

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number:

K031717

B. Analyte:

Sex hormone binding globulin

Calibrator

Quality control material

C. Type of Test:

Quantitative; electrochemiluminescent immunoassay

D. Applicant:

Roche Diagnostics Corporation

E. Proprietary and Established Names:

Elecsys® SHBG Immunoassay System

Elecsys® SHBG CalSet

Elecsys® PreciControl Universal

F. Regulatory Information:

1. Regulation section:

21 CFR 862.1680 (reagent)

21 CFR 862.1150 (calibrator)

21 CFR 862.1660 (control)

2. Classification:

Class I (reagent)

Class II (calibrator)

Class I (control)

3. Product Code:

CDZ – Radioimmunoassay, testosterone and dihydrotestosterone

JIS – Primary calibrator

JJY – Multi-analyte controls, all kinds (assayed and unassayed)

4. Panel:

75

G. Intended Use:

1. Intended use(s):

Elecsys® SHBG Immunoassay is for the in vitro quantitative determination of sex hormone-binding globulin in human serum and plasma. The electrochemiluminescence immunoassay “ECLIA” is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

Elecsys® SHBG CalSet is used for calibrating the quantitative Elecsys SHBG assay on Elecsys immunoassay systems.

PreciControl Universal is used for quality control of Elecsys immunoassay systems.

2. Indication(s) for use:

Immunoassay for the in vitro quantitative determination of sex hormone binding globulin in human serum and plasma. The Elecsys® SHBG Immunoassay is intended for use as an aid in the diagnosis of androgen disorders including hirsutism, virilization, polycystic ovarian syndrome, androgenital syndrome, and hyperandrogenism; the correct interpretation of testosterone and estradiol concentrations; investigation of the androgen-estrogen balance in gonadal and sexual dysfunction; assessment of the peripheral effect of hormones which regulate SHBG concentrations. The electrochemiluminescence immunoassay “ECLIA” is intended for use on the Roche Elecsys family of analyzers.

3. Special condition for use statement(s):

Not applicable

4. Special instrument Requirements:

Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers

H. Device Description:

The Elecsys® SHBG Immunoassay kit contains reagents sufficient for 100 tests. The reagents are as follows: 1 bottle containing streptavidin-coated microparticles and preservative; 1 bottle containing biotinylated monoclonal anti-SHBG antibody (mouse), buffer, and preservative; and 1 bottle of monoclonal anti-SHBG antibody (mouse) labeled with ruthenium complex, buffer, and preservative.

The Elecsys® SHBG CalSet kit, sold separately, contains the following: lyophilized calibrators, barcode card, calibrator barcode sheet, 4 labeled empty snap-cap bottles, and 2 x 6 bottle labels. Calibrator 1 contains approximately 0 nmol/L SHBG in equine serum, and calibrator 2 contains approximately 40 nmol/L human SHBG in human serum matrix. Each calibrator is supplied in two bottles, each for 1 mL of calibrator.

The PreciControl Universal, sold separately, contains the following: lyophilized controls, two barcode cards, control barcode sheet, 2 x 2 labeled empty snap-cap bottles, and 2 x 6 bottle labels. The control serum is based on human serum in two concentration ranges. The two controls are supplied in two bottles, each for 3 mL of control.

I. Substantial Equivalence Information:

1. Predicate device name(s):
DPC Immulite SHBG
2. Predicate K number(s):
K941797
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative determination of sex hormone-binding globulin in serum, for professional use	Quantitative determination of sex hormone-binding globulin in serum, for professional use
Principle	Immunoassay	Immunoassay
Differences		
Item	Device	Predicate
IU/Specimen	Serum and Li-heparain plasma	Serum only
Instrument(s)	Elecsys 1010/2010 and MODULAR ANALYTICS E170	Immulite
Reagents	Streptavidin-coated microparticles, biotinylated mouse monoclonal anti-SHBG, mouse monoclonal anti-SHBG labeled with ruthenium complex	Monoclonal murine anti-SHBG coated beads, alkaline phosphatase conjugated to polyclonal rabbit anti-SHBG
	Calibrators – equine serum matrix and SHBG in human serum matrix Controls – SHBG in human serum	Adjustors and controls – SHBG in nonhuman protein/buffer matrix
Reportable Range	0.350 – 200 nmol/L	0.2 - 180 nmol/L

J. Standard/Guidance Document Referenced (if applicable):

Not applicable

K. Test Principle:

The Elecsys® SHBG Immunoassay is an electrochemiluminescent, sandwich based assay.

L. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Reproducibility was determined using Elecsys reagents, pooled human serum and controls in a modified protocol (EP5-A) of the National Committee for Clinical Laboratory Standards (NCCLS). In one study $n = 60$ and in another, $n = 21$. Within-run precision results were 2.7% CV and below. Total precision results were 4.0% CV and below.

b. *Linearity/assay reportable range:*

Linearity was evaluated by diluting three patient samples with varying amounts of the low-analyte human serum. In order to demonstrate linearity at the lower end of measuring range, a patient sample was diluted with varying amounts of horse serum, as analyte-free human serum is difficult to obtain.

The expected values were generated using the concentrations measured in the diluent and the undiluted patient sample and then applying the dilution factors. The % recovery was determined by dividing the measured concentration with the expected concentration. Linearity was defined as 85-115% recovery.

The measuring range is 0.350-200 nmol/L (defined by the lower detection limit and the maximum of the master curve). Values below the detection limit are reported as <0.350 nmol/L. Values above the measuring range are reported as >200 nmol/L.

c. *Traceability (controls, calibrators, or method):*

The assay has been standardized against the 1st International Standard for SHBG from the National Institute for Biological Standards and Controls (NIBSC) code 95/560. The CalSet is traceable to NIBSC's 1st International Standard for SHBG.

d. *Detection limit:*

The 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, within-run precision, $n = 21$).

e. Analytical specificity:

The specificity of the Elecsys® SHBG was determined using human serum samples spiked with potential cross-reactant compounds and non-spiked human serum samples. The spiked and non-spiked samples were tested in duplicate. Non detectable cross reactivities were found for AFP, CBG, DHT, estradiol, fibrinogen, human IgA, human IgG, plasminogen, TBG, testosterone, Tg, transferrin, and TSH.

Endogenous interferences were evaluated by using natural and spiked samples. The assay was unaffected by icterus (bilirubin $< 1026 \mu\text{mol/L}$ or $< 60 \text{ mg/dL}$), hemolysis ($\text{Hb} < 1.8 \text{ mmol/L}$ or $< 2.9 \text{ g/dL}$), lipemia (Intralipid $< 2700 \text{ mg/dL}$), and biotin $< 60 \text{ ng/mL}$. The criterion was recovery within $\pm 10\%$ of initial value. Additionally, no interference was observed from rheumatoid factors up to 1160 U/mL .

f. Assay cut-off:

See Detection limit above.

2. Comparison studies:

a. Method comparison with predicate device:

The Elecsys® SHBG Immunoassay was compared with a commercially available SHBG assay using 109 clinical samples. Each sample was tested in singleton. SHBG values ranged from $11.2 - 155 \text{ nmol/L}$. The following linear regression resulted: $y = 1.15x - 1.82$, $r = 0.981$.

b. Matrix comparison:

A comparison of values obtained from samples drawn into serum and Li heparin plasma vacutainer tubes was conducted. Forty four samples were analyzed and included concentrations ranging from $18-244 \text{ nmol/L}$. The following linear regression resulted: $y = 0.99x - 0.39$, $r = 0.998$.

3. Clinical studies:

a. Clinical sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a and b are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The following expected values are from published literature:

Males 10-80 nmol/L

Females 20-130 nmol/L

M. Conclusion:

Descriptive characteristics and performance data above demonstrate that the new device is similar to the DPC Immulite SHBG and other commercially available assays of this type. Additionally, the labeling is adequate and conforms to 21 CFR 809.10. Therefore, I recommend a substantial equivalence determination for the Elecsys® SHBG Immunoassay System, Elecsys® SHBG CalSet, and PreciControl Universal (as modified).