MAGLUMI FSH (CLIA)

Keep upright for storage

REF 130202001M

Σ 100

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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 Europe
	Manufacturer
	Attention. See Instructions For Use
CONT	Contents of kit
IVD	In vitro diagnostic medical device (In vitro diagnostic use)
LOT	Lot number
REF	Catalogue Code
	Expiry date (Use by…)
8°C 2°C	Temperature limitation (store at 2-8°C)
Σ	Number of tests
	Keep away from direct sunlight

INTENDED USE

The kit has been designed for the quantitative determination of follicular-stimulating hormone (FSH) in human serum.
The method can be used for samples over the range of 0-400 mIU/ml.
The test has to be performed on the MAGLUMI chemiluminescence immunoassay (CLIA) fully auto analyzer (Including MAGLUMI 1000, MAGLUMI 2000, MAGLUMI 2000 Plus and new developed models).

SUMMARY AND EXPLANATION OF THE TEST

Follicle-stimulating hormone (FSH) is made by the pituitary gland in the brain. Control of FSH production is a complex system involving hormones produced by the gonads (ovaries or testes), the pituitary, and the hypothalamus.
In women, FSH stimulates the growth and maturation of eggs (follicles) in the ovaries during the follicular phase of the menstrual cycle. The menstrual cycle is divided into the follicular and the luteal phases, characterized by a mid-cycle surge of FSH and luteinizing hormone (LH). Ovulation occurs shortly after this mid-cycle surge of hormones. During the follicular phase, FSH initiates the production of estradiol by the follicle, and the two hormones work together in the further development of the egg follicle. During the luteal phase, FSH stimulates the production of progesterone. Both estradiol and progesterone help the pituitary control the amount of FSH produced. FSH also facilitates the ability of the ovary to respond to LH. At the time of menopause, the ovaries stop functioning and FSH levels rise. In men, FSH stimulates the testes to produce mature sperm and also promotes the production of androgen binding proteins. FSH levels are relatively constant in males after puberty.
In infants and children, FSH levels rise shortly after birth and then fall to very low levels by 6 months in boys and 1-2 years in girls. Concentrations begin to rise again before the beginning of puberty and the development of secondary sexual characteristics.
FSH is often used in conjunction with other tests (LH, testosterone, estradiol, and progesterone) in the workup of infertility in both men and women. FSH levels are used to help determine the reason a man has a low sperm count. FSH levels are also useful in the investigation of menstrual irregularities and to aid in the diagnosis of pituitary disorders or diseases involving the ovaries or testes. In children, FSH and LH are used to diagnose delayed or precocious (early) puberty.
In women and men, FSH and LH are ordered as part of the workup of infertility and pituitary or gonadal disorders.
FSH may be ordered when a woman's menstrual cycle has stopped or become irregular, to determine if the woman has entered menopause.
In children, FSH and LH may be ordered when a boy or girl does not appear to be entering puberty at an appropriate age (either too late or too soon). Signs of early (precocious) puberty may include:
1) Breast enlargement in females;
2) Growth of pubic hair
3) Genitalia growth in males
4) Beginning of menstruation in females
Irregular timing of puberty may be an indication of a more serious problem involving the hypothalamus, the pituitary gland, the gonads (ovaries or testes), or other systems. The measurement of LH and FSH may help differentiate between benign symptoms and true disease. Once it is established that symptoms are a result of true disease, further testing can be done to discern the underlying

cause.
FSH results can be increased with use of cimetidine, clomiphene, digitalis, and levodopa. FSH results can decrease with oral contraceptives, phenothiazines, and hormone treatments. FSH has been reported to increase with age and in smokers.

PRINCIPLE OF THE TEST

Sandwich immunoluminometric assay:
Use an anti-FSH monoclonal antibody to label ABEI and use another monoclonal antibody to label FITC. Sample, Calibrator or Control are mixed thoroughly with ABEI Label, FITC Label and magnetic microbeads coated with anti-FITC in a cuvette incubated at 37℃, forming a sandwich; After sediment in a magnetic field, suck the supernatant and then cycle wash it for 1 time. Subsequently, Starter 1+2 substrates 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 FSH present in controls or 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 sheep anti-FITC polyclonal antibody.	2.5ml
Calibrator Low : bovine serum, 0.2%NaN_3	3.0ml
Calibrator High : bovine serum, 0.2%NaN_3	3.0ml
FITC Label: anti-FSH monoclonal antibody labeled FITC, containing BSA, 0.2%NaN_3.	10.5ml
ABEI Label: anti-FSH monoclonal antibody labeled ABEI, containing BSA, 0.2%NaN_3.	10.5ml
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, gently and carefully horizontally 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 components 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 direct sunlight.

TRACEABILITY AND CALIBRATION

1)Traceability

To perform an accurate calibration, we have provided the test calibrators standardized against the W.H.O 2nd International Reference Preparation 78/549

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 lots (Reagent Integral or Starter Reagents).
- Every 4 weeks and/or each time a new Integral is used (recommended).
- After each servicing of the MAGLUMI Fully Auto analyzer.
- If controls are beyond the expected range.

SPECIMEN COLLECTION AND PREPARATION

Sample material: serum
Collect samples using standard procedures.
Store at 2-8℃: 24 hours, for longer storage periods: freeze to below - 20℃
Avoid repeated freezing and thawing cycles, 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.
- be cautious 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 separator, red blood cells or clot. Specimens removed from the separator gel, cells or clot may be stored up to 24 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 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

IVD

- 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 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 make sure 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 Maglumi Fully Auto analyzer. Each test parameter is identified via a RFID tag on the Reagent Integral. For further information please refer to the Maglumi Fully Auto Operator's Manual.

80μl	Sample, calibrator or controls
+80μl	ABEI Label
+80μl	FITC Label
+20μl	Nano magnetic microbeads
15 min	Incubation
400μl	Cycle wash
3 s	Measurement

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 must be processed.

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

FSH assay values may only be interpreted in context with the clinical picture and other diagnostic procedures.

2) Interfering Substances

No interference with test results is seen by concentrations of bilirubin＜0.06mg/ml, haemoglobin＜16mg/dl or triglycerides＜12.5mg/ml.

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.

4) High-Dose Hook

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For

the MAGLUMI FSH assay, no high dose hook effect was observed when samples containing up to 3,000 mIU/ml.

RESULTS

1) Calculation of Results

The analyzer automatically calculates the FSH 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 mIU/ml. For further information please refer to the MAGLUMI® Chemiluminescence Analyzer Operating Instructions.

2) Interpretation of Results

- Reference values:

  Male：1.5-11.8mIU/ml

  Female： Follicular phase 3.2-15mIU/ml
  ovulatory phase 7.5-20mIU/ml
  luteal phase 1.3-11mIU/ml
  postmenopause 36-138mIU/ml
- Results may differ between laboratories due to variations in population and test method. 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(mIU/ml)	SD(mIU/ml)	CV%
Level 1	5.62	0.29	5.09%
Level 2	21.04	1.10	5.23%
Level 3	41.83	2.02	4.83%

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(mIU/ml)	SD(mIU/ml)	CV%
Level 1	5.78	0.50	8.73%
Level 2	20.56	1.79	8.69%
Level 3	41.67	3.75	9.01%

2) Analytical Sensitivity

The sensitivity is defined as the concentration of FSH 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 0.1mIU/ml.

3) Specificity

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

Compound	Concentration	Cross reactivity
LH	200 mIU/ml	0.8%
HCG	500 mIU/ml	1%

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
94.574 mIU/ml	93.2mIU/ml	98.3%

5) Linearity

Use FSH 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 mIU/ml	Absolute linear correlation coefficient (r)
A	0	
B	2	r=0.9880
C	10	
D	20	
E	50	
F	150	

6)Method comparison Reference values:

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

Linear regression

y=1.01x-5.92

r=0.97

Sys.x=12.3

Number of samples measured:200

The sample concentrations were between 0.5-360.58mIU/ml

REFERENCES

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