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T3

cobas®

Triiodothyronine

REF	Σ	SYSTEM
11731360 122	200	Elecsys 2010 MODULAR ANALYTICS E170 **cobas e** 411 **cobas e** 601 **cobas e** 602

English

Intended use

Immunoassay for the in vitro quantitative determination of total triiodothyronine in human serum and plasma.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on Elecsys and **cobas e** immunoassay analyzers.

Summary

Triiodothyronine (T3) is the hormone principally responsible for the development of the effects of the thyroid hormones on the various target organs.

T3 (3,5,3'-triiodothyronine) is mainly formed extrathyroidally, particularly in the liver, by enzymatic 5'-deiodination of T4. Accordingly, the T3 concentration in serum is more a reflection of the functional state of the peripheral tissue than the secretory performance of the thyroid gland.

A reduction in the conversion of T4 to T3 results in a decrease in the T3 concentration. It occurs under the influence of medicaments such as propranolol, glucocorticoids or amiodarone and in severe non-thyroidal illness (NTI), and is referred to as "low T3 syndrome". As with T4, over 99 % of T3 is bound to transport proteins. However, the affinity of T3 to them is around 10-fold lower.[1,2,3,4]

The determination of T3 is utilized in the diagnosis of T3-hyperthyroidism, the detection of early stages of hyperthyroidism and for indicating a diagnosis of thyrotoxicosis factitia.[5,6,7]

The Elecsys T3 assay employs a competitive test principle with polyclonal antibodies specifically directed against T3. Endogenous T3, released by the action of 8-anilino-1-naphthalene sulfonic acid (ANS), competes with the added biotinylated T3-derivative for the binding sites on the antibodies labeled with the ruthenium complex[a)].

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

Test principle

Competition principle. Total duration of assay: 18 minutes.

- 1st incubation: 30 µL of sample and a T3-specific antibody labeled with a ruthenium complex; bound T3 is released from the binding proteins in the sample by ANS.
- 2nd incubation: After addition of streptavidin-coated microparticles and biotinylated T3, the still-free binding sites of the labeled antibody become occupied, with formation of an antibody-hapten complex. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

Reagents - working solutions

The reagent rackpack is labeled as T3.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 12 mL:

Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-T3-Ab~$Ru(bpy)_3^{2+}$ (gray cap), 1 bottle, 16 mL:

Polyclonal anti-T3-antibody (sheep) labeled with ruthenium complex 75 ng/mL; ANS 0.8 mg/mL; phosphate buffer 100 mmol/L, pH 7.4; preservative.

R2 T3~biotin (black cap), 1 bottle, 16 mL:

Biotinylated T3 3 ng/mL; ANS 0.8 mg/mL; phosphate buffer 100 mmol/L, pH 7.4; preservative.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.

All information required for correct operation is read in from the respective reagent barcodes.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the analyzers	8 weeks

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-, Na-, NH_4^+-heparin, K_3-EDTA, sodium citrate and sodium fluoride/potassium oxalate plasma.

Criterion: Recovery within 90-110 % of serum value or slope 0.9-1.1 + intercept within < ± 2x analytical sensitivity (LDL) + coefficient of correlation > 0.95.

Stable for 7 days at 2-8 °C, 1 month at -20 °C.[4] Freeze only once.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- REF 11731548122, T3 CalSet, for 4 x 1 mL

- REF 11731416190, PreciControl Universal, for 2 x 3 mL each of PreciControl Universal 1 and 2
- REF 11731416160, PreciControl Universal, for 2 x 3 mL each of PreciControl Universal 1 and 2 (for USA)
- General laboratory equipment
- Elecsys 2010, MODULAR ANALYTICS E170 or **cobas e** analyzer

Accessories for Elecsys 2010 and **cobas e** 411 analyzers:

- REF 11662988122, ProCell, 6 x 380 mL system buffer
- REF 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- REF 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- REF 11933159001, Adapter for SysClean
- REF 11706802001, Elecsys 2010 AssayCup, 60 x 60 reaction vessels
- REF 11706799001, Elecsys 2010 AssayTip, 30 x 120 pipette tips

Accessories for MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers:

- REF 04880340190, ProCell M, 2 x 2 L system buffer
- REF 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- REF 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- REF 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- REF 12102137001, AssayTip/AssayCup Combimagazine M, 48 magazines x 84 reaction vessels or pipette tips, waste bags
- REF 03023150001, WasteLiner, waste bags
- REF 03027651001, SysClean Adapter M

Accessories for all analyzers:

- REF 11298500316, Elecsys SysClean, 5 x 100 mL system cleaning solution
- REF 11298500160, Elecsys SysClean, 5 x 100 mL system cleaning solution (for USA)

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibration

Traceability: This method has been standardized against reference standards by weighing T3 into analyte-free human serum matrix.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows:

- after 8 weeks when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl Universal.

In addition, other suitable control material can be used.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

The analyzer automatically calculates the analyte concentration of each sample (either in nmol/L, ng/mL or ng/dL).

Conversion factors:	nmol/L x 0.651 = ng/mL
	nmol/L x 65.09998 = ng/dL
	ng/mL x 1.536 = nmol/L

Limitations - interference

The assay is unaffected by icterus (bilirubin < 599 µmol/L or < 35 mg/dL), hemolysis (Hb < 1.2 mmol/L or < 2.0 g/dL), lipemia (Intralipid < 1800 mg/dL) and biotin (< 40.9 nmol/L or < 10 ng/mL).

Criterion: Recovery within ± 10 % of initial value.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL and samples from dialysis patients.

In vitro tests were performed on 26 commonly used pharmaceuticals. No interference with the assay was found.

Therapy with amiodarone can lead to depressed T3 values.

Phenytoin, phenylbutazone, and salicylates cause release of T3 from the binding proteins, thus leading to a reduction in the total T3 hormone level at normal fT3 levels.[8]

Autoantibodies to thyroid hormones can interfere with the assay.

Binding protein anomalies seen with FDH (familial dysalbuminemic hyperthyroxinemia), for example, may cause values which, while characteristic of the condition, deviate from the expected results.[9]

Pathological concentrations of binding proteins (TBG, albumin) can lead to total T3 values outside the normal range being found despite a euthyroid metabolic state (e.g. in NTI[b)]-patients, pregnancy, use of oral contraceptives). In such cases a fT3 or fT4 determination is indicated.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

b) NTI = non thyroidal illness

Limits and ranges

Measuring range

0.300-10.0 nmol/L or 0.195-6.51 ng/mL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.300 nmol/L or < 0.195 ng/mL. Values above the measuring range are reported as > 10.0 nmol/L or > 6.51 ng/mL.

Lower limits of measurement

Lower detection limit of the test

Lower detection limit: 0.300 nmol/L or 0.195 ng/mL

The lower detection limit represents the lowest analyte level that can be distinguished from 0.

Dilution

Not necessary due to the broad measuring range.

Expected values

1.3-3.1 nmol/L or 0.8-2.0 ng/mL: euthyroid

The values correspond to the 2.5th and 97.5th percentiles of findings from a total of 514 healthy test subjects.

Status: MCE Elecsys 2010, status 1996, verified 1st quarter 1998

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For detailed information about reference intervals in children, adolescents and pregnant women, refer to the brochure "Reference Intervals for Children and Adults", English: REF 04640292, German: REF 04625889.

This booklet also contains results of a detailed study about influencing factors on thyroid parameters in a well characterized reference group of adults. Different inclusion and exclusion criteria were applied (e.g. sonographic results (thyroid volume and density) as well as criteria according to the guidelines of the National Academy of Clinical Biochemistry - NACB).

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, pooled human sera, and controls in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days (n = 60); repeatability on MODULAR ANALYTICS E170 analyzer, n = 21. The following results were obtained:

Elecsys 2010 and **cobas e** 411 analyzers								
			Repeatability			**Intermediate precision**		
Sample	Mean		SD		CV	SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%	nmol/L	ng/mL	%
HS[c)] 1	1.22	0.79	0.04	0.03	3.6	0.07	0.05	5.4
HS 2	2.87	1.87	0.12	0.08	4.2	0.14	0.09	4.7
HS 3	5.09	3.31	0.27	0.18	5.3	0.27	0.18	5.4
PC U[d)]1	2.12	1.38	0.09	0.06	4.1	0.10	0.07	4.8
PC U2	6.31	4.11	0.22	0.14	3.5	0.26	0.17	4.1

c) HS = human serum

d) PC U = PreciControl Universal

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers					
	Repeatability				
Sample	Mean		SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%
HS 1	1.19	0.77	0.04	0.02	3.1
HS 2	2.16	1.41	0.05	0.03	2.2
HS 3	6.83	4.45	0.11	0.07	1.5
PC U1	2.36	1.54	0.03	0.02	1.3
PC U2	5.83	3.79	0.07	0.05	1.3

MODULAR ANALYTICS E170, **cobas e** 601 and **cobas e** 602 analyzers					
	Intermediate precision				
Sample	Mean		SD		CV
	nmol/L	ng/mL	nmol/L	ng/mL	%
HS 1	1.24	0.80	0.06	0.04	4.5
HS 2	2.28	1.49	0.08	0.05	3.4
HS 3	7.08	4.61	0.26	0.17	3.7
PC U1	2.42	1.58	0.08	0.05	3.4
PC U2	5.81	3.78	0.20	0.13	3.4

Method comparison

A comparison of the Elecsys T3 assay (y) with the Enzymun-Test T3 method (x) using clinical samples gave the following correlations (nmol/L):

Number of samples measured: 300

Passing/Bablok[10]	Linear regression
y = 1.26x - 0.56	y = 1.18x - 0.35
τ = 0.754	r = 0.957

The sample concentrations were between approximately 0.5 and 9 nmol/L (0.3 and 5.9 ng/mL).

Analytical specificity

For the antibody derivative used, the following cross-reactivities were found:

D-T3 100 %; L-T4 < 0.16 %; D-T4 < 0.16 %; L-rT3 < 0.04 %; L-T2 < 1.0 %; 3,3',5-triiodothyroacetic acid 106 %; 3,3',5,5'-tetraiodothyroacetic acid < 0.01 %.

References

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For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information and the Method Sheets of all necessary components (if available in your country).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume after reconstitution or mixing

T3

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