

REF



SYSTEM

07026919190

07026919500

300

cobas e 801

English

System information

Short name	ACN (application code number)
ATG	10065

Please note

The measured anti-Tg value of a patient's sample can vary depending on the testing procedure used. The laboratory finding must therefore always contain a statement on the anti-Tg assay method used. Anti-Tg values determined on patient samples by different testing procedures cannot be directly compared with one another and could be the cause of erroneous medical interpretations. If there is a change in the anti-Tg assay procedure used while monitoring therapy, then the anti-Tg values obtained upon changing over to the new procedure must be confirmed by parallel measurements with both methods.

Intended use

Immunoassay for the in vitro quantitative determination of antibodies to thyroglobulin in human serum and plasma. The anti-Tg determination is used as an aid in the detection of autoimmune thyroid diseases.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the **cobas e 801** immunoassay analyzer.

Summary

Thyroglobulin (Tg) is produced in the thyroid gland and is a main component in the lumen of the thyroid follicle. In synergy with the enzyme thyroid-specific peroxidase (TPO), Tg has an essential function in the iodination of L-tyrosine and in the formation of the thyroid hormones T4 and T3.¹ Both Tg and TPO are potentially autoantigenic.^{2,3}

Elevated serum concentrations of antibodies against Tg (Tg-autoantibodies) are found in subjects with autoimmunity-based thyroiditis.^{2,3} High concentrations of anti-Tg together with anti-TPO are present in most patients with chronic lymphocytic-infiltrative thyroiditis (Hashimoto's disease).³ The frequency of thyroglobulin antibodies is approximately 50-80 % in subjects with autoimmune-thyroiditis, including Hashimoto's disease, and approximately 30-50 % in individuals with Graves' disease.^{3,4,5,6} The anti-Tg assay can also provide useful information for monitoring the course of Hashimoto's thyroiditis and for differential diagnosis.^{3,7} This includes cases of suspected autoimmune thyroiditis of unknown origin with negative anti-TPO test results,^{8,9} and to distinguish Hashimoto's thyroiditis from nontoxic nodular goiter or from other forms of thyroiditis.⁴

Anti-Tg has also been reported as a useful surrogate diagnostic marker for differentiated thyroid cancer when serum Tg is negative,¹⁰ and for ruling out interference by Tg autoantibodies when measuring serum Tg using a Tg test.^{11,12}

Although the sensitivity of the procedure can be increased by simultaneously determining additional thyroid antibodies (anti-TPO, anti-TSHR), a negative result does not definitively rule out the presence of an autoimmune disease. The antibody titer does not correlate with the clinical activity of the disease. Titers that are elevated initially can become negative if the disease persists for a longer period of time or if remission occurs. If antibodies reappear after remission, relapse is likely.

The Elecsys Anti-Tg assay uses human antigen and monoclonal human anti-Tg antibodies.¹³

Test principle

Competition principle. Total duration of assay: 18 minutes.

- 1st incubation: 6 µL of sample are incubated with biotinylated Tg and the antibodies of the sample bind the antigen.
- 2nd incubation: After addition of anti-Tg antibodies labeled with ruthenium complex⁹ and streptavidin-coated microparticles, the immunocomplex produced 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 II 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 **cobas** link.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex (Ru(bpy)₃²⁺)

Reagents - working solutions

The **cobas e** pack is labeled as ATG.

- M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Tg-biotin, 1 bottle, 19.7 mL:
Biotinylated Tg (human) 0.200 mg/L; TRIS buffer 100 mmol/L, pH 7.0; preservative.
- R2 Anti-Tg-Ab~Ru(bpy)₃²⁺, 1 bottle, 19.7 mL:
Monoclonal anti-Tg antibodies (human) labeled with ruthenium complex 0.620 mg/L; TRIS buffer 100 mmol/L, pH 7.0; 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.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

2-methyl-2H-isothiazol-3-one hydrochloride

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

All human material should be considered potentially infectious.

All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.

The initial thyroid glandular tissue extract containing the human thyroglobulin has shown to be free from HBsAg and antibodies to HCV and HIV.

The testing methods used assays approved by the FDA or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.

However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.^{14,15}

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 available via the **cobas** link.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the **cobas e** pack **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
on the cobas e 801 analyzer	16 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.

K₂-EDTA and K₃-EDTA plasma.

Criterion: Slope 0.9-1.1 + intercept within ± 20 IU/mL + coefficient of correlation ≥ 0.95 .

Stable for 4 days at 20-25 °C, 4 days at 2-8 °C, 2 months at -20 °C (± 5 °C). 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 and calibrators are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples and calibrators 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] 06368603190, Anti-Tg CalSet, for 4 x 1.5 mL
- [REF] 05042666191, PreciControl ThyroAB, for 4 x 2.0 mL
- General laboratory equipment
- **cobas e** 801 analyzer

Additional materials for the **cobas e** 801 analyzer:

- [REF] 06908799190, ProCell II M, 2 x 2 L system solution
- [REF] 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution
- [REF] 07485409001, Reservoir Cup, 8 cups to supply ProCell II M and CleanCell M
- [REF] 06908853190, PreClean II M, 2 x 2 L wash solution
- [REF] 05694302001, Assay Tip/Assay Cup tray, 6 magazines x 6 magazine stacks x 105 assay tips and 105 assay cups, 3 wasteliners
- [REF] 07485425001, Liquid Flow Cleaning Cup, 2 adaptor cups to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning Detection Unit
- [REF] 07485433001, PreWash Liquid Flow Cleaning Cup, 1 adaptor cup to supply ISE Cleaning Solution/Elecsys SysClean for Liquid Flow Cleaning PreWash Unit
- [REF] 11298500316, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

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.

Place the cooled (stored at 2-8 °C) **cobas e** pack on the reagent manager. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the **cobas e** pack.

Calibration

Traceability: This method has been standardized against the NIBSC (National Institute for Biological Standards and Control) 65/93 Standard.

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 **cobas e** pack was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 12 weeks when using the same reagent lot
- after 28 days when using the same **cobas e** pack on the analyzer
- as required: e.g. quality control findings outside the defined limits

Quality control

For quality control, use PreciControl ThyroAB.

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 **cobas e** pack, 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.

If necessary, repeat the measurement of the samples concerned.

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

Calculation

The analyzer automatically calculates the analyte concentration of each sample (either in IU/mL or kIU/L).

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	$\leq 1129 \mu\text{mol/L}$ or $\leq 66 \text{ mg/dL}$
Hemoglobin	$\leq 0.373 \text{ mmol/L}$ or $\leq 600 \text{ mg/dL}$
Intralipid	$\leq 2000 \text{ mg/dL}$
Biotin	$\leq 246 \text{ nmol/L}$ or $\leq 60 \text{ ng/mL}$
Rheumatoid factors	$\leq 300 \text{ IU/mL}$

Criterion: For concentrations of 10-75 IU/mL the deviation is ≤ 11 IU/mL. For concentrations > 75 IU/mL the deviation is ≤ 15 %.

For samples ≤ 115 IU/mL no interference was observed for hemoglobin concentrations ≤ 600 mg/dL. In samples with a concentration of > 115 IU/mL a lower hemoglobin concentration may result in increased anti-Tg values.

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.

Pharmaceutical substances

In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

In addition, the following special drugs were tested. No interference with the assay was found.

Special drugs

Drug	Concentration tested mg/L
Iodide	0.200
Carbimazole	30
Methimazole	80
Propylthiouracil	300
Perchlorate	2000
Propranolol	48
Amiodarone	40
Prednisolone	100

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- 6 Iddah MA, Macharia BN. Autoimmune thyroid disorders. *ISRN Endocrinol* 2013:509764.
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- 8 Feldt-Rasmussen U. Analytical and clinical performance goals for testing autoantibodies to thyroperoxidase, thyroglobulin, and thyrotropin receptor. *Clin Chem* 1996;42(1):160-163.
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- 10 Nam HY, Paeng JC, Chung JK, et al. Monitoring differentiated thyroid cancer patients with negative serum thyroglobulin. Diagnostic implication of TSH-stimulated antithyroglobulin antibody. *Nuklearmedizin* 2014;53(2):32-38.
- 11 Spencer CA, Takeuchi M, Kazarosyan M, et al. Serum Thyroglobulin Antibodies: Prevalence, Influence on Serum Thyroglobulin Measurement, and Prognostic Significance in Patients with Differentiated Thyroid Carcinoma. *J Clin Endocrin Metabol* 1998;83(4):1121-1127.
- 12 Spencer C. International Thyroid Testing Guidelines. National Academy of Clinical Biochemistry, August 2001;Section 3E,11-14.
- 13 Prentice L, Kiso Y, Fukuma N, et al. Monoclonal Thyroglobulin Autoantibodies: Variable Region Analysis and Epitope Recognition. *J Clin Endocrin Metabol* 1995;80:977.
- 14 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.
- 15 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.
- 16 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. *J Clin Chem Clin Biochem* 1988 Nov;26(11):783-790.



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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 (for USA: see dialog.roche.com for definition of symbols used):

	Contents of kit
	Analyzers/Instruments on which reagents can be used
	Reagent
	Calibrator
	Volume after reconstitution or mixing
	Global Trade Item Number

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