values obtained for a buffer with no binding capacity and a normal human serum pool, assigned a value of 1.0 T-Uptake unit (a dimensionless unit). Abbott maintains a set of internal rare primary calibrators, which represent different levels of T_4 binding capacity, and also T-Uptake ratios, less than and greater than the original normal pool. The kit calibrators are manufactured and signal matched at each level to the internal Abbott reference standards.

CONTROLS
AxSYM T-Uptake Controls (7A56-10)

3 Bottles (8 mL each) of AxSYM T-Uptake Controls contain sheep thyroxine antibody prepared in a phosphate buffered protein matrix (human, donor units nonreactive for HBsAg, HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2) to yield the following T-Uptake ranges:

Bottle	T-Uptake Unit	T-Uptake Unit Range
CONTROL L	0.5	0.41 - 0.59
CONTROL M	1.0	0.90 - 1.10
CONTROL H	1.5	1.35 - 1.65

Preservative: Sodium Azide.

The AxSYM T-Uptake reporting unit is factory set to T-Uptake Units. For alternate result unit, refer to the Conversion of AxSYM T-Uptake Units to %Uptake section in this package insert.

OTHER REAGENTS

Solution 4 (Line Diluent) (8A46)

SOLUTION 4 LINE DILUENT 1 Bottle (10 L) Solution 4 (Line Diluent) containing 0.1M Phosphate Buffer. Preservatives: Sodium Azide and Antimicrobial Agents.

AxSYM Probe Cleaning Solution (9A35-05)

PROBE CLEANING SOLUTION 2 Bottles (220 mL each) AxSYM Probe Cleaning Solution containing 2% Tetraethylammonium Hydroxide (TEAH).

WARNINGS AND PRECAUTIONS

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

SAFETY PRECAUTIONS

CAUTION: This product contains human sourced and/or potentially infectious components. For a specific listing, refer to the **REAGENTS** section of this package insert. Donor units of components sourced from human blood have been tested and found to be nonreactive for HBsAg, HIV-1 Ag, anti-HCV, and anti-HIV-1/HIV-2. 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.[12] Biosafety Level 2[13] or other appropriate biosafety practices[14,15] should be used for materials that contain or are suspected of containing infectious agents.

- The AxSYM Probe Cleaning Solution (2% TEAH) may cause mild eye irritation. If this solution comes in contact with eyes, rinse immediately with water. If irritation persists, seek medical attention.

Some components of this product contain Sodium Azide. For a specific listing, refer to the **REAGENTS** section of this package insert. The T_4 Fluorescein Tracer (Reagent Bottle 1), AxSYM T-Uptake Master and Standard Calibrators, AxSYM T-Uptake Controls, and Solution 4 (Line Diluent) are classified per applicable European Community (EC) Directives as: Harmful (Xn). The following are the appropriate Risk (R) and Safety (S) phrases.

R22 Harmful if swallowed.
R32 Contact with acids liberates very toxic gas.
S35 This material and its container must be disposed of in a safe way.
S36 Wear suitable protective clothing.
S46 If swallowed, seek medical advice immediately and show this container or label.

The AxSYM T-Uptake Pretreatment Solution (Reagent Bottle 3) containing Sodium Azide and Triethylenediamine is classified per applicable European Community (EC) Directives as: Harmful (Xn). The following are the appropriate Risk (R) and Safety (S) phrases.

R22 Harmful if swallowed.
R32 Contact with acids liberates very toxic gas.
R36/38 Irritating to eyes and skin.
S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
S35 This material and its container must be disposed of in a safe way.
S36 Wear suitable protective clothing.
S46 If swallowed, seek medical advice immediately and show this container or label.

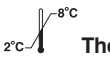
Information for European customers: For product not classified as dangerous per European Directive 1999/45/EC - Safety data sheet available for professional user on request.

HANDLING PRECAUTIONS

- Do not use Reagent Pack beyond the expiration date or a maximum of 336 cumulative hours on-board the AxSYM System.
- Do not mix reagents from different reagent packs.

Refer to the AxSYM System Operations Manual, Sections 7 and 8, for a more detailed discussion of the safety and handling precautions during system operation.

STORAGE INSTRUCTIONS

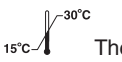


The AxSYM T-Uptake Reagents are light sensitive. When the AxSYM T-Uptake Reagent Pack is not on-board the AxSYM System, the reagent pack must be stored protected from light.

The AxSYM T-Uptake Reagent Pack must be stored at 2-8°C (do not freeze). The AxSYM T-Uptake Calibrators and Controls must be stored at 2-8°C. The AxSYM T-Uptake Reagent Pack, Calibrators and Controls may be used immediately after removing them from the refrigerator. Calibrators and Controls should be returned to 2-8°C storage immediately after use.

Reagents are stable until the expiration date when stored and handled as directed.

The AxSYM T-Uptake Reagent Pack may be on-board the AxSYM System for a maximum of 336 cumulative hours; for example, 42 eight hour shifts. After 336 hours the reagent pack must be discarded. Refer to the AxSYM System Operations Manual, Sections 2, 5 and Appendices, for further information on tracking on-board time.



The AxSYM Probe Cleaning Solution and Solution 4 (Line Diluent) must be stored at 15-30°C.

INSTRUMENT PROCEDURE

Assay File Installation

The AxSYM T-Uptake assay file must be installed on the AxSYM System from one of the following software disks, prior to performing T-Uptake assays:

- 2G37-01, or higher

Refer to the AxSYM System Operations Manual, Section 2, for proper installation procedures.

Note: AxSYM T-Uptake Assay must be run with AxSYM System software version 3.60 or higher.

AxSYM T-Uptake Assay Parameters

The default values for the visible assay parameters used for the AxSYM T-Uptake assay are listed below. Assay parameters that can be edited contain a (>) symbol. These parameters can be displayed and edited according to the procedure in the AxSYM System Operations Manual, Section 2. However, some parameters that contain a (>) symbol may not be editable if there are no additional options. In order to obtain values for the parameters with an asterisk (*), review the specific Assay Parameter screen. Press PRINT to print the assay parameters.

Assay Parameters	
1	Long Assay Name (English): T-Uptake
6	Abbrev Assay Name (English): T-Uptake
11	Assay Number: 253
12	Assay Version: *
13	Calibration Version: *
14	Assay File Revision: *
15	Assay Enabled > ON
17	Assay Type: FPIA
18	Standard Cal Reps > 2
19	Master Cal Reps > 2
21	Cal A Concentration: 0.00
22	Cal B Concentration: 0.40
23	Cal C Concentration: 0.80
24	Cal D Concentration: 1.20
25	Cal E Concentration: 1.60
26	Cal F Concentration: 2.00
27	Master Calibrator 1 Concentration: 0.00
28	Master Calibrator 2 Concentration: 1.20
43	Default Dilution Protocol > UNDILUTED
44	Default Calibration Method > Standard Cal
45	Selected Result Concentration Units > Uptake
46	Selected Result Decimal Places > 2
62	Blank I-Max background intensity: *
63	Min Tracer-Min net intensity: *
73	Low Limit-Normal/Therapeutic Range lower limit > 0.00
74	High Limit-Normal/Therapeutic Range upper limit > 0.00
75	Low Extreme Value > 0.10
76	High Extreme Value > 99999.99
77	Lo Norm-% Uptake Normal Range Low > 0.0000
78	Hi Norm-% Uptake Normal Range High > 99999.9900
91	Low Range Neat: *
92	High Range Neat: *

NOTE: Parameter 45 can be edited to the alternate result unit (%Uptake).

Values associated with the Low and High Extreme flags, Assay Parameters #75 and 76, are assay specific and should not be edited.

We recommend that you set General Configuration Parameters Release Mode to the "Manual" or "Hold" Release Mode to ensure that all flagged results are reviewed prior to reporting assay results. Refer to the AxSYM System Operations Manual, Section 2, for a detailed description of Instrument Procedures. If General Configuration Parameter Release Mode is configured in the "Automatic" Release Mode, ensure that all flagged results are reviewed prior to reporting assay results.

Retest Rules

For details on Automatic Sample Retest Configuration refer to the AxSYM System Operations Manual, Section 2, Installation Procedures and Special Requirements.

If reporting results in the alternate result unit, %Uptake, the Retest Min. Limit and the Retest Max. Limit values must be inverted due to the inverse relationship to T-Uptake units.

Example	Retest Range:	55.00-78.00
	Retest Min. Limit:	78.00
	Retest Max. Limit:	55.00

SAMPLE COLLECTION AND PREPARATION FOR ANALYSIS

- Serum (including serum collected in separator tubes) or plasma (collected in sodium heparin or tripotassium EDTA) may be used in the AxSYM T-Uptake Assay. Follow the manufacturer's processing instructions for serum or plasma collection tubes.
- The AxSYM System does not provide the capability of verifying sample type. It is the responsibility of the operator to verify the correct sample types are used in the T-Uptake assay.
- Ensure that complete clot formation has taken place prior to centrifugation. Some samples, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the sample is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.
- For optimal results, samples should be free of fibrin, red blood cells or other particulate matter.
- Patient samples should be mixed and centrifuged after any freeze-thaw cycle or to remove red cells or particulate matter.
- Multiple freeze-thaw cycles should be avoided. Samples must be mixed thoroughly after thawing, by LOW speed vortexing or by gently inverting, and centrifuged prior to use to remove particulate matter and to ensure consistency in the results.
- Samples may be stored for up to 24 hours at 2-8°C prior to being tested. If testing will be delayed more than 24 hours, serum or plasma should be separated from the clot or red blood cells and stored frozen (-10°C or colder). Samples stored frozen at -10°C or colder for 12 months showed no performance difference.
- To minimize the effects of evaporation, all samples (patient samples, controls and calibrators) should be tested within 3 hours of being placed on-board the AxSYM System. Refer to the AxSYM System Operations Manual, Section 5, for a more detailed discussion of on-board sample storage constraints.
- Inspect all samples for bubbles. Remove bubbles prior to analysis.
- When shipped, samples must be packaged and labeled in compliance with applicable federal and international regulations covering the transport of clinical samples and etiologic agents.

SAMPLE VOLUME

The sample volume required to perform a single undiluted T-Uptake test on the AxSYM System varies depending on the type of sample container used. For sample cups, a ROUTINE test requires 150 µL and a STAT test requires 94 µL. For every additional T-Uptake test performed (ROUTINE or STAT) from the same container, an additional 44 µL of sample is required.

The sample cup minimum volumes for both STAT and ROUTINE tests are calculated by the AxSYM System. It is displayed on the Order screen at the time the test(s) is (are) ordered. The STAT sample cup minimum volume is printed on the Orderlist Report. When using Host Query, the Order screen information and Orderlist report are not available. Refer to the AxSYM System Operations Manual, Section 5: Ordering Patient Samples, for a description of the Host Order Query option.

If the assay is configured for auto retest the additional sample volume needed for the retest will not be displayed on the order screen at the time the test(s) is (are) ordered. Therefore, the total sample volume should include the additional 44 µL of sample.

To obtain the recommended volume requirements for AxSYM T-Uptake 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.

Refer to the AxSYM System Operations Manual, Section 5, for sample volume requirements in primary or aliquot tubes and calibrator/control volume requirements for multiple reagent lots.

AxSYM T-UPTAKE PROCEDURE

Materials Provided

- 7A56-99 — AxSYM T-Uptake Reagent Kit, containing:
  AxSYM T-Uptake REAGENT PACK
  100 REACTION VESSELS

Materials Required But Not Provided

- AxSYM System
- 7A56-10 — AxSYM T-Uptake Controls
- 7A56-01 — AxSYM T-Uptake Standard Calibrators or
- 7A56-30 — AxSYM T-Uptake Master Calibrators
- 8A46 — SOLUTION 4 LINE DILUENT
- 9A35-05 — AxSYM PROBE CLEANING SOLUTION
- 8A76-01 — SAMPLE CUPS
- Pipettes/pipette tips (optional) to deliver the volumes specified on the Order screen.

CAUTION:

- When manually dispensing sample into sample cups, verify that the dispensing equipment does not introduce cross contamination and delivers the specified sample volume.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the AxSYM System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

Assay Procedure

Sections 5 and 6 of the AxSYM System Operations Manual contain detailed steps for performing assay calibration and sample testing procedures.

Prior to ordering tests, confirm that the System inventory of bulk solutions and waste levels are acceptable.

The Orderlist Report contains sample placement information and sample cup volume requirements for all ordered tests. It is recommended that this report be referenced when loading samples into sample segments.

CAUTION: When operating the AxSYM System, always observe the following:

- The System status must be WARMING, PAUSED, READY or STOPPED before adding or removing sample segments, reagent packs or reaction vessels (RVs).
- When performing only FPIA assays, the instrument homes all motors and may display "Error Code 5066 Matrix cell not detected, trap door, processing center". Select OK to proceed with testing the FPIA assays.
- Do not open the Interior Waste Door or the AxSYM Processing Center Cover while any test is in process. If opened, all processing will stop. Tests in process will be terminated and must be repeated.
- When testing is completed, it is recommended that samples and the AxSYM T-Uptake Reagent Pack are removed from the Sampling Center to maximize the on-board reagent pack use. Store at 2-8°C.

SAMPLE DILUTION PROCEDURES

Specimens with a T-Uptake value exceeding 2.0 are flagged with the code ">2.0". The test result should be reported as "greater than 2.0", since an accurate result cannot be determined by diluting the sample.

FTI PROCEDURE

The AxSYM System can ***automatically*** calculate FTI values for test samples when AxSYM Total T_4 and AxSYM T-Uptake are ordered on the same sample at the same time. The FTI Value is calculated and printed with the Total T_4 and T-Uptake results, for the specific specimen.

FTI System Configuration

The following steps configure the AxSYM System to calculate FTI values.

1. Ensure that AxSYM Total T_4, AxSYM T-Uptake and FTI are installed and enabled on your AxSYM. The FTI file is located on the AxSYM T-Uptake assay disk. Refer to the AxSYM System Operations Manual, Section 2, for the Assay Installation procedure.
2. Ensure that Active assay calibration curves are stored on the system for the AxSYM Total T_4 and AxSYM T-Uptake assays.
3. Enable the FTI Ratio calculation. Refer to the AxSYM System Operations Manual, Section 2, for the Ratio Configuration procedure. When the Configuration/Ratio screen is displayed, select the FTI ratio option and **one** of the following formulas:
   - Ratio Disabled
   - $\dfrac{\text{Total } T_4}{\text{T-Uptake Unit}}$
   - Total T_4 x %Uptake
   - $\dfrac{\text{Total } T_4 \text{ x \%Uptake}}{100\%}$

NOTE: When activating the FTI ratio calculation, **a formula must be selected which uses units that are consistent with the result units currently selected for the AxSYM T-Uptake Assay.**

4. Select F6 - SAVE to update the system with the selection. To turn off the FTI option calculation, select "Ratio Disabled."

Once the FTI Ratio is configured, AxSYM Total T_4 and AxSYM T-Uptake Assays must be ordered at the same time from the same sample to obtain an FTI ratio calculation.

As the Total T_4 and T-Uptake assays are completed, the FTI value will automatically be calculated and reported with the Total T_4 and T-Uptake results.

The AxSYM T-Uptake Assay better compensates for extreme thyroxine binding protein levels than a converted T_3 Uptake value. Therefore, the T-Uptake Unit derived FTI calculation may have better clinical utility, in situations of abnormally low or high thyroxine binding protein levels, than FTI values derived using transformed %Uptake values.

QUALITY CONTROL PROCEDURES

CALIBRATION

The AxSYM T-Uptake Assay must be calibrated using either a Master Calibration (2-point), or a Standard Calibration (6-point) procedure. The use of a particular calibration procedure is dependent on individual laboratory policy.

Master Calibration

Each AxSYM T-Uptake Reagent Pack is shipped with a bar coded label "insert" that contains the Master Curve information for that specific lot of reagent. When using a lot number for the first time, the bar coded Master Curve information must be entered into the AxSYM System. Refer to the AxSYM System Operations Manual, Section 6, for additional information on entering Master Curve bar codes. Once this bar code information is entered, a Master Calibration must be performed.

To perform an AxSYM T-Uptake Master Calibration, test Master Calibrators 1 and 2 in duplicate. A single sample of all levels of T-Uptake controls must be tested as a means of evaluating the assay calibration.

Standard Calibration

The Standard Calibration procedure may be used without prior entry of the bar coded Master Curve information. To perform an AxSYM T-Uptake Standard Calibration, test Standard Calibrators A, B, C, D, E, and F in duplicate. A single sample of all levels of T-Uptake controls must be tested as a means of evaluating the assay calibration.

Once the AxSYM T-Uptake calibration is accepted and stored, all subsequent samples may be tested without further calibration. Calibration is required once a reagent pack with a new lot number is placed on-board the system.

Refer to the AxSYM System Operations Manual, Section 6, for:

- Setting up an assay calibration
- When recalibration may be necessary
- Calibration verification

The AxSYM System verifies the results of an assay calibration meet the specifications assigned to selected validity parameters. An error message occurs when the calibration fails to meet a specification. Refer to the AxSYM System Operations Manual, Section 10, for an explanation of the corrective actions for the error code. Refer to the AxSYM System Operations Manual, Appendices, for an explanation of the calibration validity parameters that may be used by the AxSYM System.

QUALITY CONTROL

The recommended control requirement for an AxSYM T-Uptake Assay is a single sample of all T-Uptake control levels tested once every 24 hours each day of use. Controls may be placed in any position in the Sample Carousel.

If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow those procedures.

To achieve maximum on-board reagent stability more frequent use of controls may be required to monitor reagent performance with the same lot.

Ensure that assay control values are within the concentration ranges specified in the package insert. Refer to the **REAGENTS**, CONTROLS section of this package insert for AxSYM T-Uptake Control ranges.

Control Configuration

For details on Control Configuration refer to the AxSYM System Operations Manual, Section 2, Installation Procedures and Special Requirements.

If reporting results in the alternate result unit, %Uptake, the minimum and maximum values must be inverted due to the inverse relationship to T-Uptake units. All editable ranges must be within the dynamic range of the assay.

Example	Control Range Configuring:	57.83-69.16
	Minimum Value:	69.16
	Maximum Value:	57.83
	Expected S.D.	2.84
	Control Mean:	63.50

INDICATIONS OF INSTABILITY OR DETERIORATION OF REAGENTS

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 require retesting. Assay recalibration may be indicated. Refer to the AxSYM System Operations Manual, Section 10, Subsection: Observed Problems, for further troubleshooting information.

The AxSYM System has a capability to generate a Levey-Jennings plot of each assay's quality control performance. Refer to the AxSYM System Operations Manual, Section 5. At the discretion of the laboratory, selected quality control rules may be applied to the quality control data.

RESULTS

AxSYM T-Uptake utilizes a linear least squares regression to generate a Standard Calibration curve and a Linear Transformation to generate the instrument-specific Master Calibration.

To review the protocol for the calculation of the Free Thyroxine Index (FTI) values, refer to FTI PROCEDURE section in this package insert.

Alternate Result Units

The default result unit for AxSYM T-Uptake is T-Uptake Units. When selecting the alternate result unit, %Uptake, follow the conversion procedure in the following section.

Conversion of AxSYM T-Uptake Units to %Uptake

The AxSYM System is programmed to provide the AxSYM T-Uptake values in T-Uptake units. T-Uptake units are the suggested way to report the AxSYM T-Uptake values. This suggestion is based on the ability of the T-Uptake unit to better compensate for extremes in thyroxine binding protein levels than classical %Uptake calculations. T-Uptake values are unitless numbers which are referenced to a normal T-Uptake value of 1.0.

The AxSYM System provides an option for transforming the T-Uptake units into %Uptake equivalents. This mathematical transformation can be used since both T-Uptake and T_3 Uptake by radioimmunoassay measure changes in TBG concentration. However, since T-Uptake and %T_3 Uptake do not measure the same exact phenomena, a direct conversion of units to % transformed is not possible and this % transformed value should be viewed as an approximation only.

To select for the conversion of T-Uptake units to %Uptake values, you must EDIT the following assay parameters:

1. The LO NORM and HI NORM values are used to obtain a mean normal that is factored into the transformation equation.
   - LO NORM, assay parameter 77, Lower limit value of your reference radioimmunoassay T_3 Uptake normal range
   - HI NORM, assay parameter 78, Upper limit value of your reference radioimmunoassay T_3 Uptake normal range

This transformation, which is based on the following equation, is automatically performed by the AxSYM System.

$$\text{Transformed \%Uptake} = \frac{\text{*MEAN NORMAL RANGE}}{\sqrt{0.8(T-U)^2 + 0.2}}$$

$$\text{*MEAN NORMAL RANGE (Reference } T_3 \text{ Uptake)} = \frac{\text{LO NORM + HIGH NORM}}{2}$$

NOTE: If you are reporting the results in the AxSYM T-Uptake units **only**, the LO NORM, assay parameter 77 and HI NORM, assay parameter 78 will not need to be edited. The LO NORM and HI NORM should remain at the default values of "0.0000" and "99999.9900", respectively.

2. To convert T-Uptake units to the transformed %Uptake equivalent, assay parameter 45 must be edited to the alternate result unit (%Uptake).

NOTE: To ensure consistency, please report all proficiency testing results in T-Uptake units. Refer to the EXPECTED VALUES section in this package insert.

3. The transformed %Uptake values may differ from measured T_3 Uptake values on a given specimen for a number of reasons:
   - The two assays measure different parameters of Thyroxine Binding Proteins:
     T-Uptake - Total binding protein.
     T_3 Uptake - Unsaturated binding protein.
   - T-Uptake levels for Hypothyroid and Hyperthyroid subjects are generally within the normal range.
   - T_3 Uptake is sensitive not only to binding protein concentration, but also T_4 concentration.

Flags

Some results may contain information in the Flags field. **Samples flagged as low extreme values (LL), Assay Parameter #75, must be reviewed prior to reporting assay results.** For a description of the flags that may appear in this field, refer to the AxSYM System Operations Manual, Section 1.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, the AxSYM T-Uptake values should be used in conjunction with a T_4 determination to yield a Free Thyroxine Index (FTI).
- Performance of this assay has not been established with neonatal specimens.
- Samples which contain high levels of fatty acids will give correct results by this procedure, but may not correlate well with results from radioactive T_3 Uptake methods, which have a fatty acid interference.[2]
- The T-Uptake underestimates its binding capacity in patients with inherited absence of TBG and in patients with Familial Dysalbuminemic Hyperthyroxinemia (FDH).

Refer to the **SAMPLE COLLECTION AND PREPARATION FOR ANALYSIS** section in this package insert.

EXPECTED VALUES

AxSYM T-Uptake results are expressed in unitless numbers which represent ratios relative to a normal value. The suggested normal range for AxSYM T-Uptake is 0.66-1.27 T-Uptake Units. This range (central 95%) represents the T-Uptake values obtained by testing serum specimens from 511 apparently healthy individuals. It is recommended that each laboratory establish its own normal range.

Women who are pregnant or taking oral contraceptives can be expected to have elevated T-Uptake values. Individuals with low serum TBG levels will tend to have a lower T-Uptake value than normal.[7-9]

NOTE: PROFICIENCY TESTING RESULTS

To ensure consistency, all Proficiency testing results should be reported in T-Uptake units. Do not report Transformed %Uptake values because reference ranges differ between laboratories and will not accurately reflect inter-laboratory variation.

THE FTI VALUE

The suggested normal range for AxSYM FTI (T_4/T-Uptake Units) is 6.33-12.40 µg/dL. This range (central 95%) represents the FTI values obtained by testing serum specimens from 511 apparently healthy individuals.

Due to potential differences in the methods of calculation, the FTI normal ranges may vary for different methodologies. It is recommended that each laboratory establish its own normal range.

SPECIFIC PERFORMANCE CHARACTERISTICS

PRECISION

Precision was determined as described in National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-T2.[16] A three member phosphate buffered protein based panel was assayed, using a single lot of reagents and a single calibration per instrument, in replicates of 2 at two separate times per day for twenty days. Data from this study are summarized in the following table.

PANEL MEMBER 1

Inst.	Mean Conc. Value (T-Uptake Units)	n	Within Run S.D.	Within Run CV(%)	Between Run S.D.	Between Run CV(%)	Between Day S.D.	Between Day CV(%)	Total Run S.D.	Total Run CV(%)
1	0.50	80	0.013	2.66	0.017	3.38	0.000	0.00	0.022	4.30
2	0.48	80	0.020	4.10	0.004	0.90	0.000	0.00	0.020	4.20
3	0.49	80	0.018	3.58	0.013	2.68	0.000	0.00	0.022	4.48
4	0.49	80	0.022	4.46	0.000	0.00	0.000	0.00	0.022	4.46

PANEL MEMBER 2

Inst.	Mean Conc. Value (T-Uptake Units)	n	Within Run S.D.	Within Run CV(%)	Between Run S.D.	Between Run CV(%)	Between Day S.D.	Between Day CV(%)	Total Run S.D.	Total Run CV(%)
1	0.98	80	0.019	1.89	0.008	0.85	0.005	0.54	0.021	2.14
2	0.94	80	0.019	2.05	0.000	0.00	0.009	0.97	0.021	2.27
3	0.97	80	0.016	1.70	0.014	1.42	0.000	0.00	0.021	2.21
4	0.95	80	0.019	1.98	0.000	0.00	0.007	0.75	0.020	2.12

PANEL MEMBER 3

Inst.	Mean Conc. Value (T-Uptake Units)	n	Within Run S.D.	Within Run CV(%)	Between Run S.D.	Between Run CV(%)	Between Day S.D.	Between Day CV(%)	Total Run S.D.	Total Run CV(%)
1	1.48	80	0.017	1.17	0.000	0.00	0.015	0.98	0.023	1.53
2	1.45	80	0.021	1.48	0.000	0.00	0.005	0.32	0.022	1.51
3	1.47	80	0.015	1.04	0.011	0.73	0.000	0.00	0.019	1.27
4	1.46	80	0.016	1.10	0.000	0.00	0.008	0.54	0.018	1.23

SPECIFICITY

The tracer binds to thyroxine binding globulin (TBG) with a relative polarization signal vs. albumin of about 21,500 to 1 on a molar basis. At normal serum concentrations of these proteins, the T-Uptake value is primarily due to TBG binding with a small contribution from albumin. Tracer will also bind to thyroxine antiserum, such as the type used in the T-Uptake calibrators. The affinity for tracer and the resulting polarization signal will vary for different antiserum. Occasionally, a patient serum will contain a high enough titer of thyroxine antibody to bind tracer.

INTERFERENCE

The AxSYM T-Uptake assay demonstrated the stated interference in the presence of the following:

- Bilirubin - <10% interference at 15 mg/dL
- Hemoglobin - <5% interference at 1.0 g/dL
- Cholesterol - <5% interference at 330 mg/dL
- Triglycerides - <10% interference at 1500 mg/dL
- Separator (SST), sodium heparin, tripotassium EDTA anticoagulants - <10% interference

ACCURACY BY CORRELATION

The AxSYM T-Uptake assay was compared to a commercially available diagnostic kit. The results of the specimen testing are shown in the following table.

Manufacturer	Number of Observations	Intercept	Slope	Correlation Coefficient
Abbott AxSYM T-Uptake vs. Abbott TDx® T-Uptake	a) 310	-0.01	0.98	0.98
Abbott AxSYM T-Uptake vs. Abbott IMx® T-Uptake	b) 1446	0.01	0.96	0.98

In this evaluation, serum samples tested a) ranged from 0.58 to 1.72 T-Uptake Units and b) ranged from 0 to 1.94 T-Uptake Units by AxSYM T-Uptake.

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