

REF			SYSTEM
11732234122	11732234501	100	cobas e 411 cobas e 601 cobas e 602

English

For use in the USA only

System information

For **cobas e 411** analyzer: test number 140

For **cobas e 601** and **cobas e 602** analyzers: Application Code Number 020

Intended use

Immunoassay for the in vitro quantitative determination of luteinizing hormone in human serum and plasma.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

Summary

LH (luteinizing hormone), together with FSH (follicle stimulating hormone), belongs to the gonadotropin family. LH and FSH regulate and stimulate the growth and function of the gonads (ovaries and testes) synergistically.^{1,2}

Like FSH, TSH and hCG, LH is a glycoprotein dimer consisting of 2 glycosylated noncovalently-linked subunits designated α and β . The α subunit is composed of 92 amino acids and is encoded on the long arm of chromosome 6. The β subunit is composed of 121 amino acids.³

In women, the gonadotropins act within the hypothalamus-pituitary-ovary regulating circuit to control the menstrual cycle.^{4,5}

LH and FSH are released in pulses from the gonadotropic cells of the anterior pituitary and pass via the bloodstream to the ovaries. Here the gonadotropins stimulate the growth and maturation of the follicle and hence the biosynthesis of estrogens and progesterones. The highest LH-concentrations occur during the mid-cycle peak and induce ovulation and formation of the corpus luteum, the principal secretion product of which is progesterone. In the Leydig cells of the testes, LH stimulates the production of testosterone.¹

Determination of the LH concentration is used in the elucidation of dysfunctions within the hypothalamus-pituitary-gonads system.

The determination of LH in conjunction with FSH is utilized for the following indications: congenital diseases with chromosome aberrations (e.g. Turner's syndrome), polycystic ovaries (PCO), clarifying the causes of amenorrhea, menopausal syndrome, and suspected Leydig cell insufficiency.^{6,7}

The Elecsys LH assay employs 2 monoclonal antibodies specifically directed against human LH. The 2 specific antibodies used recognize particular conformations, with the biotinylated antibodies detecting an epitope constructed from both subunits whereas the antibody with the ruthenium complex^{a)} label detects an epitope from the β -subunit. As a result, the Elecsys LH assay shows negligible cross-reactivity with FSH, TSH, hCG, hGH, and hPL.

a) Tris(2,2'-bipyridyl)ruthenium(II)-complex ($\text{Ru}(\text{bpy})_3^{2+}$)

Test principle

Sandwich principle. Total duration of assay: 18 minutes.

- 1st incubation: 20 μL of sample, a biotinylated monoclonal LH-specific antibody, and a monoclonal LH-specific antibody labeled with a ruthenium complex form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell/ProCell M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode or e-barcode.

Reagents - working solutions

The reagent rackpack is labeled as LH.

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-LH-Ab~biotin (gray cap), 1 bottle, 10 mL:
Biotinylated monoclonal anti-LH antibody (mouse) 2.0 mg/L; TRIS buffer 50 mmol/L, pH 8.0; preservative.
- R2 Anti-LH-Ab~ $\text{Ru}(\text{bpy})_3^{2+}$ (black cap), 1 bottle, 10 mL:
Monoclonal anti-LH antibody (mouse) labeled with ruthenium complex 0.3 mg/L; TRIS buffer 50 mmol/L, pH 8.0; preservative.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:

Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:

Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:



Warning

- H317 May cause an allergic skin reaction.

Prevention:

- P261 Avoid breathing mist or vapours.
- P272 Contaminated work clothing should not be allowed out of the workplace.
- P280 Wear protective gloves.

Response:

- P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
- P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

- P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

Avoid foam formation in all reagents and sample types (specimens, calibrators and controls).

Reagent handling

The reagents in the kit have been assembled into a ready-for-use unit that cannot be separated.

All information required for correct operation is read in from the respective reagent barcodes.

Storage and stability

Store at 2-8 °C.

Do not freeze.

Store the Elecsys reagent kit **upright** in order to ensure complete availability of the microparticles during automatic mixing prior to use.

Stability:	
unopened at 2-8 °C	up to the stated expiration date
after opening at 2-8 °C	12 weeks
on the analyzers	8 weeks

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Serum collected using standard sampling tubes or tubes containing separating gel.

Li-heparin, K₂-EDTA and K₃-EDTA plasma.

Criterion: Slope 0.9-1.1 + intercept within ± 0.3 mIU/mL + coefficient of correlation ≥ 0.95 .

Stable for 5 days at 20-25 °C, 14 days at 2-8 °C, 6 months at -20 °C (± 5 °C). Freeze only once.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Do not use heat-inactivated samples.

Do not use samples and controls stabilized with azide.

Ensure the samples, calibrators and controls are at 20-25 °C prior to measurement.

Due to possible evaporation effects, samples, calibrators and controls on the analyzers should be analyzed/measured within 2 hours.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- [REF] 03561097190, LH CalSet II, for 4 x 1.0 mL
- [REF] 09557423190, LH CalSet II, for 4 x 1.0 mL
- [REF] 11731416160, PreciControl Universal, for 4 x 3.0 mL
- General laboratory equipment
- cobas e** analyzer

Additional materials for the **cobas e** 411 analyzer:

- [REF] 11662988122, ProCell, 6 x 380 mL system buffer
- [REF] 11662970122, CleanCell, 6 x 380 mL measuring cell cleaning solution
- [REF] 11930346122, Elecsys SysWash, 1 x 500 mL washwater additive
- [REF] 11933159001, Adapter for SysClean
- [REF] 11706802001, AssayCup, 60 x 60 reaction cups
- [REF] 11706799001, AssayTip, 30 x 120 pipette tips
- [REF] 11800507001, Clean-Liner

Additional materials for **cobas e** 601 and **cobas e** 602 analyzers:

- [REF] 04880340190, ProCell M, 2 x 2 L system buffer
- [REF] 04880293190, CleanCell M, 2 x 2 L measuring cell cleaning solution

- [REF] 03023141001, PC/CC-Cups, 12 cups to prewarm ProCell M and CleanCell M before use
- [REF] 03005712190, ProbeWash M, 12 x 70 mL cleaning solution for run finalization and rinsing during reagent change
- [REF] 12102137001, AssayTip/AssayCup, 48 magazines x 84 reaction cups or pipette tips, waste bags
- [REF] 03023150001, WasteLiner, waste bags
- [REF] 03027651001, SysClean Adapter M

Additional material for all analyzers:

- [REF] 11298500160, ISE Cleaning Solution/Elecsys SysClean, 5 x 100 mL system cleaning solution

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Resuspension of the microparticles takes place automatically prior to use. Read in the test-specific parameters via the reagent barcode. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

Bring the cooled reagents to approximately 20 °C and place on the reagent disk (20 °C) of the analyzer. Avoid foam formation. The system automatically regulates the temperature of the reagents and the opening/closing of the bottles.

Calibration

Traceability: This method has been standardized against the 2nd International Standard (NIBSC) 80/552.

Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.

Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer).

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Renewed calibration is recommended as follows:

- after 1 month (28 days) when using the same reagent lot
- after 7 days (when using the same reagent kit on the analyzer)
- as required: e.g. quality control findings outside the defined limits

Quality control

Use PreciControl Universal or other suitable controls for routine quality control procedures.

Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

If necessary, repeat the measurement of the samples concerned.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

The analyzer automatically calculates the analyte concentration of each sample (either in mIU/mL or IU/L).

Limitations - interference

The effect of the following endogenous substances and pharmaceutical compounds on assay performance was tested. Interferences were tested up to the listed concentrations and no impact on results was observed.

Endogenous substances

Compound	Concentration tested
Bilirubin	$\leq 1129 \mu\text{mol/L}$ or $\leq 66 \text{ mg/dL}$
Hemoglobin	$\leq 0.621 \text{ mmol/L}$ or $\leq 1000 \text{ mg/dL}$

Compound	Concentration tested
Intralipid	≤ 1900 mg/dL
Biotin	≤ 205 nmol/L or ≤ 50 ng/mL
Rheumatoid factors	≤ 1500 IU/mL

Criterion: For concentrations from 0.100-20 mIU/mL the deviation is ± 2.5 mIU/mL. For concentrations from 20-200 mIU/mL the deviation is ± 10 %.

Samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

There is no high-dose hook effect at LH concentrations up to 1150 mIU/mL.

In vitro tests were performed on 17 commonly used pharmaceuticals. No interference with the assay was found.

Samples of neonates have not been tested with the Elecsys LH assay.

In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Limits and ranges

Measuring range

0.100-200 mIU/mL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.100 mIU/mL. Values above the measuring range are reported as > 200 mIU/mL.

Lower limits of measurement

Lower detection limit of the test

Lower detection limit: 0.100 mIU/mL

The Lower Detection Limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 2 standard deviations above that of the lowest standard (master calibrator, standard 1 + 2 SD, repeatability study, n = 21).

Dilution

Not necessary due to the broad measuring range.

Expected values

Studies with the Elecsys LH assay have revealed the following LH values:

Test subjects	N	LH mIU/mL		
		Percentile		
		50 th	5 th	95 th
Men	322	4.0	1.7	8.6
Women				
• Follicular phase	316	5.9	2.4	12.6
• Ovulation phase	56	30.8	14.0	95.6
• Luteal phase	280	4.3	1.0	11.4
• Postmenopause	132	29.1	7.7	58.5

LH/FSH quotient: Quotients have been calculated from the results obtained with the Elecsys LH assay and the Elecsys FSH assay in the samples of healthy women of child-bearing age. The following medians have been calculated:

Follicular phase: 0.82 (n = 315)

Luteal phase: 1.12 (n = 279)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using Elecsys reagents, pooled human sera, and controls in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days (n = 60); repeatability on MODULAR ANALYTICS E170 analyzer, n = 21. The following results were obtained:

cobas e 411 analyzer					
		Repeatability		Intermediate precision	
Sample	Mean mIU/mL	SD mIU/mL	CV %	SD mIU/mL	CV %
Human serum 1	0.54	0.01	1.8	0.03	5.2
Human serum 2	27.2	0.21	0.8	0.54	2.0
Human serum 3	50.7	0.41	0.8	1.01	2.0
PC ^{b)} Universal 1	9.38	0.11	1.1	0.19	2.0
PC Universal 2	44.8	0.42	0.9	0.83	1.9

b) PC = PreciControl

cobas e 601 and cobas e 602 analyzers						
		Repeatability			Intermediate precision	
Sample	Mean mIU/mL	SD mIU/mL	CV %	Mean mIU/mL	SD mIU/mL	CV %
Human serum 1	6.15	0.08	1.2	5.81	0.12	2.0
Human serum 2	92.2	0.68	0.7	89.1	1.47	1.6
Human serum 3	164	1.41	0.9	159	3.47	2.2
PC Universal 1	6.67	0.05	0.8	6.63	0.14	2.1
PC Universal 2	54.6	0.35	0.6	54.2	1.13	2.1

Method comparison

A comparison of the Elecsys LH assay (y) with the Enzygum-Test LH method (x) using clinical samples gave the following correlations:

Number of samples measured: 166

Passing/Bablok⁸ Linear regression

y = 1.09x - 0.46

y = 1.14x - 0.80

r = 0.929

r = 0.993

The sample concentrations were between 1.3 and 123 mIU/mL.

Analytical specificity

For the monoclonal antibodies used, the following cross-reactivities were found:

FSH, TSH, hCG, hGH, hPL < 0.1 %

References

- Franchimont P. Regulation of gonadal androgen secretion Horm Res 1983;18(1-3):7-17.
- Johnson MR, Carter G, Grint C, et al. Relationship between ovarian steroids, gonadotropin and relating during the menstrual cycle. Acta Endocrinol 1993;129/2:121-125.
- Armand MK, Crister JK. Reproductive Tissue Banking: Scientific Principles - 186.
- Runnebaum B, Rabe T. Gynäkologische Endokrinologie und Fortpflanzungsmedizin Springer Verlag 1994. Band 1:17,202-205,252-253, Band 2:350,360-362. ISBN 3-540-57345-3, ISBN 3-540-57347-x.
- Scott MG, Ladenson JH, Green ED, et al. Hormonal evaluation of female infertility and reproductive disorders. Clin Chem 1989;35:620-630.
- Howell SJ, Radford JA, Adams JE, et al. Randomized placebo-controlled trial of testosterone replacement in men with mild Leydig cell insufficiency following cytotoxic chemotherapy. Clin Endocrinol (Oxf). 2001;55(3):315-24

- 7 Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Fertil Steril. 2004;81(1):19-25.
- 8 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

For further information, please refer to the appropriate user guide or operator's manual for the analyzer concerned, the respective application sheets and the Method Sheets of all necessary components (if available in your country).

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

	Contents of kit
	Analyzers/Instruments on which reagents can be used
	Reagent
	Calibrator
	Volume for reconstitution
	Global Trade Item Number

Rx only For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

COBAS, NAVIFY, ELECSYS and PRECICONTROL are trademarks of Roche. INTRALIPID is a trademark of Fresenius Kabi AB.

All other product names and trademarks are the property of their respective owners.

Additions, deletions or changes are indicated by a change bar in the margin.

© 2024, Roche Diagnostics

For USA: Rx only



Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

+800 5505 6606



Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336