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Luteinizing Hormone (CLIA) PACKAGE INSERT

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INTENDED USE

Luteinizing Hormone (CLIA) is a Chemiluminescence Immunoassay test for the quantitative measurement of circulating Luteinizing Hormone (LH) in human serum or plasma, which is intended as an aid to diagnosis of Pituitary endocrine function.
The assay can be used for samples over the range of 0.1mIU/mL～200 mIU/mL
The test must to be performed at the ACCRE series analyzers (including ACCRE 6, ACCRE 8, ACCRE 90, ACCRE 100, ACCRE 120 and other ACCRE series analyzers).

For *in vitro* diagnostic use only. For professional use only.

SUMMARY AND EXPLANATIONS

Human Luteinizing Hormone (LH, lutropin) is a glycoprotein hormone with two dissimilar subunits (α and β). The α -subunit is essentially identical to the α-subunits of follicle stimulating hormone (FSH, follitropin), thyroid stimulating hormone (TSH, thyrotropin), and human chorionic gonadotropin (hCG). It is the differences in the β-subunit of these glycoproteins which contributes to immunological and physiological specificity.
LH, together with FSH, is secreted by the gonadotroph cells in the pituitary in response to the secretion of the gonadotropin releasing hormone (LHRH, GnRH) from the medial basal hypothalamus. Ovarian steroids, principally estrogens, modulate the secretion of LH and FSH which in turn regulate the menstrual cycle in females. When the follicle, and the ovum contained within it, reach maturity, a surge of LH causes the follicle to rupture releasing the ovum. The follicular remnant is transformed into a corpus luteum, which secretes progesterone and estradiol. During the follicular and luteal phases, LH concentrations are much lower than the levels observed at the time of the LH surge. During the follicular and luteal phases, the estrogens exert a negative feedback on the release of LH. Shortly before the mid-cycle surge in LH, ovarian steroids, specifically estradiol, exert a positive feedback on the release of LH.
Determination of the concentration of LH is essential for the prediction of ovulation, in the evaluation of infertility, and the diagnosis of pituitary and gonadal disorders. Increasing concentrations of LH precede ovulation and in cases in which the period of optimal fertility needs to be defined for the timing of intercourse or artificial insemination, daily concentrations of LH are important for the prediction of ovulation. More frequent sampling is required if the precise time of follicular rupture is needed for egg aspiration for in vitro fertilization.

ASSAY PRINCIPLES

The principle of Luteinizing Hormone (CLIA) hereinafter also referred to as the "LH" combines a two-sites immunoassay sandwich method with enzyme catalytic chemiluminescence detection (CLIA). The principle is described as following:
Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent cartridges. All of the assay steps are performed automatically by the ACCRE analyzer.
The sample is manually pipetted into the sample well of reagent cartridge. The sample and the mouse anti-LH monoclonal antibody labeled alkaline phosphatase are added to the magnetic beads coated with the mouse anti-LH monoclonal antibody, and after mixing and incubation, the antigen in the sample and the antibody on the magnetic beads and the antibody labeled alkaline phosphatase binds to form an antibody-antigen complex.
After the reaction is completed, the magnetic field adsorbs the magnetic beads and the unbound material is removed by washing. After the reaction substrate is added, the luminescence intensity is measured by a photomultiplier tube. The concentration of the substance to be detected in the sample is proportional to the intensity of the luminescence. At the end, the results were automatically calculated by the ACCRE analyzer in relation to the calibration curve stored.

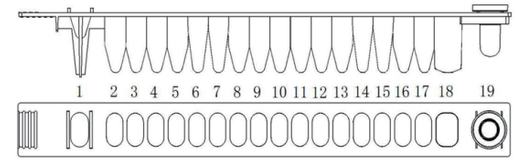
CONTENT OF THE KIT

Package: 60tests/kit with quality controls, 36 tests/kit with quality controls, 60 tests/kit without quality controls, 36 tests/kit without quality controls
The calibration kit has been traced to the national standard 150531 for Luteinizing Hormone immunoassay. The exact calibrator concentration values are detailed in the Calibrator Barcode Sheet.

Contents	Quantities				Notice
	REF W42A	REF W42C	REF W50A	REF W50C	
LH reagent cartridge	60 strips	36 strips	60 strips	36 strips	Ready to Use
LH Calibrator 1 (CAL1)	1.0 mL x 1 vial	1.0 mL x 1 vial	1.0 mL x 1 vial	1.0 mL x 1 vial	Phosphate buffer, 50mM; ProClin300, 0.48g/L; BND, 0.2g/L
LH Calibrator 2 (CAL2)	1.0 mL x 1 vial	1.0 mL x 1 vial	1.0 mL x 1 vial	1.0 mL x 1 vial	Phosphate buffer, 50mM; ProClin300, 0.48g/L; BND, 0.2g/L; LH recombinant protein, 5mIU/mL
LH Calibrator3 (CAL3)	1.0 mL x 1 vial	1.0 mL x 1 vial	1.0 mL x 1 vial	1.0 mL x 1 vial	Phosphate buffer, 50mM; ProClin300, 0.48g/L; BND, 0.2g/L; LH recombinant protein, 50mIU/mL
LH Quality Control Level 1 (QC1)	1.0 mL x 1 vial	1.0 mL x 1 vial	/	/	Phosphate buffer, 50Mm; ProClin300, 0.48g/L; BND, 0.2g/L; LH recombinant protein, 10mIU/mL Only for the configuration with Quality Controls
LH Quality Control Level 2(QC2)	1.0 mL x 1 vial	1.0 mL x 1 vial	/	/	Phosphate buffer, 50mM; ProClin300, 0.48g/L; BND, 0.2g/L; LH recombinant protein, 40mIU/mL Only for the configuration with Quality Controls
Instruction for Use	1	1	1	1	N/A
Reagent Registration Card	1	1	1	1	N/A
Calibrator Barcode Sheet	1	1	1	1	N/A
Quality Control Sheet	1	1	/	/	Only for the configurations with Quality Controls

Note: Refer to the target value list of the controls from Quality Control Sheet within the kit.

Reagent Cartridge
The strip consists of 19 wells. The 1st well is the sample well and the last well 19th is the reading well for chemiluminescent signal. From the 2nd to the 18th well are all covered with a label, aluminum foil seal. The label comprises a barcode which mainly indicates the reagent assay information, reagent lot number and expiration date. All reagents components needed for the assay are ready-to-use and pre-dispensed in the cartridges. And please do not interchange integral component from different reagents or lots.



Description of The Reagent Cartridge

Well	Component	Content	Volume
5	Enzyme Label(R2)	ALP (alkaline phosphatase) labeled anti-LH antibody (Rat), 3.0mg/L; MES buffer, 50mmol/L; ProClin300, 0.48g/L; BND, 0.2g/L	50μL
7	Magnetic Particles(R1)	Anti-LH antibody coated magnetic particles, 0.15g/L; Tris buffer, 50mmol/L; ProClin300, 0.48g/L; BND,0.2g/L	50μL
10, 11, 12, 14	Wash Solutions	Tris buffer, 50mmol/L; ProClin300, 0.48g/L; BND, 0.2g/L	350μL
16	Substrate	APS-5	100μL

Note: Well 1, 2, 3, 4, 6, 8, 9, 13, 15, 17, 18 are empty.

MATERIALS AND DISPOSABLES REQUIRED BUT NOT PROVIDED

- Pipette with disposable tip to dispense 200μL.
- Powderless, disposable gloves.
- For other specific materials and disposables, please refer to the Instrument User Manual.
- Instruments of the ACCRE series analyzers.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- For professional use only by qualified laboratory personnel.
- This kit contains products of animal origin. Certified knowledge of the origin and/or sanitary state of the animals does not totally guarantee the absence of transmissible pathogenic agents. It is therefore recommended that these products be treated as potentially infectious, and handled observing the usual safety precautions (do not ingest; do not inhale)
- Do not use reagents after the expiration date indicated on the box label.
- Do not use if the packaging of reagent cartridge is damaged or leaked.
- Do not use the reagents if the quantity is obviously insufficient.
- If any component adheres to inside wall of wells or aluminum film of the reagent cartridge, please gently switch the reagent cartridge to let the component back the wells.
- Do not reverse the reagent cartridge. Otherwise, the result will be unreliable.
- Do not mix reagents (or disposables) from different lots.
- 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.
- Use powderless gloves, as powder has been reported to cause false results for certain enzyme immunoassay tests.

STORAGE

- Store the Luteinizing Hormone (CLIA) kits including reagent cartridges, calibrators and quality controls **upright** at 2~8°C in dark place and the kit can be valid for 18 months from manufactured date..
- After the reagent cartridge is on-board in the ACCRE analyzer, the testing should be finished within 2 hours.
- When opened, the calibrators will be stable for 30 days at 2~8°C, and 3 months at -20°C and below -20°C. Calibrators can only be frozen and thawed once. Quality controls will be stable for 30 days at 2~8°C.

SAMPLES

The sample volume for Luteinizing Hormone (CLIA) assay is 50μL, please note that at least 70μL of sample has to be pipetted manually into the reagent cartridge.

Sample Type and Sample Collection
Human serum or plasma (Heparin sodium, EDTA-K_2 or EDTA-K_3) are recommended.
Types of tubes:
- Plastic tube with clot activator,
- Plastic tube with clot activator and separation gel,
- Plastic tube with Heparin sodium,
- Plastic tube with EDTA-K_2,
- Plastic tube with EDTA-K_3.

It is recommended to validate collection tubes before using them as some may contain substances which interfere with test results.
Note: Blood sampling tube results may vary from one manufacturer to another depending on the materials and additives used.
It is the responsibility of each laboratory to validate the type of sample tube used and to follow the manufacturer's recommendations for use.

Sample Preparation
The current revision of the WHO/DIL/LAB/99.1 document provides recommendations for the preparation of samples.
For use of the sample tubes, follow the tube manufacturer's instructions for use.
The pre-analytical step, including the preparation of blood samples, is an essential part of medical analyses. In accordance with Good Laboratory Practice, this step is performed under the responsibility of the laboratory manager.
Insufficient clot time can result in the formation of fibrin with micro-clots that are invisible to the naked eye. The presence of fibrin, red blood cells, or suspended particles can lead to erroneous results.
Samples containing suspended fibrin particles or erythrocyte stroma should be centrifuged before testing.
If there is a lipid layer over the sample after centrifuging, please transfer the clear sample into a new sample tube without transferring the lipid layer.
Severe hemolysis samples (hemoglobin >500mg/dL) or heat-inactivated samples are not recommended for applying on the reagents.
Preparation of frozen-stored samples: after thawing, these samples must be thoroughly mixed before testing.
Mix using with a vortex-type mixer. If necessary, clarify samples by centrifuging before testing.

Sample Stability
Samples (serum and plasma) can be stored at 15-30°C for up to 4 hours or at 2~8°C for up to 24 hours; if longer storage is required, freeze the serum or plasma at -20°C or below -20°C for up to 6 months, without exceeding 1 freeze/thaw cycle.

INSTRUCTIONS FOR USE

For complete instructions, see the Instrument User Manual.
When using the assay for the first time. Register the assay using the registration code in the reagent kit before any assay is used in the ACCRE analyzer for the first time. Calibration, QC and sample test are only available after assay was registered successfully.
When opening a new lot of reagents. Each new lot of reagent must be registered by using the registration code in Reagent Registration Card within the reagent kit.

Calibration
Calibration must be performed with the reagents and calibrators from Manufacturer.
Calibration is necessary under the following conditions:
(1) New reagent lot number applied;
(2) Same lot of reagents used more than 4 weeks;
(3) Quality Control out of control;
(4) When necessary, for example: system maintenance or repair that may affect the

analytic performance.

Test Procedure

1. Remove the kit from storage at 2-8°C and take out the required number of reagent cartridge. Allow the reagent cartridges, specimens, calibrators, and/or controls to equilibrate to room temperature (15-30°C) prior to testing.
2. Use each assay LH strips for each sample, calibrator or control respectively.
3. Place the reagent cartridge into the reagent rack.
4. Manually pipette the Sample, Calibrator, or Controls into the sample well of each reagent cartridge

Please note that at least 70μl of sample has to be pipetted manually into the reagent cartridge and 50μL sample is needed for each test.

** Before pipetting: Mix the samples using a vortex-type mixer if necessary, and ensure that the samples and sample diluent (if applicable) DO NOT have any bubbles. The same for calibrators and controls.*

5. Put the sample rack into the reagent chamber of the ACCRE analyzer.
6. Place the assay tips into the reagent chamber of the ACCRE analyzer.
7. Input Sample ID, sample type etc. into the software as directed in the USER MANUAL.
8. Luteinizing Hormone (CLIA) assay will be completed within approximately 15 minutes. Assays will be performed automatically by the ACCRE analyzer.
9. After the assay is completed, remove the reagent rack from the ACCRE analyzer. Dispose the used reagent cartridge into an appropriate recipient.

Quality Control

Quality control can be performed in accordance with local regulations or requirements related to accreditation, as well as requirements defined in the laboratory's quality control procedure.

RESULTS AND INTERPRETATION

Calculation of Results

The results are automatically calculated by the ACCRE analyzer using stored calibration curve which generate by 3-point calibration, and calculated according to a predefined mathematical model, the results expressed in mIU/mL.

Interpretation of Results

The detection range is from 0.1mIU/mL～200mIU/mL. For samples with LH below the upper limit of detection, quantitative determination can be performed; if the sample is lower than the lower limit of detection, the reported result is <0.1mIU/mL; if the sample is higher than the upper limit of detection, the reported result is >200mIU/mL.

Results of Luteinizing Hormone (CLIA) assays are determined by testing serum specimens from a study in clinical centers with group of totally 716 healthy adult individuals in China (138 male and 578 female). The2.5th - 97.5th percentile value is as follows:

Group		Cases	2.5th - 97.5th Percentile value（mIU/mL）
Healthy Males		138	1.562-8.893
Healthy Females	Follicular Phase	135	2.148-13.01
	Period of Ovulation	147	12.93-92.57
	Luteal Phase	142	1.084-12.39
	Post menopause	154	8.046-56.72

** Please note that results may differ between laboratories due to variations in population and test method. If necessary, each laboratory should establish its own reference range.*

In interpreting the results, patient's clinical condition including symptoms, diseases history, and other relevant data and information should be considered.

LIMITATIONS

1. If the test results are inconsistent with clinical evidence, additional other testing is suggested to confirm the result.
2. For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
3. Please note that heterophile antibody in human serum or plasma can interfere the test result.
4. High concentration of HAMA can also cause a false positive or false negative result.

PERFORMANCE CHARACTERISTICS

Detection limits

LOB (Limit of Blank) = 0.1mIU/mL.
LOB was determined according to CLSI® EP17-A2 recommendations.

Measurement range

The measurement range is the range of values corresponding to the acceptable performance limits (precision and linearity).

The measurement range of the Luteinizing Hormone (CLIA) assay is: 0.1mIU/mL ~ 200 mIU/mL.

Linearity

Linearity was evaluated according to CLSI® EP06-A recommendations.
The Luteinizing Hormone (CLIA) assay is linear between 0.2mIU/mL to 200mIU/mL.
The absolute linear correlation coefficient (r) should be bigger than 0.9900.

Precision

A precision study was performed according to CLSI® EP05-A3 recommendations.
The Within-lot precision CV% is less than 8.0%.
The between-lot precision CV% is less than 15.0%.

Accuracy

The sample which is a control product with trueness traceability is used for the detection, and the relative deviation between the detection result and the calibration concentration is within ±10%.

Specificity

No significant cross-reactivity was observed when TSH (200μIU/mL), FSH (200mIU/mL), or HCG (2000mIU/mL) were added to the LH Calibrator CAL1 respectively. The results of LH in these samples were less than 0.1mIU/mL.

Interference

Potential interference substances was studied according to CLSI® EP07-A3 recommendations. No significant interference was detected up to the maximum concentrations tested.

Substance	Concentration
Hemoglobin	≤500mg/dL
Bilirubin	≤20 mg/dL
Triglyceride	≤1500 mg/dL
Total Protein	≤10 g/dL
Rheumatoid factors	≤1000 IU/mL

Hook effect

No hook effect was found up to LH concentrations of 1000 mIU/mL.

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.

WASTE DISPOSAL

Dispose used or unused reagents as well as any other contaminated disposable materials following procedures for infectious or potentially infectious products.
It is the responsibility of each laboratory to handle waste and effluents produced according to their nature and degree of hazardousness and to treat and dispose of them (or have them treated and disposed of) in accordance with any applicable regulations.

INDEX OF SYMBOLS

Symbol	Meaning	Symbol	Meaning	Symbol	Meaning
	Consult instructions for use		Contains sufficient for <n> tests		Date of manufacture
IVD	*In vitro* diagnostic medical device		Use-by date		Do not re-use
	Temperature limit	LOT	Batch code	REF	Catalogue number
	Keep away from sunlight		Keep dry		Manufacturer
EC REP	Authorized representative in the European Community/ European Union		Do not use if package is damaged and consult instructions for use	BIO	Contains biological material of animal origin
	Biological risks		Caution	CE	CE marking
	Upright		Fragile, handle with care		Do not roll
CONTROL	Control				

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