03000087500V20.0

# Elecsys DHEA-S

cobas®

| REF | | Σ | SYSTEM |
|---|---|---|---|
| | | | **cobas e** 411 |
| 03000087122 | 03000087500 | 100 | **cobas e** 601 |
| | | | **cobas e** 602 |

**English**

**System information**

For **cobas e** 411 analyzer: test number 740
For **cobas e** 601 and **cobas e** 602 analyzers: Application Code Number 142

**Intended use**

Immunoassay for the in vitro quantitative determination of dehydroepiandrosterone sulfate (DHEA-S) in human serum and plasma.

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

**Summary**

DHEA-S is a steroid hormone for which the adrenal glands is the sole source in females and the principle source in males. DHEA-S is found in the fetus but declines rapidly in the first year of life. Around 5-7 years of age, DHEA-S production slowly resumes, increases during puberty and reaches a maximum between 20 and 30 years of age. Thereafter DHEA-S levels steadily decline to approximately 10 % of peak levels by the age of 80.[1,2] DHEA-S has a relatively long half-life of 7-10 hours and its concentration is approximately constant over the day.[1]

Measurement of DHEA-S can be useful in the diagnostic work-up of female patients presenting with clinical symptoms of hyperandrogenism.[3] Elevated DHEA-S levels are indicative of an involvement of the adrenal gland. A decrease of DHEA-S and total serum testosterone by more than 50 % upon dexamethasone suppression, is seen as confirmation of hyperandrogenism of the adrenal gland.[4] The most common cause is missense mutations in the 21-hydroxylase gene resulting in a mild or adult-onset or non-classical congenital adrenal hyperplasia (NCCAH). It has been estimated that the incidence of NCCAH is around 1 % in the population of New York.[4] In rare cases the cause is an adrenal tumor; in a study by Carmina et al.,[5] the incidence of an adrenal tumor was 0.2 % (2 out of 950 women with hyperandrogenism). Tumor relevant values in women are those values exceeding 700 µg/dL DHEA-S.[6]

The Elecsys DHEA-S assay makes use of a competition test principle using a polyclonal antibody (rabbit) specifically directed against DHEA-S. Endogenous DHEA-S in the sample competes with added DHEA-S derivative labeled with a ruthenium complex[a)] for the binding sites on the biotinylated antibody.

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

**Test principle**

Competition principle. Total duration of assay: 18 minutes.

- 1st incubation: By incubating the sample (15 µL) with a DHEA-S-specific biotinylated antibody, an immunocomplex is formed, the amount of which is dependent upon the analyte concentration in the sample.
- 2nd incubation: After addition of streptavidin-coated microparticles and a DHEA-S derivative labeled with a ruthenium complex, the still-vacant sites of the biotinylated antibodies become occupied, with formation of an antibody-hapten complex. The entire 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 DHEA-S.

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

R1 Anti-DHEA-S-Ab~biotin (gray cap), 1 bottle, 9 mL:
Biotinylated polyclonal anti-DHEA-S antibody (rabbit) 450 ng/mL; phosphate buffer 100 mmol/L, pH 6.8; preservative.

R2 DHEA-S~$Ru(bpy)_3^{2+}$ (black cap), 1 bottle, 9 mL:
DHEA-S derivative (synthetic) labeled with ruthenium complex 0.32 ng/mL; phosphate buffer 100 mmol/L, pH 6.8; preservative.

**Precautions and warnings**

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
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:

2-methyl-2H-isothiazol-3-one hydrochloride

EUH 208 May produce an allergic reaction.

Product safety labeling follows EU GHS guidance.

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

Plasma tubes containing separating gel can be used.

Criterion: Slope 0.9-1.1 + coefficient of correlation ≥ 0.95.

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 03000095122, DHEA-S CalSet, for 4 x 1.0 mL
- REF 11731416190, 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 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 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.

**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 gravimetrically produced master calibrators consisting of exactly defined DHEA-S concentrations in depleted human serum matrix.

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**

For quality control, use PreciControl Universal.

In addition, other suitable control material can be used.

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 µmol/L, µg/dL or µg/mL).

Conversion factors: µmol/L x 36.846 = µg/dL
µg/dL x 0.02714 = µmol/L
µg/dL x 0.01 = µg/mL

**Limitations - interference**

*Endogenous substances*

| Compound | Concentration tested |
|---|---|
| Bilirubin | ≤ 222 µmol/L or ≤ 13 mg/dL |
| Hemoglobin | ≤ 0.35 mmol/L or ≤ 0.56 g/dL |
| Intralipid | ≤ 2000 mg/dL |
| Biotin | ≤ 123 nmol/L or ≤ 30 ng/mL |
| Rheumatoid factors | ≤ 80 IU/mL |

Criterion: For concentrations of 0.100-50 µg/dL the deviation is ≤ ± 5 µg/dL. For concentrations > 50 µg/dL 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.

In vitro tests were performed on 17 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**

0.003-27.1 µmol/L or 0.100-1000 µg/dL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.003 µmol/L or < 0.100 µg/dL. Values above the measuring range are reported as > 27.1 µmol/L or > 1000 µg/dL (or up to 135 µmol/L or 5000 µg/dL for 5-fold diluted samples).

**Lower limits of measurement**

*Lower detection limit of the test*

Lower detection limit: 0.003 µmol/L (0.100 µg/dL)

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

**Dilution**

Samples with DHEA-S concentrations above the measuring range can be diluted using human samples with a low analyte concentration. The

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recommended dilution is 1:5. The concentration of the diluted sample must be > 1.22 µmol/L (> 45 µg/dL).

If the endogenous DHEA-S concentration is negligible, multiply the result by the dilution factor or calculate using the following equation:

C = c + 4 (c - D)

C = true DHEA-S concentration of the sample

c = measured DHEA-S concentration

D = DHEA-S concentration in the diluent (human sample)

**Expected values**

Extended studies with the Elecsys DHEA-S assay conducted in two clinical centers in Germany covering a total of 519 samples from female individuals, a total of 489 samples from male individuals and a total of 269 samples from children gave the following values for the age groups listed below (study protocols No.: C00P032 and C01P005):

| Age (years) | N | 50th percentile | | 5-95th percentile | |
|---|---|---|---|---|---|
| | | µmol/L | µg/dL | µmol/L | µg/dL |
| Females: | | | | | |
| 10-14 | 73 | 3.34 | 123 | 0.92-7.60 | 33.9-280 |
| 15-19 | 55 | 4.26 | 157 | 1.77-9.99 | 65.1-368 |
| 20-24 | 36 | 6.46 | 238 | 4.02-11.0 | 148-407 |
| 25-34 | 64 | 4.96 | 183 | 2.68-9.23 | 98.8-340 |
| 35-44* | 85 | 4.38 | 161 | 1.65-9.15 | 60.9-337 |
| 45-54* | 89 | 3.28 | 121 | 0.96-6.95 | 35.4-256 |
| 55-64 | 59 | 2.08 | 76.7 | 0.51-5.56 | 18.9-205 |
| 65-74 | 29 | 1.75 | 64.4 | 0.26-6.68 | 9.40-246 |
| ≥ 75 | 29 | 1.65 | 60.9 | 0.33-4.18 | 12.0-154 |
| Males: | | | | | |
| 10-14 | 74 | 2.74 | 101 | 0.66-6.70 | 24.4-247 |
| 15-19 | 67 | 7.57 | 279 | 1.91-13.4 | 70.2-492 |
| 20-24 | 28 | 9.58 | 353 | 5.73-13.4 | 211-492 |
| 25-34 | 60 | 7.68 | 283 | 4.34-12.2 | 160-449 |
| 35-44 | 70 | 6.00 | 221 | 2.41-11.6 | 88.9-427 |
| 45-54 | 45 | 5.94 | 219 | 1.20-8.98 | 44.3-331 |
| 55-64 | 69 | 3.75 | 138 | 1.40-8.01 | 51.7-295 |
| 65-74 | 55 | 2.45 | 90.2 | 0.91-6.76 | 33.6-249 |
| ≥ 75 | 21 | 1.53 | 56.2 | 0.44-3.34 | 16.2-123 |
| Children: | | | | | |
| < 1 week | 37 | 7.60 | 280 | 2.93-16.5 | 108-607 |
| 1-4 weeks | 25 | 3.91 | 144 | 0.86-11.7 | 31.6-431 |
| 1-12 months | 69 | 0.59 | 21.6 | 0.09-3.35 | 3.4-124 |
| 1-4 years | 59 | 0.14 | 5.0 | 0.01-0.53 | 0.47-19.4 |
| 5-9 years | 79 | 0.63 | 23.1 | 0.08-2.31 | 2.8-85.2 |

* Effects of the menopause on the results obtained for the women of the corresponding age groups were tested and found to be negligible.

DHEA-S values of newborns are strongly influenced by maternal hormonal exchange via placenta.

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 | | SD | | CV | SD | | CV |
| | µmol/L | µg/dL | µmol/L | µg/dL | % | µmol/L | µg/dL | % |
| HS[b] 1 | 3.18 | 117 | 0.09 | 3.28 | 2.8 | 0.11 | 4.16 | 3.6 |
| HS 2 | 10.7 | 395 | 0.26 | 9.46 | 2.4 | 0.50 | 18.4 | 4.7 |
| HS 3 | 26.7 | 984 | 0.46 | 17.0 | 1.7 | 0.63 | 23.3 | 2.4 |
| PC U[c]1 | 4.15 | 153 | 0.09 | 3.33 | 2.2 | 0.11 | 3.99 | 2.6 |
| PC U2 | 3.34 | 123 | 0.09 | 3.41 | 2.8 | 0.10 | 3.83 | 3.1 |

b) HS = human serum

c) PC U = PreciControl Universal

| **cobas e** 601 and **cobas e** 602 analyzers | | | | | |
|---|---|---|---|---|---|
| | | | **Repeatability** | | |
| Sample | Mean | | SD | | CV |
| | µmol/L | µg/dL | µmol/L | µg/dL | % |
| HS 1 | 2.60 | 96.0 | 0.08 | 3.03 | 3.2 |
| HS 2 | 10.9 | 402 | 0.29 | 10.5 | 2.6 |
| HS 3 | 21.3 | 784 | 0.49 | 18.0 | 2.3 |
| PC U1 | 5.81 | 214 | 0.10 | 3.60 | 1.7 |
| PC U2 | 14.1 | 519 | 0.21 | 7.71 | 1.5 |

| **cobas e** 601 and **cobas e** 602 analyzers | | | | | |
|---|---|---|---|---|---|
| | | | **Intermediate precision** | | |
| Sample | Mean | | SD | | CV |
| | µmol/L | µg/dL | µmol/L | µg/dL | % |
| HS 1 | 2.53 | 93.2 | 0.06 | 2.29 | 2.5 |
| HS 2 | 10.7 | 395 | 0.29 | 10.6 | 2.7 |
| HS 3 | 20.4 | 753 | 0.48 | 17.7 | 2.4 |
| PC U1 | 5.69 | 210 | 0.14 | 4.99 | 2.4 |
| PC U2 | 13.6 | 501 | 0.29 | 10.8 | 2.2 |

**Analytical specificity**

For the Elecsys DHEA-S assay, the following cross-reactivities were found:

| Substance | **Cross-reactivity %** | **Additive concentration µg/dL** |
|---|---|---|
| Androstenedione | 10.8 | 1000 |
| DHEA | 8.90 | 1000 |
| Androsterone | 2.10 | 2000 |
| Testosterone | 2.55 | 2000 |
| Aldosterone | 0.320 | 5000 |
| Androsterone-sulfate | 1.10 | 5000 |
| DHEA-glucuronide | 2.08 | 5000 |
| Estradiol | n. d.[d] | 5000 |
| Estriol | n. d. | 5000 |
| Estrone | 0.740 | 5000 |
| Estrone-3-sulfate | 0.500 | 5000 |
| Progesterone | 1.32 | 5000 |

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| Substance | Cross-reactivity % | Additive concentration µg/dL |
|---|---|---|
| 5-α-Dihydrotestosterone | 1.12 | 5000 |
| 19-Hydroxyandrostendione | 1.66 | 5000 |
| Cortisol | 0.060 | 10000 |

d) n. d. = not detectable

**References**


1 Leowattana W. DHEAS as a new diagnostic tool. Clin Chim Acta. 2004;341(1-2):1-15.

2 Enea C, Boisseau N, Diaz V, et al. Biological factors and the determination of androgens in female subjects. J Steroids 2008;73(12):1203-1216.

3 Huang A, Brennan K, Azziz R. Prevalence of Hyperandtrogenemia in the Polycystic Ovary Syndrome by the NIH 1990 Criteria. J Fertil Steril. 2010;93(6):1938-1941.

4 Rachon D. Differential Diagnosis of Hyperandrogenism in Women with Polycystic Ovary Syndrome. J Exp Clin Endocrinol Diabetes 2012;120:205-209.

5 Carmina E, Rosato F, Janni A, et al. Relative Prevalence of Different Androgen Excess Disorders in 950 Women Referred because of Clinical Hyperandrogenism. J Clin Endocrinol Metab 2006;91(1):2-6.

6 Sciarra F, Tosti-Croce C, Toscano V. Androgen-secreting adrenal tumors. Minerva Endocrinol. 1995;20(1):63-8.


For further information, please refer to the appropriate operator's manual for the analyzer concerned, the respective application sheets, the product information 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.

**Symbols**

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.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 after reconstitution or mixing |
| GTIN | Global Trade Item Number |



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