

LH

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Read Highlighted Changes
Revised February, 2007

This package insert must be read carefully prior to use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.



Key to symbols used	
REF	List Number
IVD	<i>In Vitro</i> Diagnostic Medical Device
	Store at 2-8°C
	CAUTION: Consult accompanying documents
SN	Serial Number
REAGENT LOT	Reagent Lot
	Expiration Date
	Abbott Laboratories Diagnostics Division Abbott Park, IL 60064 USA Manufacturer
EC REP	Authorized Representative
LOT	Lot Number
CAL 1	Calibrator (1,2)
CONTROL L	Control Low, Medium, High (L, M, H)
ASSAY CD-ROM	Assay CD-ROM
REACTION VESSELS	Reaction Vessels
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
REPLACEMENT CAPS	Replacement Caps

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NAME

ARCHITECT LH

INTENDED USE

The ARCHITECT LH assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of human luteinizing hormone (LH) in human serum and plasma.

SUMMARY AND EXPLANATION OF TEST

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).¹⁻⁴ The β -subunit is considerably different from that of FSH and TSH.^{1,4,5} However, the β -subunits of LH and hCG are very similar.^{1,5,6}

LH, together with FSH, is secreted by the gonadotroph cells in the pituitary^{5,7} in response to the secretion of the gonadotropin releasing hormone (LHRH, GnRH) from the medial basal hypothalamus.⁸⁻¹⁰ 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.¹¹⁻¹³

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.^{11,14} 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.¹⁵

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.^{11,15,16}

The primary role of LH in the male is to stimulate the production of testosterone by the Leydig cells. LH, through the production of testosterone together with FSH, regulates spermatogenesis in the Sertoli cells of the seminiferous tubules of the testes. Testosterone exerts a negative feedback on the release of LH.¹⁴

In sexually mature adults, gonadotropin deficiency is usually an early indication of the development of panhypopituitarism. Low concentrations of LH, FSH, and steroids are observed with this disorder. In contrast, gonadotropin secreting tumors of the hypothalamus and pituitary result in elevated concentrations of LH and FSH.¹⁵

Gonadal failure, a cause of infertility, is indicated by elevated concentrations of LH and FSH accompanied by low concentrations of gonadal steroids.^{11,14,15} In the female, elevated concentrations of LH can indicate primary amenorrhea,¹¹ menopause,^{11,15,16} premature ovarian failure,^{15,17} polycystic ovarian syndrome,^{17,18} hypergonadotropic hypogonadism,^{11,15} or ovulation. In the male, elevated concentrations of LH can result from primary testicular failure, seminiferous tubule dysgenesis (Klinefelter's syndrome), Sertoli cell failure, anorchia, or hypergonadotropic hypogonadism.^{19,20}

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT LH assay is a two-step immunoassay to determine the presence of luteinizing hormone in human serum and plasma using Chemiluminescent Microparticle Immunoassay (CMIA) technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample and anti- β LH coated paramagnetic microparticles are combined. LH present in the sample binds to the anti- β LH coated microparticles. After washing, anti- α LH acridinium labeled conjugate is added in the second step. Pre-Trigger and Trigger Solutions are then added to the reaction mixture; the resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of LH in the sample and the RLUs detected by the ARCHITECT *i* optical system.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100 Tests/500 Tests

NOTE: Some kit sizes are not available in all countries or for use on all Architect *i* Systems. Please contact your local distributor.

NOTE: Reagent Kit Configurations vary based on order.

ARCHITECT LH Reagent Kit (6C25)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL/27.0 mL) Anti- β LH (mouse, monoclonal) coated Microparticles in HEPES buffer with sucrose stabilizers. Preservative: antimicrobial agents.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL/26.3 mL) Anti- α LH (mouse, monoclonal) acridinium labeled Conjugate in MES buffer with protein (bovine) stabilizers. Minimum concentration: 85 ng/mL. Preservative: antimicrobial agents.

Manual Diluent

ARCHITECT *i* Multi-Assay Manual Diluent (7D82-50)

- **MULTI-ASSAY MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT *i* Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

NOTE: Bottle and volume varies based on order.

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: antimicrobial agent.

WARNINGS AND PRECAUTIONS

- **For *In Vitro* Diagnostic Use.**
- Package insert instructions must be followed accordingly. 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 are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens²¹. Biosafety Level 2²² or other appropriate biosafety practices^{23,24} should be used for materials that contain or are suspected of containing infectious agents.

- For product not classified as dangerous per European Directive 1999/45/EC **as amended** - Safety data sheet available for professional user on request.
- For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not mix reagents from different reagent kits.**
- Prior to loading the ARCHITECT LH Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
- Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- 2°C  8°C The ARCHITECT LH Reagent Kit must be stored at 2-8°C and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT LH Reagent Kit may be stored on-board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking on-board time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, you must initiate a scan to update the on-board stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results may be invalid and may require retesting. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT LH assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM prior to performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.
- The default result unit for the ARCHITECT LH assay is mIU/mL. An alternate result unit, IU/L, may be selected for reporting results by editing assay parameter "Result concentration units", to IU/L. The conversion factor used by the system is 1.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Human serum (including serum collected in serum separator tubes) or plasma collected in potassium EDTA may be used in the ARCHITECT LH assay. Other anticoagulants have not been validated for use with the ARCHITECT LH assay. Follow the tube manufacturer's processing instructions for serum or plasma collection tubes.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify the correct specimen types are used in the ARCHITECT LH assay.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, 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.
- For optimal results, serum and plasma 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.
- If testing will be delayed more than 24 hours, remove serum or plasma from the clot, serum separator or red blood cells. Specimens may be stored for up to 7 days at 2-8°C prior to being tested. If testing will be delayed more than 7 days, specimens should be frozen at -10°C or colder. Specimens stored frozen at -10°C or colder for 12 months showed no performance difference.
- Multiple freeze-thaw cycles of specimens should be avoided. 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.

- 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 may be shipped under thermally controlled refrigerated conditions or frozen (dry ice). Prior to shipment, it is recommended that specimens be removed from the clot, serum separator or red blood cells.

PROCEDURE

Materials Provided:

- 6C25 ARCHITECT LH Reagent Kit

ARCHITECT LH Reagent Kit **MUST** be used with matched Calibrators. If using Abbott Controls they must also be matched per labeling. Matching lot information is provided in a card supplied with each kit of reagents, calibrators and controls.

Materials Required but not Provided:

- ARCHITECT *i* System
- ARCHITECT *i* **ASSAY CD-ROM**
- 7G94-01 ARCHITECT LH Calibrators
- 6C25-10 ARCHITECT LH Controls
- 7D82-50 ARCHITECT *i* Multi-Assay Manual Diluent
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

Assay Procedure

- Before loading the ARCHITECT LH Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment:
 - Invert the microparticle bottle 30 times.
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
 - Once the microparticles have been resuspended, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Carefully snap the septum onto the top of the bottle.
 - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
- Order tests.
- Load the ARCHITECT LH Reagent Kit on the ARCHITECT *i* System. Verify that all necessary assay reagents are present. Ensure that septums are present on all reagent bottles.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation verify adequate sample cup volume is present prior to running the test.
 - Priority: 115 µL for the first LH test plus 65 µL for each additional LH test from the same sample cup
 - ≤ 3 hours onboard: 150 µL for the first LH test plus 65 µL for each additional LH test from the same sample cup
 - > 3 hours onboard: additional sample volume is required. Refer to the ARCHITECT System Operations Manual, Section 5 for information on sample evaporation and volumes.
- If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- ARCHITECT LH Calibrators and Controls should be mixed by gentle inversion prior to use.
- To obtain the recommended volume requirements for the ARCHITECT LH Calibrators and Controls, hold the bottles **vertically** and dispense 4 drops of each calibrator or 3 drops of each control into each respective sample cup.
- Load samples
 - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5

- Press RUN. The ARCHITECT *i* System performs the following function:
 - Moves the sample to the aspiration point
 - Loads a reaction vessel (RV) into the process path
 - Aspirates and transfers sample into the RV
 - Advances the RV one position and transfers microparticles into the RV
 - Mixes, incubates and washes the reaction mixture
 - Adds conjugate to the RV
 - Mixes, incubates and washes the reaction mixture
 - Adds Pre-Trigger and Trigger Solutions
 - Measures chemiluminescent emission to determine the quantity of LH in the sample
 - Aspirates contents of RV to liquid waste and unloads RV to solid waste
 - Calculates the result
- For information on ordering patient specimens, calibrators and controls, and general operating procedures refer to the ARCHITECT System Operations Manual, Section 5.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens with a LH value exceeding 250.00 mIU/mL are flagged with the code ">250.00" and may be diluted with the Manual Dilution Procedure.

- Manual dilutions should be performed as follows:
 - The recommended dilution for LH is 1:4. The manual dilution should not exceed 1:4.
 - For a 1:4 dilution, add 50 μ L of the patient specimen to 150 μ L of ARCHITECT *i* Multi-Assay Manual Diluent (7D82-50).
 - The reported result will be that of the diluted sample. This result (before dilution factor is applied) should be greater than 2 mIU/mL.

Calibration

- To perform an ARCHITECT LH calibration, test Calibrators 1 and 2 in duplicate. A single sample of all levels of LH controls must be tested to evaluate the assay calibration. Ensure that assay control values are within the concentration ranges specified in the package insert. Calibrators should be priority loaded.
- Calibration Range: 0.00 - 250.00.
- Once an ARCHITECT LH calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
 - A reagent kit with a new lot number is used
 - Controls are out of range
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT LH assay is a single sample of all control levels tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures. Ensure that assay control values are within the concentration ranges specified in the package insert.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT LH assay belongs to method group 6.

RESULTS

The ARCHITECT LH assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y weighted) to generate a calibration curve.

Alternate Result Units

- The default result unit for the ARCHITECT LH assay is mIU/mL. When the alternate result unit, IU/L, is selected, the conversion factor used by the system is 1.
- Conversion Formula: (Concentration in mIU/mL) x (1) = IU/L.

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- If the LH results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies.^{25,26} Additional information may be required for diagnosis.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.²⁷ Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.

EXPECTED VALUES

The suggested normal range for the ARCHITECT LH assay represents the LH values obtained from 130 normal males, 125 postmenopausal females (not on hormone replacement therapy), and 44 normal cycling females. For this study, the follicular phase was defined as the period of time from 10 to 4 days prior to the mid-cycle peak. The luteal phase was defined as the period of time from 4 to 10 days following the mid-cycle peak. Cycle days were synchronized to the mid-cycle peak, the day on which the LH concentration was most elevated. The results are presented in the following table.

	n	Median	LH Values (mIU/mL)	
			2.5 Percentile	97.5 Percentile
Males	130	2.75	1.14	8.75
Normally Menstruating Females				
Follicular Phase	148	4.21	2.39	6.60
Mid-Cycle Peak	44	31.58	9.06	74.24
Luteal Phase	138	3.60	0.90	9.33
Postmenopausal Females				
without HRT	125	26.45	10.39	64.57

It is recommended that each laboratory establish its own normal range.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

Precision was determined as described in National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-T2.²⁸ A three member calf serum based panel was assayed, using two lots of reagents, on two instruments, in replicates of two at two separate times per day for 20 days. Data from this study are summarized in the following table.

Note: Precision of this assay was designed to be ≤ 10 Total %CV. Data shown are representative and may vary from data obtained by your laboratory.

Panel Member	Reagent Lot	Instrument	n	Mean Conc. Value (mIU/mL)		Within Run		Total	
				Conc. Value	SD	%CV	SD	%CV	
1	1	1	80	5.07	0.108	2.1	0.170	3.4	
1	1	2	80	5.23	0.157	3.0	0.188	3.6	
1	2	1	80	5.24	0.162	3.1	0.215	4.1	
1	2	2	80	5.03	0.104	2.1	0.167	3.3	
2	1	1	80	38.14	0.738	1.9	1.191	3.1	
2	1	2	80	40.06	0.999	2.5	1.148	2.9	
2	2	1	80	41.43	0.976	2.4	1.297	3.1	
2	2	2	80	39.25	0.829	2.1	1.294	3.3	
3	1	1	80	73.18	1.527	2.1	2.282	3.1	
3	1	2	80	76.50	1.975	2.6	2.243	2.9	
3	2	1	80	79.21	1.957	2.5	2.668	3.4	
3	2	2	80	74.03	1.786	2.4	1.805	2.4	

Accuracy by Recovery

Accuracy by Recovery of this assay was designed to be $\pm 10\%$ of the spike level. Known concentrations of the World Health Organization (W.H.O.) Luteinizing Hormone (LH) Human, Pituitary 2nd International Standard 80/552 were added to 5 aliquots of human serum. The concentration of LH was determined using the ARCHITECT LH assay. The percent recovery was calculated to be within $\pm 10\%$ of spike level.

Analytical Sensitivity

The analytical sensitivity of the ARCHITECT LH assay was calculated to be better than 0.07 mIU/mL (n = 51 runs). Analytical sensitivity is defined as the concentration at two standard deviations from the mean RLU value of the ARCHITECT LH MasterCheck Level 0 (0.00 mIU/mL), and represents the lowest measurable concentration of LH that can be distinguished from zero.

Specificity

The specificity of the ARCHITECT LH assay was determined by studying the cross reactivity of FSH, TSH, and hCG. Aliquots of processed human serum were supplemented with 150 mIU/mL FSH, 100 µIU/mL TSH, and 200,000 mIU/mL hCG and assayed for LH. The cross reactivity was calculated as a percent cross reactivity and was shown to be 0.00% for FSH, 0.84% for TSH, and 0.00% for hCG.

Interference

Potential interference from hemoglobin, bilirubin, triglycerides, and protein was studied in the ARCHITECT LH assay. The ARCHITECT LH assay demonstrated the following interferences.

- Hemoglobin - ≤ 10% at 500 mg/dL
- Bilirubin - ≤ 10% at 20 mg/dL
- Triglycerides - ≤ 10% at 3000 mg/dL
- Protein - ≤ 10% at 4 g/dL and 11 g/dL

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