

# MAGLUMI® GH (CLIA)

## INTENDED USE

The kit is an *in vitro* chemiluminescence immunoassay for the quantitative determination of Growth Hormone (GH) in human serum using the MAGLUMI series Fully-auto chemiluminescence immunoassay analyzer (including Maglumi 600, Maglumi 800, Maglumi 1000, Maglumi 1000 Plus, Maglumi 2000, Maglumi 2000 Plus, Maglumi 4000, Maglumi 4000 Plus, MAGLUMI X8, MAGLUMI X3 and MAGLUMI X6) and Biolumi series Integrated System (including Biolumi CX8).

## SUMMARY AND EXPLANATION OF THE TEST

Growth hormone (GH), also known as somatotropin (or as human growth hormone [hGH or HGH] in its human form), is a peptide hormone that stimulates growth, cell reproduction, and cell regeneration in humans and other animals. It is thus important in human development. It is a type of mitogen which is specific only to certain kinds of cells. Growth hormone is a 191-amino acid, single-chain polypeptide that is synthesized, stored, and secreted by somatotrophic cells within the lateral wings of the anterior pituitary gland<sup>1-2</sup>.

The most common disease of GH excess is a pituitary tumor composed of somatotroph cells of the anterior pituitary. These somatotroph adenomas are benign and grow slowly, gradually producing more and more GH. For years, the principal clinical problems are those of GH excess. Eventually, the adenoma may become large enough to cause headaches, impair vision by pressure on the optic nerves, or cause deficiency of other pituitary hormones by displacement<sup>1</sup>. Prolonged GH excess thickens the bones of the jaw, fingers and toes. Accompanying problems can include sweating, pressure on nerves (e.g., carpal tunnel syndrome), muscle weakness, excess sex hormone-binding globulin (SHBG), insulin resistance or even a rare form of type 2 diabetes, and reduced sexual function<sup>3-4</sup>. The effects of growth hormone deficiency (GHD) vary depending on the age at which they occur. In children, growth failure and short stature are the major manifestations of GH deficiency, with common causes including genetic conditions and congenital malformations<sup>5</sup>. It can also cause delayed sexual maturity. In adults, deficiency is rare, with the most common cause a pituitary adenoma, and others including a continuation of a childhood problem, other structural lesions or trauma, and very rarely idiopathic GHD<sup>6</sup>.

## PRINCIPLE OF THE TEST

The GH assay is a sandwich chemiluminescence immunoassay.

The sample (or calibrator/control, if applicable), ABEI labeled with anti-GH monoclonal antibody, FITC labeled with another anti-GH monoclonal antibody, magnetic microbeads coated with anti-FITC polyclonal antibody are mixed thoroughly and incubated, forming sandwich of immuno-complexes. After precipitation in a magnetic field, the supernatant is decanted and then a wash cycle is performed. Subsequently, the Starter 1+2 are added to initiate a chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLUs), which is proportional to the concentration of GH present in the sample (or calibrator/control, if applicable).

## KIT COMPONENTS

### Material Provided

Components	Contents	100 tests (REF: 130298001M)	50 tests (REF: 130698001M)
<b>Magnetic Microbeads</b>	Magnetic microbeads coated with sheep anti-FITC polyclonal antibody, NaN <sub>3</sub> (<0.1%).	2.5 mL	2.0 mL
<b>Calibrator Low</b>	GH antigen, containing bovine serum, NaN <sub>3</sub> (<0.1%).	2.5 mL	2.0 mL
<b>Calibrator High</b>	GH antigen, containing bovine serum, NaN <sub>3</sub> (<0.1%).	2.5 mL	2.0 mL
<b>FITC Label</b>	Anti-GH monoclonal antibody labeled with FITC, containing BSA, NaN <sub>3</sub> (<0.1%).	6.5 mL	4.0 mL
<b>ABEI Label</b>	Anti-GH monoclonal antibody labeled with ABEI, containing BSA, NaN <sub>3</sub> (<0.1%).	6.5 mL	4.0 mL
<b>Internal Quality Control</b>	GH antigen, containing bovine serum, NaN <sub>3</sub> (<0.1%).	2.0 mL	2.0 mL

All reagents are provided ready-to-use.

### Accessories Required But Not Provided

MAGLUMI and Biolumi Series:

Reaction Module	REF: 630003
Starter 1+2	REF: 130299004M, 130299027M
Wash Concentrate	REF: 130299005M
Light Check	REF: 130299006M
Reaction Cup	REF: 130105000101

Please order accessories from Shenzhen New Industries Biomedical Engineering Co., Ltd. (SNIBE) or our authorized representatives.

## CALIBRATION

Traceability: This method has been traceable to the WHO 2nd International Standard 98/574.

Test of assay specific calibrators allows the RLU values to adjust the assigned master curve. Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve (10 calibrations) provided via the reagent Radio Frequency Identification (RFID) CHIP.

Recalibration is recommended if any of the following conditions occurs:

- After each change of lots (Reagent or Starter 1+2).
- Every 2 weeks and/or each time a new reagent kit is used (recommended).
- After instrument service is required.
- If controls lie outside the expected range.

## QUALITY CONTROL

Follow government regulations or accreditation requirements for quality control frequency.

Internal quality control is only applicable with MAGLUMI and Biolumi systems. For instructions for use and target value refer to **GH (CLIA) Quality Control Information**. User needs to judge results with their own standards and knowledge.

For detailed information about entering quality control values, refer to the corresponding Analyzer Operating Instructions.

To monitor system performance and chart trends, commercially available quality control materials are required. Treat all quality control samples the same as patient samples. A satisfactory level of performance is achieved when analyte values obtained are within the acceptable Control Range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme. If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical supporters or distributors for assistance.

## SPECIMEN COLLECTION AND PREPARATION

- Use standard sampling tubes or tubes containing separating gel. Collect blood aseptically following the universal precautions for venipuncture.
- Ensure that complete clot formation in 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 clotting, the presence of fibrin may cause erroneous results. Samples must be free of fibrin and other particulate matter.
- Do not use hemolyzed or grossly lipemic specimens as well as specimens containing particulate substance or exhibiting obvious microbial contamination. Inspect all specimens for bubbles, and remove bubbles before analysis for optimal results.
- Avoid repeated freezing and thawing. The serum sample can be frozen and thawed for two times. Stored samples should be thoroughly mixed prior to use (Vortex mixer). Frozen specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing. Please ask local representative of SNIBE for more details if you have any doubt.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care should be taken to transfer only the clarified specimen without the lipemic material.
- All samples (patient specimens and controls) should be tested within 3 hours when placed on board the MAGLUMI and Biolumi Systems. Refer to the SNIBE service for more details of onboard sample storage constraints.
- Specimens removed from the separator, red blood cells or clot may be stored up to 24 hours at 2-8°C, and stored up to 28 days frozen at -20°C or colder.
- Before shipping specimens, it is recommended that specimens be removed from the serum separator, red blood cells or clot. When shipped, specimens should be packaged and labeled in compliance with applicable state, federal and international regulations covering the transport of clinical specimens and infectious substances. Specimens should be shipped frozen.
- The sample volume required for a single determination of GH is 20 µL.

## WARNING AND PRECAUTIONS FOR USERS

- **IVD**
- For *In Vitro* Diagnostic Use.
- Follow the package insert carefully. 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. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the 29 CFR 1910.1030 Occupational exposure to bloodborne pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
- All samples, biological reagents and materials used in the assay should be considered potentially able to transmit infectious agents. They should therefore be disposed in accordance with the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.
- This product contains Sodium Azide. Dispose of contents and containers must be in accordance with all local, regional and national regulations.
- Refer to safety data sheets which are available on request.

### Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not interchange reagent components from different reagents or lots.
- Prior to loading the reagent kit on the system for the first time, the reagent kit requires mixing to re-suspend magnetic microbeads that have settled during shipment.
- For magnetic microbeads mixing instructions, refer to the Preparation of the Reagent section of this package insert.
- To avoid contamination, wear clean gloves when operating with a reagent kit and samples.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For detailed discussion of handling precautions during system operation, refer to the SNIBE service information.

## STORAGE AND STABILITY

- Sealed: Stored at 2-8°C until the expiration date.
- Opened at 2-8°C: Minimum stability is 4 weeks.
- On-board: Minimum stability is 4 weeks.
- To ensure the best kit performance, it is recommended to place opened kits in the refrigerator after the end of the intraday test work. It is still possible to keep on using the kit beyond the opened or on-board period if the controls are found within the expected ranges.
- Keep upright for storage to facilitate later proper resuspension of magnetic microbeads.
- Keep away from sunlight.

## TEST PROCEDURE

### Preparation of the Reagent

- Resuspension of the magnetic microbeads takes place automatically when the kit is loaded successfully, ensuring the magnetic microbeads are totally resuspended homogenous prior to use.
- To ensure proper test performance, strictly adhere to the corresponding Analyzer Operating Instructions. Each test parameter is identified via a RFID CHIP on the Reagent kit. For further information please refer to the corresponding Analyzer Operating Instructions.

## DILUTION

Sample dilution by analyzer is not available in this reagent kit.

Samples with concentrations above the measuring range can be diluted manually. After manual dilution, multiply the result by the dilution factor. Please

choose applicable diluents or ask SNIBE for advice before manual dilution.

#### High-Dose Hook

No high-dose hook effect was seen for GH concentrations up to 1,000 ng/mL.

#### LIMITATION

- A skillful operation and strict adherence to the instructions are necessary to obtain reliable results. Procedural directions should be followed exactly and careful operation should be used to obtain valid results. Any modification of the procedure is likely to alter the results.
- For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or received immunotherapy may contain human anti-mouse antibodies (HAMA), which may result in falsely elevated or decreased values. Moreover, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples as well. Additional clinical or diagnostic information may be required to determine patient status.
- For diagnostic purposes, the results should always be assessed and verified in conjunction with the patient's medical history, clinical examination and other findings.

#### RESULTS

##### Calculation of Results

The analyzer automatically calculates the GH 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 corresponding Analyzer Operating Instructions.

##### Interpretation of Results

Expected values:

Sample type	ng/mL
Normal adult	<5.0
Cord blood	10-50
Neonatal	15-40

Age	Male(ng/mL)	Female(ng/mL)
1-7 days	1.18-27.0	2.4-24.0
8-15 days	0.69-17.3	1.07-17.6
1-3 years	0.43-2.4	0.50-3.5
4-6 years	0.09-2.5	0.10-2.2
7-8 years	0.15-3.2	0.16-5.4
9-10 years	0.09-1.95	0.08-3.1
11 year	0.08-4.7	0.12-6.9
12 year	0.12-8.9	0.14-11.2
13 year	0.10-7.9	0.21-17.8
14 year	0.09-7.1	0.14-9.9
15 year	0.10-7.8	0.24-10.0
16 year	0.08-11.4	0.26-11.7
17 year	0.22-12.2	0.30-10.8
18-19 year	0.97-4.7	0.24-4.3

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

##### Precision

Precision for the GH assay was determined as described in the CLSI EP5-A2. 3 human serum pools and 3 controls containing different concentration of analyte were assayed in duplicate of two at two independent runs per day for 20 testing days. The results are summarized in the following table:

Sample	Mean(ng/mL) (N=80)	Within-Run		Between-Run		Total	
		SD(ng/mL)	%CV	SD(ng/mL)	%CV	SD(ng/mL)	%CV
Serum Pool 1	5.167	0.272	5.26	0.234	4.53	0.358	6.93
Serum Pool 2	15.543	0.585	3.76	0.735	4.73	0.939	6.04
Serum Pool 3	25.975	0.517	1.99	1.366	5.26	1.461	5.62
Control 1	3.558	0.230	6.46	0.065	1.83	0.239	6.72
Control 2	10.678	0.501	4.69	0.643	6.02	0.816	7.64
Control 3	19.259	0.584	3.03	0.812	4.22	1.000	5.19

##### Limit of Blank (LoB)

The LoB for the GH assay is 0.05 ng/mL.

##### Limit of Detection (LoD)

The LoD for the GH assay is 0.1 ng/mL.

### Measuring Range

0.05-50 ng/mL (defined by the limit of blank and the maximum of the master curve). Values below the limit of blank are reported as <0.05 ng/mL. Values above the measuring range are reported as >50 ng/mL.

### Linearity

The assay is linear between 0.1 ng/mL and 50 ng/mL based on a study performed with guidance from CLSI EP6-A. Nine equally distributed levels of samples were prepared by spiking a serum sample containing GH 55 ng/mL with a serum sample free of GH (0.0ng/mL). The mean sample recovery ranged from 90% to 110%.

### Method Comparison

A total of 133 samples in the range of 0.10 to 38 ng/mL were tested using the GH assay(y) and a commercially available immunoassay(x). The data from the resulting linear regressions are summarized as:  $y=0.959x+0.4389$ ,  $r^2=0.976$ .

### Analytical Specificity

The specificity of the assay was obtained by adding HPL (1000ng/mL), TSH (100  $\mu$ IU/mL), FSH (200  $\mu$ IU/mL), LH (200 mIU/mL), HCG (1000 mIU/mL), PRL (20 mIU/mL) and IGF-1 (500 ng/mL) to serum samples at the indicated concentrations. No interference was found.

### Endogenous Interference

Substances up to the following concentrations did not interfere with the assay:

- Bilirubin 40 mg/dL
- Hemoglobin 2000 mg/dL
- Triglyceride 1250 mg/dL

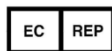
### REFERENCES

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### SYMBOLS EXPLANATIONS

	Consult instructions for use		Manufacturer
	Temperature limit (Store at 2-8 °C)		Use-by date
	Contains sufficient for		Keep away from sunlight
	This way up		Authorized representative in the European Community
	In vitro diagnostic medical device		Kit components
	Catalogue number		Batch code