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Thyroglobulin (TG) Assay Reagent Kit(CMIA)

Package Insert

For professional in vitro diagnostic use only.

INTENDED USE

Thyroglobulin (TG) Assay Reagent Kit (CMIA) is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of Thyroglobulin (TG) in human serum and plasma.

PACKING SIZE

24 Device/Kit,30Device/Kit,48 Device/Kit,60 Device/Kit

SUMMARY

The thyroid is a small endocrine gland located in the base of the neck. It consists of two lateral lobes connected by an isthmus. The gland produces a variety of metabolic hormones in a negative biofeedback loop.

Thyroglobulin (Tg) is a large glycoprotein (MW = 660,000) that is stored in the follicular colloid of the thyroid gland. Thyroglobulin functions as a prohormone in the intrathyroid synthesis of T4 and T3. Lysosomes containing proteases cleave T4 and T3 from Tg, resulting in release of T4 and T3.

Thyroglobulin is present in the serum of normal healthy individuals and can be elevated in numerous disorders which disrupt thyroid tissue. Elevated circulating levels of Tg have been reported in a number of thyroid conditions including Hashimoto's disease,Graves' disease, thyroid adenoma, subacute thyroiditis and thyroid carcinoma.

Thyroid cancer is a relatively common form of cancer. It is not generally highly malignant, and normal life span can be obtained with appropriate follow-up and treatment.Females are affected 2 to 3 times more frequently than males. Thyroglobulin has become a useful tool in the follow-up of patients with differentiated thyroid carcinoma (i.e. papillary-follicular or follicular carcinoma of the thyroid). The thyroid is the only source of Tg; therefore, the serum Tg level will drop to a very low or undetectable level after total or near-total thyroidectomy and successful radioiodine ablation of the residual thyroid tissue. A rise in the serum level of Tg points to the recurrence of the disease. Thyroglobulin levels in patients who have undergone only a partial thyroidectomy will retain measurable levels of Tg, depending on how much tissue is remaining after surgery. These patients can be monitored by Tg measurement, but the post-surgical Tg level must betaken into account.

A limiting factor in the use of serum Tg measurements is the presence of Tg autoantibodies found in some patients.These antibodies may interfere with the immunoassay used to measure Tg and can cause false high or false low values. It is important to determine the levels of Tg autoantibodies in patients requiring serum Tg measurements.

PRINCIPLE OF TEST

The TG assay is a two-step immunoassay for the quantitative measurement of TG in human serum, plasma using CMIA technology, with flexible assay protocols.

In the first step,sample and anti-TG coated paramagnetic microparticles are combined. TG present in the sample binds to the anti-TG coated microparticles. ALP-labeled anti-TG conjugate is added to create a reaction mixture in the second step.Following wash cycle, substrate is added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of TG in the sample and the RLUs detected by the system optics.

REAGENTS

The device is pre-dispensed with buffer needed for single use.

The device is constituted with Buffers described below is the main reagent

Object	Content
Micro-particles Buffer	Anti -TG (monoclonal) coated Micro-particles in TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 0.1% solid. Preservative: ProClin-300.
Conjugate Buffer	Anti -TG (monoclonal) alkaline phosphatase (ALP) labeled conjugate in TRIS buffer with protein (bovine) stabilizer. Preservative: ProClin-300.
Wash buffer	TRIS buffer with surfactant. Preservative: ProClin-300.
Substrate buffer	AMPPD, Enhancer, surfactant, ProClin-300.

Reagent Handing

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.

MATERIALS PROVIDED

·TG Test Device
·Product Insert
·Calibration Solution (optional)
·Control Solution (optional)

MATERIALS REQUIRED BUT NOT PROVIDED

·Analyzer

STORAGE AND STABILITY

▪Store at 2-8℃.
▪Do not freeze.
▪Store the reagent kit upright prior to use.
▪Expiration date: up to the stated expiration date.

Note: The TG Reagent Kit must be stored at 2-8℃ in an upright position, and must be used immediately after removal from 2-8℃ storage or the device was opened.

SPECIMEN COLLECTION AND STORAGE

Specimen Types

Validated specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human serum	Serum Serum separator tubes
Human plasma	Sodium heparin Lithium heparin Potassium EDTA Sodium EDTA

Other anticoagulants have not been validated for use with this assay.

The instrument does not provide the capability to verily specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  heat-inactivated
  pooled
  grossly hemolyzed
  obvious microbial 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 especial 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.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for specimen collection tubes.
- Specimens must be mixed THOROUGHLY after thawing, by LOW speed vortex, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum/Plasma	2-8℃	6 days

- If testing will be delayed more than 24 hours, remove serum or plasma from the clot, serum separator or red blood cells.
- If testing will be delayed more than 6 days, specimens should be frozen at -10℃ or colder.
- Specimens stored frozen at -20℃ or colder for 3 months showed no performance difference.
- Avoid more than 3 freeze/thaw cycles.

Specimen Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped ambient, at 2-8℃ (wet ice), or frozen (dry ice). Do not exceed the storage time limitations listed above.

INSTRUMENT

The TG Test Device is designed for use on the REALY or Cybereagen Analyzer System.

TEST PROCEDURE

Assay Procedure

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 digit sequence of numbers. Bring the cooled reagents to approx. 20℃ and place on the reagent disk of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

For this test device, the transfer volume of specimens, calibrators or controls into the sample hole is 80 µL. (No less than 80 µL.)

Reagent strips should be left at room temperature between 20 and 25 ℃ for more than 30 minutes before use and kept away from light.

In order to avoid the magnetic beads adsorbed on the side wall and top due to the upside down and side placement of the reagent strip during transportation, the reagent strip should be mixed by shaking and mixing before use. The reagent strip should be mixed upside down for about 30 seconds, and then the reagent strip should be mixed upward for about 30 seconds.The reagent strip was then gently shaken so that the magnetic beads fell completely to the bottom of the strip.

Calibration

Every Test Device has a barcoded label containing specific information for calibration of the particular reagent lot. The pre-defined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed before new lot of device be used. Renewed calibration is recommended as follows:

- After 90 days (when using the same reagent lot on the analyzer);
- As required: e.g. quality control findings outside the defined limits.

Note: Refer to Instruction of Analyzer for the procedure of calibration.

Quality Control

For quality control, please use Control of REALY or Control 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.

Specimen Dilution Procedures

Specimens with an TG concentration greater than 500 ng/mL will be flagged as "> 500 ng/mL" and may be diluted using Manual Dilution Procedure. Use the 1:10 dilution is recommended. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution.

EXPECTED VALUES

Reference values: 3.5-77 ng/mL

The concentration of thyroglobulin in 350 sera was tested. These human serum samples were from healthy men and women with negative TgAb. The reference range is 2.98 to 82.88 ng/mL, with 2.5 and 97.5 percentiles of 3.5 and 77 ng/mL, respectively.

Serum samples from patients with Graves disease, Hashimoto disease and other benign diseases were tested. The results ranged from undetectable levels to>500 ng/mL.

The concentration of Tg in the body of patients who have undergone thyroidectomy related surgery is close to zero or the functional sensitivity measured.

When interpreting the change of serum Tg concentration, it is necessary to consider the overall clinical situation of the patient, including but not limited to: medical history, data from other tests and other corresponding information. In order to make an overall assessment of the patient's symptoms, a single determination of thyroglobulin has only a limited effect. Continuous testing is required and the baseline of postoperative Tg results should be used as a reference.

If necessary, advice each laboratory set up your own reference range to assure proper representation of specific populations.

INTERPRETATION OF RESULTS

As interpret the results, the patient's overall clinical situation, including symptoms, medical history and other related data, should be referred to.

LIMITATIONS

- If the TG results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- The presence of serum autoantibodies to thyroglobulin (TgAb) can interfere with assays for thyroglobulin (Tg). Therefore, sera which contain TgAb, even at very low levels, should not be tested for Tg. and samples which are TgAb antibody positive should be interpreted with caution as the true value may be higher than that obtained.
- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Specimens containing HAMA may produce anomalous values when tested with assay kits such as REALY TG that employ mouse monoclonal antibodies.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous results may be observed. Additional information may be required for diagnosis.
- Although the REALY TG assay is specifically designed to minimize the effects of HAMA and heterophilic antibodies, assay results that are not consistent with other clinical observations may require additional information for diagnosis.

PERFORMANCE CHARACTERISTICS

Linearity

The linearity of TG Reagent Kit was determined by use TG calibrator to prepare 6 different specimens, measuring all these specimens follow the test instruction and then do linear fitting, the results show that the linear correlation coefficient (r) was not less than 0.9900.

Precision / Reproducibility

Intra-assay coefficient of variation was evaluated on 3 different levels of control serum. Repeatedly measured 20 times, calculating the coefficient of variation.

Intra-assay Precision			
Control	Mean (ng/mL)	SD (ng/mL)	CV
Level 1	0.50	0.04	8.00%
Level 2	9.69	0.72	7.43%
Level 3	236.74	12.45	5.26%

Inter-assay coefficient of variation was evaluated on three batches of kits. Repeatedly measured 3 different levels of control serum 30 times, calculating the coefficient of variation.

Inter-assay Precision			
Control	Mean (ng/mL)	SD (ng/mL)	CV
Level 1	0.47	0.03	6.38%
Level 2	9.77	0.84	8.60%
Level 3	250.68	22.54	8.99%

Analytical Sensitivity

The analytical sensitivity is defined as the concentration of TG equivalent to the mean RLU of 20 replicates of the zero standard plus two standard deviations corresponding to the concentration from the standard curve. The analytical sensitivity is typically less than0.5 ng/mL.

Analytical Specificity

The specificity of the TG assay system was assessed by measuring the apparent response of the assay to various potentially cross-reactive analytes.

Compound	Concentration	Cross-reactivity
TSH	1000 mIU/L	< 1%
TBG	200000 ng/mL	< 1%

Interference

The following compounds in both low-level specimen and high-level specimen show no cross-reactivity when tested with the TG Assay Reagent Kit at a concentration below:

Compound	Concentration
Hemoglobin	0.6 g/dL
Bilirubin	66 mg/dL
Triglycerides	2000mg/dL

Method Comparison

The comparison between the TG Assay Reagent Kit (y) and a commercially available TG test kit (x), using clinical samples gave the following correlations (ng/mL):

Linear regression
y=0.9239x-2.1953
r=0.9940
Number of samples measured: 116
The sample concentrations were between about 0.5-450 ng/mL.

WARNINGS AND PRECAUTIONS

- For *In Vitro* Diagnostic Use.
- Do not use expired or clearly damaged kits.
- Operating according to the steps described, can make the risk of daily handling patients` samples and blood products into a minimum, however, no matter what the source of the products, handling mode or the previous proof, these potentially infectious substances were used shall be in accordance with the unified considerations and Good Laboratory Practice (GLP).
- Proper disinfectant should be used to eliminate pollution.
- Follow local rules and regulations to keep and dispose of these items and containers for these items.
- The ProClin-300 is a potential skin sensitizer. Avoid dumping or splashing this reagent on your skin and clothing. In case of contact with this reagent, wash thoroughly with soap and water.
- Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

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SYMBOLS

Symbol	Meaning	Symbol	Meaning
IVD	In vitro diagnostic medical device		Storage temperature limit
	Manufacturer	EC REP	Authorized representative in the European Community /European Union
	Date of Manufacture		Use-by date
	Do not re-use		Consult instructions for use or consult electronic instructions for use
LOT	Batch code		Do not use if package is damaged and consult instructions for use
REF	Catalogue number	Σ	Contains sufficient for <n> tests

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