# Instruction For Use

**【Product Name】**

Thyroglobulin (Electrochemiluminescence Immunoassay)

**【Order Information】**

| REF NO. | Package Size |
|---|---|
| 690033 | 50T |
| 690034 | 2×50T |
| 690030 | 100T |
| 690029 | 2×100T |

**【Intended Use】**

Immunoassay for the in vitro quantitative determination of thyroglobulin in human serum and plasma. Determination of Tg is used as an aid in monitoring after thyroid ablation.

**【Summary】**

Thyroglobulin (Tg) is a glycoprotein with a molecular weight of approximately 660 kDa[1]. Tg is synthesized in large quantities by the thyrocytes and released into the lumina of the thyroid follicles. Production of Tg is stimulated by TSH, intrathyroidal iodine deficiency and the presence of thyroid-stimulating immunoglobulins. Tg plays a decisive role in the synthesis of the peripheral thyroid hormones T3 and T4. During synthesis of Tg by the thyrocytes and transport of Tg to the follicles, small quantities of the protein can pass into the bloodstream. Accordingly, low concentrations of Tg can be found in the blood of healthy individuals not suffering from thyroid diseases[2,3]. Elevated Tg concentrations have been reported in different thyroid conditions like Hashimoto's disease, Graves' disease, thyroid adenoma, and thyroid carcinoma[4,5]. In cases of congenital hypothyroidism the determination of Tg can be used to differentiate between the complete absence of the thyroid gland and thyroid hypoplasia or other pathological conditions. The main application of Tg testing is the post-operative follow-up of patients with differentiated thyroid carcinoma (DTC).

All Tg results should be interpreted in conjunction with the total clinical presentation of the patient, including symptoms, clinical history, data from additional tests (i.e. neck ultrasound, whole body scan) and other appropriate information.

Tg determinations can be affected by the presence of Tg autoantibodies causing false high or false low Tg values. Therefore anti-TG determinations are recommended for all Tg samples to rule out this interference[6].

**【Test Principle】**

Sandwich principle. Total duration of assay: 18 minutes.

35 µL of sample, biotinylated anti-thyroglobulin antibody, and anti-thyroglobulin antibody labeled with ruthenium complex react to form a sandwich complex. After addition of streptavidin-coated microparticles, the 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 system reagent. 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 RFID.

**【Main Component】**

The reagent pack consists of MB, RA, RB, calibrators and control materials (Optional). Different batch of reagent components should not be used interchangeably.

| Component | Ingredients | Volume (50T) | Volume (2×50T) | Volume (100T) | Volume (2×100T) |
|---|---|---|---|---|---|
| Magnetic Beads (MB) | Streptavidin-coated microparticles; preservative | 1×1.3 mL | 2×1.3 mL | 1×2.5 mL | 2×2.5 mL |
| Reagent B (RB) | Tg-Ab~Biotin: 0.05M ME;S preservative | 1×3.5 mL | 2×3.5 mL | 1×7.0 mL | 2×7.0 mL |
| Reagent A (RA) | Tg-Ab~Ru(bpy)$^{2+}_3$: 0.05M MES; preservative | 1×3.5 mL | 2×3.5 mL | 1×7.0 mL | 2×7.0 mL |
| Calibrators | Bovine serum, preservative | High: 1×1.0 mL<br>Low: 1×1.0 mL | | | |
| Control Materials (Optional) | Bovine serum, preservative | High: 1×1.0 mL<br>Low: 1×1.0 mL | | | |

Traceability: This method can be traceable to CRM (Certified Reference Material) 457 of the BCR (Community Bureau of Reference) of the European Union.

See the control material value sheet for the target values and ranges of control materials.

Supporting instruments and materials required but not provided in this pack (provided by Lifotronic)

Additional materials for Automated ECL Immunoassay Analyzer eCL8000, eCL8000i, eCL8000p, eCL8000x:

- REF 679005, Auffer, 480 mL, or REF 679004, Auffer, 6×480 mL
- REF 679007, Buffer, 480 mL, or REF 679006, Buffer, 6×480 mL
- REF 679009, Concentrated Washing Buffer, 1 L, or REF 679008, Concentrated Washing Buffer, 6×1 L

Additional materials for Automated ECL Immunoassay Analyzer eCL8600, eCL8600i, eCL8600p, eCL8800, eCL8800i, eCL8800p:

- REF 0320501804, Auffer, 2×1 L, or REF 0320501805, Auffer, 4×1 L
- REF 0320501904, Buffer, 2×1 L, or REF 0320501905, Buffer, 4×1 L
- REF 0320507502, PreClean, 2×800 mL, or REF 0320507503, PreClean, 4×800 mL
- REF 0320510001, Assay Cup/Assay Tip, 6×6×105, or REF 032120111, Assay Cup/Assay Tip, 12×2×105

Additional materials for Automated ECL Immunoassay Analyzer eCL9000, eCL9600, eCL9900, eCL9900i:

- REF 0320501801, Auffer, 2×2 L, or REF 0320501806, Auffer, 4×2 L
- REF 0320501901, Buffer, 2×2 L, or REF 0320501906, Buffer, 4×2 L
- REF 0320507501, PreClean, 2×2 L, or REF 0320507504, PreClean, 4×2 L
- REF 320510001, Assay Cup/Assay Tip, 6×6×105, or REF 0320510002, Assay Cup/Assay Tip, 1×6×105

**【Storage and Shelf Life】**

Store at 2ºC-8ºC.

Do not freeze.

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

| *Stability of the reagents* | |
|---|---|
| Unopened store at 2ºC~8ºC | 18 months |
| Store at 2ºC~8ºC after opening | 8 weeks |
| on the analyzers at 2ºC~15ºC | 8 weeks |

The calibrators and control materials are stable up to the stated expiration date.

| *Stability of the calibrators and control materials* | |
|---|---|
| Unopened store at 2ºC~8ºC | 18 months |
| Store at 2ºC~8ºC after opening | 8 weeks |

The expiration date is labeled on the box, rackpack and bottles.

Damaged, expired or contaminated reagents should be discarded.

**【Applicable Instrument】**

Automated ECL Immunoassay Analyzers: eCL8000, eCL8000i, eCL8000p, eCL8000x, eCL8600, eCL8600i, eCL8600p, eCL8800, eCL8800i, eCL8800p, eCL9000, eCL9600, eCL9900, eCL9900i.

**【Specimen collection, handling and storage】**

Human serum and plasma added with heparin lithium, EDTA-K3 and EDTA-K2 anti-coagulants are recommended. Blood samples should be collected by standard operation of venous puncture; after complete coagulation, the tangible component should be removed by centrifugation. The sample should avoid bubbling during testing. Lipid layer floating on the upper of the sample should be removed. Samples with severe hemolysis are not recommended. Samples would better to be tested in 48 hours after collection, otherwise, should be stored 2~8ºC for no more than 3 days or -25~-15ºC for 1 month. Freezing and thawing cycle is permitted only once.

**【Assay Procedure】**

**Testing procedures and precautions**

Previous to operation, one should read the operational manual carefully to obtain system operation procedure, sample processing, security precaution, maintenance and other related information.

Set up Tg test according to the operational manual.

Put the Tg rackpack into the correct analyzer slot to automatically suspend magnetic beads at least 30 min before testing.

**Calibration**

Calibration should be performed using lot-matching reagent and calibrators.

Before calibration, the reagent and main curve information should be imported into the analyzer via radio frequency identification (RFID) reagent card(refer to instrument user manual). The analyzer adjusts the main curve to produce working curve according to the calibrator results, and identifies validity of the working curve automatically.

Recalibration is recommended when:

(1) the reagents of different lot are used;

(2) the same lot of reagents were used on the analyzer beyond 28 days;

(3) quality control misses the target.

**Quality control**

For quality control, use Tg control materials.

In addition, other suitable control material can be used.

Control materials 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.

If necessary, repeat the measurement of the samples concerned.

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

Please make sure that the correct values are used.

**Calculation**

The system software automatically calculates the analyte concentration using particular algorithm, and the result unit is ng/mL or µg/L. 1ng/mL=1µg/L.

**Specimen dilution**

Samples exceeding the measuring range would be manually diluted with Tg-negative serum.

The recommended dilution ratio is 1:10, the concentration of the diluted sample must be > 50 ng/mL, and the diluted sample test results need to multiply dilution ratio.

**【Biological reference interval】**

According to serum test results of 381 heathy human serum samples (male 218,and female 163), the percentile 2.5$^{th}$ to 97.5$^{th}$ gives reference range 3.3~74.0 ng/mL.

Due to differences in the region, race, gender and age, laboratories are recommended to set up their own reference ranges.

**【Result Interpretation】**

For explaining the result, the patient's overall clinical manifestation should be referred to, including symptoms, medical history and other relevant data and information.

**【Limitations】**

Test results are used only for clinical reference and cannot be used as the basis for diagnosis or rule-out of diseases alone.

When the sample has bilirubin ≤66 mg/dL, hemoglobin ≤0.6 g/dL, triglyceride ≤2000 mg/dL, biotin ≤30 ng/mL, total protein ≤10g/dL, rheumatoid factor ≤600 IU/mL and HAMA ≤100 ng/mL, the interference deviation of the measurement results is within ±10%.

Tg determinations can be affected by the presence of anti-thyroglobulin antibodies (anti-Tg) or by non-specific effects in patient sera. Results should be either confirmed with the determination of anti-Tg.

**【Measuring Range】**

The measuring range of the kit is 0.04～500 ng/mL. For samples with Tg content below the lower detection limit, the results are reported as < 0.04 ng/mL; If the Tg content is above the upper detection limit, , the results are reported as > 500 ng/mL.

**【Analytical Performance】**

**Lower limits of measurement**

Lower detection limit is 0.04 ng/mL.

**Accuracy**

Test samples with different concentrations of Tg were added, and the recovery rate was in the range of 90% to 110%.

**Linearity**

The correlation coefficient (Pearson's r) is not less than 0.9900 in the interval of 0.04~ 500 ng/mL.

**Within-run precision (repeatability)**

The coefficient of variation (CV) ≤ 6%.

**Between-lot precision**

The coefficient of variation (CV) ≤ 10%.

**Analytical specificity**

Test results of blank samples spiked with analogs below are lower than 0.04ng/mL.

| Analog | Concentration |
|---|---|
| TSH | 1000 mIU/L |
| TBG | 200000 ng/mL |

**Method comparison**

A comparison of the Lifotronic Tg assay (y) with the Roche Elecsys Tg Method (x) using clinical samples gave the following correlations:

Linear regression:

y=1.0407x+2.4802

r =0.9856

Number of samples measured: 145

The samples concentration were between approx 0.053 ng/mL and 410.4 ng/mL.

**【Precaution and Warning】**

The kit is only used for in vitro diagnostics.

When using the kit, it's necessary to exercise the normal precautions in the laboratory.

All reagents and samples including specimen, calibrators and control materials, should avoid foaming before and during test.

Test results of the kit are for clinical reference only, and clinical evaluation of patients should be combined with their symptoms and signs, medical history, other laboratory examination results and treatment responses.

Thyroglobulin (Tg) determinations can be affected by the presence of Tg autoantibodies (anti-Tg) in some patient samples. These autoantibodies may interfere with the assay used to measure Tg, causing false high or false low Tg values.

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

Due to factors such as methodology or antibody specificity, testing identical samples with reagents from different manufacturers may get different results, and the results from different kits should not compare directly, lest cause the wrong medical explanation; It's suggested that laboratorians should point out the characteristics of used reagent in the test report to the clinician. In serial monitoring, if the reagent type is changed, a continuous parallel test should be performed and comparison of the results to the former should be to determine new baseline value.

This product contains animal-sourced materials and may have potential biological risk. All samples and test wastes should be treated as the source of infection, and all wastes must be disposed according to local regulations.

Any serious incident that would be occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

The preservative ProClin™300 which contain Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-Methyl-2H-isothiazol-3-one (3:1): May cause an allergic skin reaction. thus, proper personal protection should be adopt while handling the reagent: avoid breathing dust/fume/gas/mist/vapours/spray, wear protective gloves and contaminated work clothing should not be allowed out of the workplace. If skin irritation or rash occurs: get medical advice/attention, take off contaminated clothing and wash it before reuse, and dispose of contents/container to an approved waste disposal plant.

**【Reference】**

1. Malthiery Y, Lissitzky S. Primary structure of human thyroglobulin deduced from sequence of its 8448-base complementary DNA ,Eur J Biochem 1987; 165:491-498.
2. Torrens JI, Burch HB.Serum thyroglobulin measurement. Utility in clinical practice. Endocrinol Metab Clin Nerth Am 2001;30(2):429-467
3. Knudsen N, Bulow L, et al. Serum Tg-a Sensitive Maker of Thyroid Abnormalities and Iodine Deficiency in Epidemiological Studies, J Clin Endocrinol Metab,2001,86(8):359-363.
4. Erali M, Bigelow RB, Meikle AW. ELISA for thyroglobulin in serum:recovery studies to evaluate autoantibody interference and reliability of thyroglobulin values. Clin Chem 1996;42(5):766-770.
5. Spencer CA, Lopresti JS. Technology Insigth: measuring thyroglobulin and thyroglobulin autoantibody in patients with differentiated thyroid cancers. Nat Clin Pract Endocrinol Metab 2008; 4(4):223-233.
6. Clark P, Franklyn J. Can we interpret serum thyroglobulin results? Ann Clin Biochem 2012; 49:313-322.

**【Symbols Explanation】**

| Symbol | Title of Symbol | Symbol | Title of Symbol |
|---|---|---|---|
|  | Manufacturer |  | Consult instructions for use |
|  | Use-by date |  | In vitro diagnostic medical device |
|  | Batch code |  | Sufficient for <n> tests |
|  | Serial number |  | Biological risks |
|  | Temperature limit |  | This way up |
|  | Authorized representative in the European Community |  | Indicates this device is in compliance with Europe Directive. |
|  | Catalogue number | P/N | Material code |
|  | Warning |  | Date of manufacture |
|  | Unique device identifier | | |

**【Manufacturer】**

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