# Elecsys HCG STAT

cobas®

| REF | | Σ | SYSTEM |
|---|---|---|---|
| 08890587190 | 08890587500 | 100 | **cobas e** 411<br>**cobas e** 601<br>**cobas e** 602 |

**English**

**System information**

For **cobas e** 411 analyzer: test number 2310
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 87

**Intended use**

Immunoassay for the in vitro quantitative determination of human chorionic gonadotropin in human serum and plasma. This assay is intended for use especially in the diagnosis and monitoring of pregnancy.

The **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

**Summary**

Similarly to LH, FSH and TSH, human chorionic gonadotropin (hCG) is a member of the glycoprotein family and consists of 2 subunits (α- and β-chains) which are associated to the intact hormone. The α-chains in all four of these glycoprotein hormones are virtually identical, whereas the β-chains have greatly differing structures and are responsible for the respective specific hormonal functions.

Human chorionic gonadotropin consists of a number of isohormones[1] with differing molecular size. The biological action of hCG serves to maintain the corpus luteum during pregnancy. It also influences steroid production. The serum of pregnant women contains mainly intact hCG.

Measurement of the hCG concentration permits the diagnosis of pregnancy just one week after conception. The determination of hCG in the 1st trimester of pregnancy is of particular importance.[2] Elevated values here serve as an indication of hydatidiform mole or multiple pregnancy.[3,4,5] Depressed values indicate threatening or missed abortion, ectopic pregnancy[6,7] or intra-uterine death. Elevated values in the absence of a pregnancy are indicative of a tumor.[8]

The specific monoclonal antibodies used recognize the holo-hormone.[9] The Elecsys HCG STAT assay should therefore be used in particular in the diagnosis and monitoring of pregnancy. The ruthenium-labeled and biotinylated antibodies used are directed against different epitopes of the hCG molecule.

**Test principle**

Sandwich principle. Total duration of assay: 9 minutes.

**cobas e** 411 analyzers:

- 1st incubation: 10 µL of sample, a biotinylated monoclonal hCG-specific antibody, and a monoclonal hCG-specific antibody labeled with a ruthenium complex[a)] react to 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.

**cobas e** 601 and **cobas e** 602 analyzers:

- During a 9 minute incubation, antigen in the sample (10 µL), a biotinylated monoclonal hCG-specific antibody, a monoclonal hCG-specific antibody labeled with a ruthenium complex and streptavidin-coated microparticles react to form a sandwich complex, which is bound to the solid phase.

All analyzers:

- 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.

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

**Reagents - working solutions**

The reagent rackpack is labeled as HCGST.

M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL:
Streptavidin-coated microparticles 0.72 mg/mL; preservative.

R1 Anti-hCG-Ab~biotin (gray cap), 1 bottle, 9 mL:
Biotinylated monoclonal anti-hCG antibody (mouse) 2.3 mg/L; phosphate buffer 40 mmol/L, pH 7.5; preservative.

R2 Anti-hCG-Ab~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 10 mL:
Monoclonal anti-hCG antibody (mouse) labeled with ruthenium complex 6.0 mg/L; phosphate buffer 40 mmol/L, pH 6.5; 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: all countries: +49-621-7590

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 automatically from the respective reagent barcodes.

**Storage and stability**

Store at 2-8 °C.

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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 | 4 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, $K_2$-EDTA and $K_3$-EDTA plasma.

Plasma tubes containing separating gel can be used.

Stable for 5 days at 20-25 °C, 14 days at 2-8 °C, 12 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.

**Materials provided**

See "Reagents – working solutions" section for reagents.

**Materials required (but not provided)**

- REF 09013296190, HCG STAT CalSet, for 4 x 1.0 mL
- REF 11731416190, PreciControl Universal, for 4 x 3.0 mL
- REF 05192943190, Diluent Universal 2, 2 x 36 mL sample diluent
- 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 03004899190, PreClean M, 5 x 600 mL detection cleaning solution
- 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 materials for all analyzers:

- REF 11298500316, 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 prior to use and the reading in of the test-specific parameters via the reagent barcode take place automatically. No manual input is necessary. If in exceptional cases the barcode cannot be read, enter the 15-digit sequence of numbers.

**cobas e** 601 and **cobas e** 602 analyzers: PreClean M solution is necessary.

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 4th International Standard for Chorionic Gonadotropin from the National Institute for Biological Standards and Control (NIBSC) code 75/589.

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 use a suitable control material which has the following characteristics:

The control material has two or more levels within the measuring range, at concentrations important for the clinical interpretation. Known concentrations have been assigned on **cobas e** analyzers (providing metrological traceability). The control material is commutable to the intended human sample material.

Use the quality control material in accordance with the quality control instructions for use.

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.

According to quality control guidelines, the quality control intervals should be set sufficiently tight to ensure correct patient sample classification.

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.

Contact your Local Technical Customer Support for guidance to selection and use of suitable control materials.

**Calculation**

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

**Limitations - interference**

The assay is unaffected by icterus (bilirubin ≤ 496 µmol/L or ≤ 29 mg/dL), hemolysis (Hb ≤ 0.932 mmol/L or ≤ 1.5 g/dL), lipemia (Intralipid ≤ 2400 mg/dL) and biotin (≤ 14326 nmol/L or ≤ 3500 ng/mL).

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Criterion: For concentrations of 1.0-10 mIU/mL the deviation is ≤ ± 1.0 mIU/mL. For concentrations > 10 mIU/mL the deviation is ≤ ± 10 %.

No interference was observed from rheumatoid factors up to a concentration of 667 IU/mL and samples from dialysis patients.

There is no high-dose hook effect at hCG concentrations up to 500000 mIU/mL.

In vitro tests were performed on 16 commonly used pharmaceuticals. No interference with the assay was found.

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**

1.0-10000 mIU/mL (defined by the Limit of Detection and the maximum of the master curve). Values below the Limit of Detection are reported as < 1.0 mIU/mL. Values above the measuring range are reported as > 10000 mIU/mL (or up to 1000000 mIU/mL for 100-fold diluted samples).

**Lower limits of measurement**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

Limit of Blank = 0.5 mIU/mL

Limit of Detection = 1.0 mIU/mL

Limit of Quantitation = 1.0 mIU/mL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95$^{th}$ percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples. The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 20 %.

**Dilution**

Samples with hCG concentrations above the measuring range can be diluted with Diluent Universal 2. The recommended dilution is 1:100 (either automatically by the analyzers or manually). The concentration of the diluted sample must be > 100 mIU/mL.

After manual dilution, multiply the result by the dilution factor.

After dilution by the analyzers, the software automatically takes the dilution into account when calculating the sample concentration.

**Expected values**

Results from a multicenter study in Belgium, Netherlands, and Germany with the Elecsys HCG STAT assay (REF 03300811190) in specimen from healthy individuals are listed below (Study No. B01P023):

- ≤ 1 mIU/mL hCG for 97.5 % of the values obtained from 182 healthy, non-pregnant premenopausal women. The corresponding upper 95 % confidence limit ranges up to 4.9 mIU/mL.
- ≤ 7 mIU/mL hCG for 97.5 % of the values obtained from 143 healthy, postmenopausal women. The corresponding upper 95 % confidence limit ranges up to 8.1 mIU/mL.

The following hCG values were determined during pregnancy (weeks of pregnancy completed following the start of the last menstruation cycle):

Data are given only for the weeks of gestation for which the case numbers (n) were greater than 10.

| Weeks of gestation | N | hCG mIU/mL | |
|---|---|---|---|
| | | Median | 5$^{th}$-95$^{th}$ percentile |
| 3 | 25 | 18.7 | 5.44-72.0 |
| 4 | 43 | 135 | 10.2-708 |
| 5 | 23 | 1420 | 217-8245 |
| 6 | 19 | 3475 | 152-32177 |
| 7 | 13 | 35873 | 4059-153767 |
| 8 | 23 | 83603 | 31366-149094 |
| 9 | 23 | 104475 | 59109-135901 |
| 10 | 20 | 85304 | 44186-170409 |
| 12 | 17 | 61730 | 27107-201615 |
| 14 | 20 | 37082 | 24302-93646 |
| 15 | 546 | 28696 | 12540-69747 |
| 16 | 766 | 24346 | 8904-55332 |
| 17 | 190 | 22064 | 8240-51793 |
| 18 | 64 | 22464 | 9649-55271 |

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 protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84). 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 | 3.70 | 0.192 | 5.2 | 0.260 | 7.0 |
| Human serum 2 | 4.76 | 0.238 | 5.0 | 0.339 | 7.1 |
| Human serum 3 | 3493 | 63.7 | 1.8 | 142 | 4.1 |
| Human serum 4 | 5749 | 114 | 2.0 | 249 | 4.3 |
| Human serum 5 | 9693 | 213 | 2.2 | 458 | 4.7 |
| PC[b)] Universal1 | 5.44 | 0.226 | 4.2 | 0.415 | 7.6 |
| PC Universal2 | 47.1 | 1.70 | 3.6 | 2.50 | 5.3 |

b) PC = PreciControl

| **cobas e** 601 and **cobas e** 602 analyzers | | | | | |
|---|---|---|---|---|---|
| | | **Repeatability** | | **Intermediate precision** | |
| Sample | Mean mIU/mL | SD mIU/mL | CV % | SD mIU/mL | CV % |
| Human serum 1 | 5.01 | 0.117 | 2.3 | 0.304 | 6.1 |
| Human serum 2 | 8.38 | 0.211 | 2.5 | 0.469 | 5.6 |
| Human serum 3 | 3211 | 38.3 | 1.2 | 118 | 3.7 |
| Human serum 4 | 6305 | 89.1 | 1.4 | 315 | 5.0 |
| Human serum 5 | 9691 | 139 | 1.4 | 325 | 3.4 |
| PC[b)] Universal1 | 5.50 | 0.105 | 1.9 | 0.178 | 3.2 |
| PC Universal2 | 47.3 | 1.31 | 2.8 | 1.63 | 3.4 |

# Elecsys HCG STAT

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**Method comparison**

A comparison of the Elecsys HCG STAT assay, REF 08890587190 (**cobas e** 601 analyzer; y) with the Elecsys HCG STAT assay, REF 03300811190 (**cobas e** 601 analyzer; x) gave the following correlations (mIU/mL):

Number of samples measured: 124

| Passing/Bablok[10] | Linear regression |
|---|---|
| y = 1.013x - 1.99 | y = 1.011x + 5.53 |
| τ = 0.995 | r = 1.000 |

The sample concentrations were between 6.30 and 9848 mIU/mL.

**Analytical specificity**

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

LH: 0.2 %, FSH: n. d.[c)], TSH: n. d.

c) n. d. = not detectable

**References**


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2 Seeber BE. What serial hCG can tell you, and cannot tell you, about an early pregnancy. Fertil Steril 2012;98(5):1074-1077.

3 Guth B, Hudelson J, Hifbie J, et al. Predictive Value of hCG 14 Days After Embryo Transfer. J of Assist Reprod Genet 1995;12(1):13-14.

4 Chung K, Sammel MD, Coutifaris C, et al. Defining the rise of serum HCG in viable pregnancies achieved through use of IVF. Hum Reprod 2006;21(3):823-828.

5 Cavailere A, Ermito S, Dinatale A, et al. Management of molar pregnancy. J Prenat Med 2009;3(1):15-17.

6 Dillon KE, Sioulas VD, Sammel MD, et al. How and when human chorionic gonadotropin curves in women with an ectopic pregnancy mimic other outcomes: differences by race and ethnicity. Fertil Steril 2012;98(4):911-916.

7 Ustunyurt E, Duran M, Coskun E, et al. Role of initial and day 4 human chorionic gonadotropin levels in predicting the outcome of single-dose methotrexate treatment in women with tubal ectopic pregnancy. Arch Gynecol Obstet 2013;288(5):1149-1152.

8 Iles RK, Delves PJ, Butler SA. Does hCG or hCGHβ play a role in cancer cell biology. Mol Cell Endocrinol 2010;329(1-2):62-70.

9 Whittington J, Fantz CR, Gronowski AM, et al. The analytical specificity of human chorionic gonadotropin assays determined using WHO International Reference Reagents. Clin Chim Acta 2010;411(1-2):81-85.

10 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).

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

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):

| | |
|---|---|
| CONTENT | Contents of kit |
| SYSTEM | Analyzers/Instruments on which reagents can be used |
| REAGENT | Reagent |
| CALIBRATOR | Calibrator |
| → | Volume for reconstitution |
| GTIN | Global Trade Item Number |
| Rx only | For USA: Caution: Federal law restricts this device to sale by or on the order of a physician. |



CE 0123


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