QDx Instacheck™ LH

INTENDED USE

QDx Instacheck™ LH along with **QDx Instacheck™ Reader** is a fluorescence immunoassay that quantifies concentration of Luteinizing hormone (LH) in human serum/plasma. It is useful as an aid in management and monitoring of determination of evaluating fertility issues, function of reproductive organs (ovaries or testicles), or detection of the ovulation.

INTRODUCTION

Human luteinizing hormone (LH, lutropin) is a glycoprotein hormone with two dissimilar subunits (α and β). LH has a molecular weight of approximately 29,000 daltons.[1] The α-subunit of LH contains 92 amino acid residues and is essentially identical to the β-subunits of follicle stimulating hormone (FSH, follitropin), thyroid stimulating hormone (TSH, thyrotropin), and human chorionic gonadotropin (hCG).[1-4] The β-subunit of LH contains 112 amino acid residues and is considerably different from that of FSH and TSH.[1,4,5] However, the β-subunits of LH and hCG are very similar. The structural similarities between LH and hCG are responsible for the observed similarity in biological properties.[1,5,6] In the female, hLH stimulates the final maturation of the follicle, follicular rupture, and ovulation.[7] Human LH is secreted by the gonadotropic cells of the anterior lobe of the pituitary gland in response to gonadotropin releasing hormone (GnRH) from the medial basal hypothalamus. Both hLH and hFSH are secreted in a pulsatile nature; however, this is less noticeable for hFSH perhaps due to the longer half-life in the circulation.[7] In a normal menstrual cycle negative feedback by estradiol suppresses hLH secretion in the follicular phase. As the follicle develops (in response to hFSH) estradiol production increases which triggers an increase in GnRH and an increased sensitivity of the pituitary to GnRH. A GnRH surge results in the preovulatory (mid-cycle) surge of hLH and ovulation. Following this surge, hLH is suppressed during the luteal phase due to negative feedback from progesterone and estradiol.[7-9] Variation in cycle lengths are observed in normally menstruating females due to variations in the length of the follicular phase. In the menopausal female, hLH levels are elevated in response to decreased production of ovarian estrogens and progestogens, which eliminates the negative feedback mechanism on the pituitary gland. As a result, ovulation and menstrual cycles decrease and eventually cease.[10] In the male, hLH is often referred to as interstitial cell-stimulating hormone and influences the production of testosterone by the Leydig cells of the testes.[11] At menopause, or following ovariectomy in women, concentrations of estrogens decline to low levels. The lowered concentrations of estrogens result in a loss of the negative feedback on gonadotropin release. The consequence is an increase in the concentrations of LH and FSH.[12,13,14] Concentrations of hLH and hFSH are commonly determined in investigations of menstrual cycle, fertility, and pubertal developmental abnormalities, such as premature ovarian failure, menopause, ovulatory disorders and pituitary failure.[15] The ratio of hLH/hFSH has been used to assist in the diagnosis of polycystic ovary disease. Low concentrations of hLH and hFSH may indicate pituitary failure while elevated concentrations of hLH and hFSH along with decreased concentrations of gonadal steroids may indicate gonadal failure (menopause, ovariectomy, premature ovarian syndrome, Turners Syndrome).[16] Low concentrations of gonadotropin are usually observed in females taking oral steroid based contraceptives.[17] In the male, elevated hLH and hFSH with low concentrations of gonadal steroids may indicate testicular failure or anorchia. In Klinefelter's syndrome hLH may be elevated due to Sertoli cell failure.[18]

PRINCIPLE

The test uses a sandwich immunodetection method; the detector antibodies in the buffer bind to antigens in the sample, forming antigen-antibody complexes, and these migrate onto the nitrocellulose matrix to be captured by other immobilized-antibodies on the test strip.

The more antigens in the sample, the more antigen-antibody complexes are formed. This then leads to stronger intensity of the fluorescence signal, which is processed by **QDx Instacheck™ Reader** to produce LH concentration in the sample.

COMPONENTS AND REAGENTS

QDx Instacheck™ LH consists of 'Cartridges', 'Detection Buffer Tubes' and an 'ID chip'.

- The cartridge contains a test strip, the membrane which has anti human LH at the test line, with rabbit IgG at the control line.
- Each cartridge is individually sealed in an aluminum foil pouch containing of a desiccant. 25 sealed cartridges are packed in a box which also contains an ID chip.
- The detection buffer contains anti human LH-fluorescence conjugate, anti rabbit IgG-fluorescence conjugate, bovine serum albumin (BSA) as a stabilizer and sodium azide as a preservative in CAPSO buffer.
- The detection buffer is pre-dispensed in a tube. 25 detection buffer tubes are packaged in a Box and further packed in a Styrofoam box with ice-packs for shipping.

WARNINGS AND PRECAUTIONS

- For in vitro diagnostic use only.
- Carefully follow the instructions and procedures described in this 'Instruction for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge, ID chip and detection buffer) must agree each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield misleading test result(s).
- Do not reuse. A detection buffer tube should be used for processing one sample only. So should a cartridge.
- The cartridge should remain sealed in its original pouch before use. Do not use the test cartridge, if is damaged or already opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with the regulations. Sample with severe hemolytic and hyperlipidemia cannot be used and should be recollected.
- Just before use, allow the test cartridge, detection buffer and sample to be at room temperature for approximately 30 minutes.
- **QDx Instacheck ™ LH** as well as **QDx Instacheck™ Reader** should be used away from vibration and/or magnetic field. During normal usage, it can be noted that **QDx Instacheck™ Reader** may produce minor vibration.
- Used detection buffer tubes, pipette tips and test cartridges should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.
- **QDx Instacheck™ LH** will provide accurate and reliable results subject to the following conditions.
  - **QDx Instacheck ™ LH** should be used only in conjunction with **QDx Instacheck™ Reader**.
  - Any anticoagulants other than **EDTA, sodium heparin, sodium citrate** should be avoided.

STORAGE AND STABILITY

- The test cartridge is stable for 20 months (while sealed in an aluminum foil pouch) if stored at 4-30 °C.
- The detection buffer pre-dispensed in a tube is stable for 20 months if stored at 2-8 °C.
- After the test cartridge pouch is opened, the test should be performed immediately.

LIMITATIONS OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result. The non-responsiveness of the antigen to the antibodies is most common where the epitope is masked by some unknown components, so as not to be detected or captured by the antibodies. The instability or degradation of the antigen with time and/or temperature may cause the false negative as it makes antigen unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician including clinical symptoms and other relevant test results.

SAMPLE COLLECTION AND PROCESSING

The test can be performed on human serum/plasma.

- It is recommended to test the sample within 24 hours after collection.
- The serum or plasma should be separated from the clot by centrifugation within 3 hours after the collection of whole blood. If longer storage is required, e.g. if the test could not be performed within 24 hours, serum or plasma should be immediately frozen below -20 °C. The freezing storage of sample up to 3 months does not affect the quality of results.
- Once the sample was frozen, it should be used one time only for test, because repeated freezing and thawing can result in the change test values.

MATERIALS SUPPLIED

REF **IFPC-5**

Components of QDx Instacheck™ LH

- Cartridge Box:
  - Cartridges 25
  - ID Chip 1
  - Instruction For Use 1
- Box containing Detection Buffer Tubes
  - Detection Buffer tubes 25

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **QDx Instacheck™ LH**. Please contact our sales division for more information.

- **QDx Instacheck™ Reader** REF FPRR010
- Thermal Printer

TEST SETUP

1. Check the components of **QDx Instacheck™ LH**: Sealed Cartridge, ID Chip, Detection Buffer Tube.
2. Ensure that the lot number of the test cartridge matches with that of the ID chip as well as the detection buffer tube.
3. Keep the test cartridge and detection buffer tube at room temperature for at least 30 minutes just prior to performing the test. Place the cartridge on a clean, dust-free and flat surface.
4. Turn on power supply of the **QDx Instacheck™ Reader**.
5. Insert the ID chip into the 'ID Chip Port' of the **QDx Instacheck™ Reader**.
6. Press 'Select' button on the **QDx Instacheck™ Reader**. (*Please refer to the '**QDx Instacheck™ Reader** Operation Manual' for complete information and operating instructions.*)

TEST PROCEDURE

[Single mode]

1. Transfer 150 µL (Human serum/plasma/control) of sample using a transfer pipette to a tube containing the detection buffer.
2. Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
3. Pipette out 75 µL of a sample mixture and load it into the sample well on the cartridge.
4. For scanning the sample-loaded cartridge, insert it into the test cartridge holder of the **QDx Instacheck™ Reader**. Ensure proper orientation of the test cartridge before pushing it all the way inside the cartridge holder. An arrow has been marked on the cartridge especially for this purpose.
5. Press 'Select' button on the **QDx Instacheck™ Reader** to start the scanning process .
6. **QDx Instacheck™ Reader** will start scanning the sample-loaded cartridge after 15 minutes.
7. Read the test result on the display screen of the **QDx Instacheck™ Reader**.

[Multi mode]

1. Transfer 150 µL (Human serum/plasma/control) of sample using a transfer pipette to a tube containing the detection buffer.
2. Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
3. Pipette out 75 µL of a sample mixture and load it into the sample well on the cartridge.
4. Leave the sample-loaded cartridge at room temperature for 15 minutes.
5. For scanning the sample-loaded cartridge, insert it into the test cartridge holder of the **QDx Instacheck™ Reader**. Ensure proper orientation of the test cartridge before pushing it all the way inside the test cartridge holder. An arrow has been marked on the test cartridge especially for this purpose.
6. Press 'Select' button on the **QDx Instacheck™ Reader** to start the scanning process.
7. **QDx Instacheck™ Reader** will start scanning the sample-loaded test cartridge immediately.
8. Read the test result on the display screen of the **QDx Instacheck™ Reader**.

INTERPRETATION OF TEST RESULT

- **QDx Instacheck™ Reader** calculates the test result automatically and displays LH concentration of the test sample in terms of mIU/mL.
- The cut-off (reference range)

Type		mIU/mL
Males		1.0 – 8.0
Females	Follicular phase	1.0 – 12.0
	Ovulatory phase	17.0 – 77.0
	Luteal phase	0.0 – 15.0
Postmenopausal		11.0 – 40.0

- Working range : 1.0 - 100.0 mIU/mL

QUALITY CONTROL

- Quality control tests should be performed as a part of the good testing practice to confirm the expected quality control results and validity of the assay as well as to ensure accuracy of the test results with clinical samples.
- A quality control test should be performed at regular intervals. Before testing a clinical sample using a new test lot, control reagents should be tested to confirm the test procedure, and to verify whether the test produces the expected quality control results. Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control reagents are not provided with **QDx Instacheck™ LH**. For more information regarding obtaining the control reagents, contact the technical section at **Diasys Diagnostics India Private Limited.**
- **Internal Control**: **QDx Instacheck™ LH** test has an in-built quality control indicator that satisfies the routine quality control requirements. This internal control test is performed automatically each time a clinical sample is tested. An invalid result from the internal control leads to display an error message on the **QDx Instacheck™ Reader** indicating that the test should be repeated.

PERFORMANCE CHARACTERISTICS

1. **Specificity:** There, in test samples, are biomolecules such as below the table were added to the test sample(s) at concentrations much higher than their normal physiological levels in blood. **QDx Instacheck™ LH** test results did not show any significant cross-reactivity with these biomolecules.

Cross reactivity materials	Concentration of cross reactivity materials	Cross reactivity (%)
hCG	200,000 mIU/ml	0.5
FSH	1,000mIU/ml	N/D
PRL	1,000ng/ml	N/D
TSH	1,000uIU/ml	0.7

* ND : Not Detected

2. **Interference**: Study of interference from table below with **QDx Instacheck ™ LH** showed following results.

Interference materials	Concentration of interference materials	Interference (%)
D-glucose	600 mM/L	< 1.5
L-Ascorbic acid	2 mM/L	< 1.7
Bilirubin [unconjugated]	4 mM/L	< 4.3
Hemoglobin[human]	20 g/L	< 4.9
Cholesterol	130 mM/L	< 1.5
Triglyceride	100 mg/mL	< 6.9

3. **Precision**: The intra-assay precision was calculated by one evaluator, who tested different concentration of control standard ten times each with three different lots of **QDx Instacheck™ LH.** The inter-assay precision was confirmed by 2 different evaluators with 3 different lots, testing three times each different concentrations.

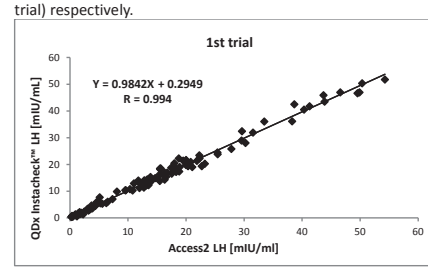
<Intra-assay>

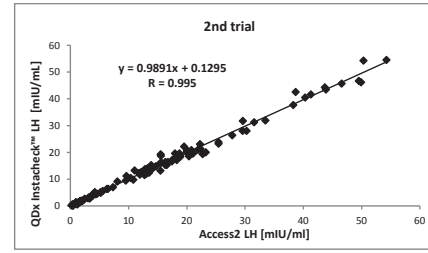
LH [mIU/mL]	Lot 1	Lot 2	Lot 3	AVG	SD	CV (%)
3.0	2.86	2.73	2.69	2.76	0.19	7.0
5.8	5.71	5.40	5.28	5.47	0.40	7.3
15.3	15.41	15.15	15.03	15.20	0.36	2.4
30.6	30.07	28.56	27.89	28.84	1.36	4.7

<Inter-assay>

LH [mIU/ml]	Lot 1	Lot 2	Lot 3	AVG	SD	CV (%)
3.0	2.76	2.68	2.65	2.70	0.22	8.3
5.8	6.10	5.78	5.63	5.84	0.49	8.5
15.3	15.66	14.99	14.36	15.00	1.16	7.7
30.6	30.12	29.16	28.53	29.72	1.29	4.4

4. **Comparability (Correlation):** LH concentrations of 117 serum samples were quantified independently with **QDx Instacheck™ LH** and Access2 (Beckman Coulter Inc. USA) as per prescribed test procedures. Test results were compared and their comparability was investigated with linear regression and coefficient of correlation (R). Linear regression and coefficient of correlation between the two tests were Y= 0.9842X + 0.2949 (1st trial), Y= 0.9891X + 0.1295 (2nd trial) and R = 0.994(1st trial), 0.995 (2nd trial) respectively.





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Note: Please refer to the table below to identify various symbols.

	Sufficient for <n> tests
	Read instruction for use
	Use by Date
LOT	Batch code
REF	Catalog number
	Caution
	Manufacturer
EC REP	Authorized representative of the European Community
IVD	In vitro diagnostic medical device
	Temperature limit
	Do not reuse
CE	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices

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