MAGLUMI TG (CLIA)

REF 130203006M Σ 100

EC REP

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CE

FOR PROFESSIONAL USE ONLY
Store at 2-8 °C

COMPLETELY READ THE INSTRUCTIONS BEFORE PROCEEDING

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SYMBOLS EXPLANATIONS

EC REP	Authorized Representative in the European community
	Manufacturer
	Consult instructions for use
CONT	Contents of kit
IVD	In vitro diagnostic medical device
LOT	Batch code
REF	Catalogue number
	Use by
8°C 2°C	Temperature limitation (store at 2-8 °C)
Σ	Sufficient for
	Keep away from sunlight
	Keep upright for storage

INTENDED USE

The kit has been designed for the quantitative determination of Thyroglobulin (TG) in human serum.
The method can be used for samples over the range of 1.0-1000.0ng/ml.
The test has to be performed on the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI (Including Maglumi 600,Maglumi 1000,Maglumi 1000 Plus, Maglumi 2000,Maglumi 2000 Plus,Maglumi 3000 and Maglumi 4000).

SUMMARY AND EXPLANATION OF THE TEST

Thyroglobulin (TG), the storage type of the thyroid gland hormones, is a dimeric, glycosylated iodoprotein with a molecular weight of approx. 660,000 dalton. TG is synthesised in the thyrocytes of the thyroid gland and is secreted into the internal parts of the follicle, where the tyrosyl residues are iodinated to become precursors of the thyroid hormones, before the free hormones T3 and T4 are liberated by proteolytic cleavage. Thyroglobulin itself is secreted into the circulation in very small amounts, its concentration in healthy persons with no thyroid disease being lower than 70ng/ml. Similar to the other thyroid hormones, synthesis and secretion of TG are subject to regulation by TSH and TRH.
Elevated TG levels at present in a variety of thyroid disorders such as Graves' disease, Hashimoto's thyroiditis, and differentiated thyroid carcinoma (papillary and follicular). In the latter, TG levels directly reflect the progression of tumour growth. Following total thyroidectomy and complete elimination of residual thyroid tissue by radiation therapy, TG concentrations (even under endogenous TSH stimulation) fall below the sensitivity in patients with no metastases or recurrences.
Residual tumor tissue and metastases cause a postoperative increase in TG levels. Thyroglobulin shows a high antigenic potential. Determination of TG may, therefore, be affected by the presence of endogenous anti-TG antibodies and other Interfering factors.

PRINCIPLE OF THE TEST

Sandwich immunoluminometric assay;
Use anti-TG monoclonal antibody to label ABEI, and use another monoclonal antibody to coat nano magnetic microbeads. Sample, Calibrator or Control with nano magnetic microbeads are mixed thoroughly and incubated at 37℃ and cycle washing for 1 time. Then add ABEI Label, incubation and form a sandwich, then washing for the 2nd time. Subsequently, the starter reagents are added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU within 3 seconds and is proportional to the concentration of TG present in samples.

CONT KIT COMPONENTS

Material Supplies

Reagent Integral for 100 determinations	
Nano magnetic microbeads: TRIS buffer, 1.2%(W/V), 0.2%NaN_3, coated with anti-TG monoclonal antibody	**2.5ml**
Calibrator Low : bovine serum, 0.2%NaN_3	**2.5ml**
Calibrator High : bovine serum, 0.2%NaN_3	**2.5ml**
Buffer: contains BSA, 0.2%NaN_3.	**6.5ml**
ABEI Label: anti-TG monoclonal antibody labeled ABEI, contains BSA, 0.2%NaN_3.	**12.5ml**
Diluent: 0.9% NaCl	**25.0ml**
All reagents are provided ready-to-use.	

Reagent Vials in kit box

Internal Quality Control: containing BSA, 0.2%NaN_3. (target value refer to Quality Control Information date sheet)	2.0ml

Accessories Required But Not Provided

MAGLUMI Reaction Module	REF: 630003
MAGLUMI Starter 1+2	REF: 130299004M
MAGLUMI Wash Concentrate	REF: 130299005M
MAGLUMI Light Check	REF: 130299006M

Preparation of the Reagent Integral

Before the sealing is removed, gentle and careful horizontal shaking of the Reagent Integral is essential (avoid foam formation!) Remove the sealing and turn the small wheel of the magnetic microbeads compartment to and fro, until the colour of the suspension has changed into brown. Place the Integral into the reagent area and let it stand there for 30 min. During this time, the magnetic microbeads are automatically agitated and completely resuspended.

Do not interchange integral component from different reagents or lots!

Storage and Stability

- Sealed: Stored at 2-8℃ until the expiry date.
- Opened: Stable for 4 weeks. To ensure the best kit performance, it is recommended to place opened kits in the refrigerator if it's not going to be used on board during the next 12 hours.
-  Keep upright for storage.
-  Keep away from sunlight.

CALIBRATION AND TRACEABILITY

1)Traceability

To perform an accurate calibration, we have provided the test calibrators standardized against the W.H.O.1st International Reference Preparation NIBSC 65/93

2) 2-Point Recalibration

Via the measurement of calibrators, the predefined master curve is adjusted (recalibrated) to a new, instrument-specific measurement level with each calibration.

3) Frequency of Recalibration

- After each exchange of lot (Reagent Integral or Starter Reagents).
- Every 2 weeks and/or each time a new Integral is used (recommendation).
- After each servicing of the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI.
- If controls are beyond the expected range.
- The room temperature has changed more than 5 ℃ (recommendation).

SPECIMEN COLLECTION AND PREPARATION

Sample material: serum

Collect 5.0ml venous blood into Blood Collection Tube. Standing at room temperature，centrifuging, separating serum part.

The serum sample is stable for up to 12 hours at 2-8℃. More than 12 hours, please packed, -20 ℃ can be stored for 30 days.

Avoid repeated freezing and thawing, the serum sample can be only frozen and thawed two times. Stored samples should be thoroughly mixed prior to use (Vortex mixer).

Please ask local representative of SNIBE for more details if you have any doubt.

Vacuum Tubes

(a) Blank tubes are recommended type for collecting samples.

(b) Please ask SNIBE for advice if special additive must be used in sample collecting.

Specimen Conditions

- Do not use specimens with the following conditions:
  (a) heat-inactivated specimens;
  (b) Cadaver specimens or body fluids other than human serum;
  (c) Obvious microbial contamination.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- Inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- Serum 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, especially 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.

Preparation for Analysis

- Patient specimens with a cloudy or turbid appearance must be centrifuged prior to testing. Following centrifugation, avoid the lipid layer (if present) when pipetting the specimen into a sample cup or secondary tube.
- Specimens must be mixed **thoroughly** after thawing by **low** speed vortexing or by gently inverting, and centrifuged prior to use to remove red blood cells or particulate matter to ensure consistency in the results. Multiple freeze-thaw cycles of specimens should be avoided.
- All samples (patient specimens or controls) should be tested within 3 hours of being placed on board the MAGLUMI System. Refer to the SNIBE service for a more detailed discussion of onboard sample storage constraints.

Storage

- If testing will be delayed for more than 8 hours, remove serum or plasma from the serum separator, red blood cells or clot. Specimens removed from the separator gel, cells or clot may be stored up to 12 hours at 2-8°C.
- Specimens can be stored up to 30 days frozen at -20°C or colder.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the serum separator, red blood cells or clot. When shipped, specimens must be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens must be shipped frozen (dry ice). Do not exceed the storage time limitations identified in this section of the package insert.

WARNING AND PRECAUTIONS FOR USERS

- For use in *IN-VITRO* diagnostic procedures only.
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

CAUTION: This product requires the handling of human specimens.

- The calibrators in this kit are prepared from bovine serum products. However, because no test method can offer complete assurance that HIV, Hepatitis B Virus or other infectious agents are absent; these reagents should be considered a potential biohazard and handled with the same precautions as applied to any serum or plasma specimen.
- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be autoclaved using an overkill approach (USP 24, 2000, p.2143). A minimum of one hour at 121℃ is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.
- It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens 13. Biosafety Level 214 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- This product contains Sodium Azide; this material and its container must be disposed of in a safe way.
- Safety data sheets are available on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not mix reagents from different reagent kits.
- Prior to loading the Reagent Kit on the system for the first time, the microbeads requires mixing to re-suspend microbeads that have settled during shipment.
- For microbeads mixing instructions, refer to the KIT COMPONENTS, Preparation of the Reagent Integral section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and sample.
- Over time, residual liquids may dry on the kit surface, please pay attention the silicon film still exists on the surface of the kit.
- For a detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

TEST PROCEDURE

To ensure proper test performance, strictly adhere to the operating instructions of the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI. Each test parameter is identified via a RFID tag on the Reagent Integral. For further information please refer to the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI Operating Instructions.

20μl +40μl +20μl	Sample, calibrator Buffer Nano magnetic microbeads
10 min	Incubation
400μl	Cycle washing
+100μl	ABEI Label
10 min	Incubation
400μl	Cycle washing
3 s	Measurement

DILUTION

Samples with concentrations above the measuring range can be diluted. After manual dilution, multiply the result by the dilution factor. After dilution by the analyzers, the analyzer software automatically takes the dilution into account when calculating the sample concentration.

Availability of sample dilution by analyzer please refers to the MAGLUMI analyzer user software program. Dilution settings please follow MALGUMI analyzer operating instructions.

QUALITY CONTROL

- Observe quality control guidelines for medical laboratories
- Use suitable controls for in-house quality control. Controls should be run at least once every 24 hours when the test is in use, once per reagent kit and after every calibration. The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined ranges. Each laboratory should establish guidelines for corrective measures to be taken if values fall outside the range.

LIMITATIONS OF THE PROCEDURE

1) Limitations

The presence of anti-thyroglobulin antibodies or other unspecific interfering factors may affect the results of TG determination by yielding false negative results. Therefore, it is strongly recommended that the reliability of the test result be confirmed by an appropriate confirmation test, via recovery.

2) Interfering Substances

No interference with test results is seen by concentrations of bilirubin< 36mg/dl, haemoglobin< 1900mg/dl or triglycerides <2000mg/dl.

3) HAMA

Patient samples containing human anti-mouse antibodies (HAMA) may give falsely elevated or decreased values. Although HAMA-neutralizing agents are added, extremely high HAMA serum concentrations may occasionally influence results.

RESULTS

1) Calculation of Results

- The analyzer automatically calculates the TG concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in ng/ml. For further information please refer to the Fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI Operating Instructions.
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2) Interpretation of Results

- Results of study in clinical centers with group of individuals, 95% of the results were: < 55 ng/ml.
- Results may differ between laboratories due to variations in population and test method. If necessary, each laboratory should establish its own reference range.

PERFORMANCE CHARACTERISTICS

1) Precision

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

Intra-assay precision			
Control	Mean(ng/ml)	SD(ng/ml)	CV%
Level 1	5.93	0.35	5.89
Level 2	45.52	2.38	5.23
Level 3	123.42	5.86	4.75

Inter-assay coefficient of variation was evaluated on three batches of kits. Repeatedly measured 3 different levels of control serum 21 times, calculating the coefficient of variation.

Inter-assay precision			
Control	Mean(ng/ml)	SD(ng/ml)	CV%

Level 1	5.81	0.53	9.13
Level 2	47.44	3.96	8.34
Level 3	125.47	10.23	8.15

2) Analytical Sensitivity

The 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 sensitivity is typically less than 1.0 ng/ml.

3) 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	50μIU/ml	6%
T3	10 ng/ml	30%
T4	300 ng/ml	1%
human IgG	80 μg/ml	10%

4) Recovery

Consider calibrator high of known concentration as a sample, dilute it by 1:2 ratio with diluents, and measure its diluted concentration for 10 times. Then calculate the recovery of measured concentration and expected concentration. The recovery should be within 90% -110%.

Expected	Mean Measuring	Recovery
281.2 ng/ml	289.6 ng/ml	103%

5) Linearity

Use TG calibrator to prepare the six-point standard curve, measuring all points' RLU except point A, and then do four-parameter linear fitting in double logarithm coordinate, the absolute linear correlation coefficient(r) should be bigger than 0.9800.

Calibrator Point	Concentration ng/ml	Absolute linear correlation coefficient (r)
A	0	
B	25	r=0.9990
C	65	
D	160	
E	400	
F	1000	

6) Method comparison

A comparison of MAGLUMI TG(y) with a commercially available TG(x) using clinical samples gave the following correlations (ng/ml):

Linear regression

y=0.5815x+5.8854

r=0.9851

Number of samples measured:100

The sample concentrations were between 3.43-119.91ng/ml

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