

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

A. 510(k) Number:

k102814

B. Purpose for Submission:

Reference range and limit of detection modified for previously cleared device (k031717)

C. Measurand:

Sex hormone-binding globulin (SHBG)

D. Type of Test:

Quantitative electrochemiluminescent immunoassay

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

Elecsys® SHBG

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1680, Testosterone test system

2. Classification:

Class I, reserved

3. Product code:

CDZ – Radioimmunoassay, testosterone and dihydrotestosterone

4. Panel:

75, Chemistry

H. 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 ELECSYS SHBG Immunoassay is intended for use as an aid in the diagnosis of androgen disorders. The electrochemiluminescence immunoassay “ECLIA” is intended for use on Elecsys and cobas e immunoassay analyzers.

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. The electrochemiluminescence immunoassay “ECLIA” is intended for use on Elecsys and cobas e immunoassay analyzers.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Elecsys 2010/cobas e 411 and MODULAR ANALYTICS E170/cobas e 601

I. 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.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Elecsys® SHBG Immunoassay

2. Predicate 510(k) number(s):

k031717

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Indications for use	Immunoassay for the in vitro quantitative determination of sex hormone-binding globulin in human serum and plasma.	same
Assay protocol	Sandwich assay	same
Detection protocol	Electrochemiluminescent immunoassay	same
Application	18 minute	same
Instrument platform	Elecsys 2010/cobas e 411; MODULAR ANALYTICS E170/cobas e 601 (Elecsys 1010 analyzer removed)	same plus Elecsys 1010 analyzer
Sample type	Serum and lithium heparin plasma	same
Traceability	The Elecsys SHBG assay has been standardized against the 1 st International Standard for SHBG, NIBSC code 95/560	same
Calibrator	Elecsys SHBG CalSet	same
Controls	Elecsys PreciControl Universal 1 and 2	same
Precision	Elecsys 2010/cobas e 411: Within run 2.1 -2.7 % CV Total 2.6 – 5.6 % CV E170/cobas e 601: Within run 1.1 -1.7 % CV Total 1.8 – 4.0 % CV	same
Hook effect	No hook effect at SHBG concentrations up to 1000 nmol/L	same
Limitations	The assay is unaffected by: <ul style="list-style-type: none"> • Hemoglobin < 2.9 g/dL • Bilirubin > 60 mg/dL • Intralipid < 2700 mg/dL • Biotin < 60 ng/mL • Rheumatoid factors up to 1160 IU/mL • In vitro tests were 	same

Similarities		
Item	Device	Predicate
	performed on 16 commonly used pharmaceuticals. No interference with the assay was found.	

Differences		
Item	Device	Predicate
Measuring range	0.800 – 200 nmol/L	0.350 – 200 nmol/L
Expected values	Males 20 – 49 years: 5 th % = 16.5 nmol/L 95 th % = 55.9 nmol/L Males ≥ 50 years: 5 th % = 19.3 nmol/L 95 th % = 76.4 nmol/L Females 21- 49 years: 5 th % = 24.6 nmol/L 95 th % = 122 nmol/L Females ≥ 50 years: 5 th % = 17.3 nmol/L 95 th % = 125 nmol/L	Males: 10 – 80 nmol/L Females, non-pregnant: 20 – 130 nmol/L

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

CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

The Elecsys® SHBG Immunoassay is an electrochemiluminescent, sandwich based assay. The total duration of the assay is 18 minutes.

- 1st incubation: 10 µL of sample, a biotinylated monoclonal SHBG-specific antibody, and a monoclonal SHBG-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. 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Previously established in k031717

b. *Linearity/assay reportable range:*

Previously established in k031717

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Previously established in k031717

d. *Detection limit:*

Limit of detection studies were performed on the Elecsys 2010 and MODULAR ANALYTICS E170 analyzers according to CLSI EP 17-A.

LoB:

The distribution of values for five analyte free samples pools was determined on two Elecsys 2010 analyzers and two MODULAR ANALYTICS E170 analyzers with 3 reagent lots over 3 days, 2 runs per day with a single replicate per run. In total, 60 determinations were obtained per reagent lot. Values for the 3 reagent lots ranged from 0.211 to 0.268 nmol/L on the Elecsys 2010 and from 0.189 to 0.274 on the E170. The sponsor set the LoB claim as 0.5 nmol/L.

LoD:

The distribution of values for five low level human serum samples pools was determined on two Elecsys 2010 analyzers and two MODULAR ANALYTICS E170 analyzers with 3 reagent lots over 3 days, 2 runs per day with a single replicate per run. In total, 60 determinations were obtained per reagent lot. LoD was determined according to EP-17-A as:

$$\text{LoD} = \text{LoB} + 1.653 \times \text{SD}_{\text{total}} \text{ (of low analyte samples)}$$

LoD values obtained for the 3 reagent lots ranged from 0.313 to 0.412 nmol/L

on the Elecsys 2010 and from 0.306 to 0.411 on the E170. The sponsor set the LoD claim as 0.8 nmol/L.

LoQ:

A low level sample set was prepared by diluting 3 human serum samples with an analyte free diluent. The low level sample set was tested in single replicates for 3 days, 2 runs per day on 2 Elecsys 2010 analyzers and 2 MODULAR ANALYTICS E170 analyzers with 3 reagent lots (N = 12) Each reagent lot was evaluated separately. Two lots of calibrators and one lot of controls were used for the study. To determine the LoQ, the differences between the expected value and the measured mean value were calculated for each member of the low level sample set to determine the total error. The average bias and SDs for each member of the low level sample set were calculated. LoQ values obtained for the 3 reagent lots ranged from 0.780 to 1.500 nmol/L on the Elecsys 2010 and from 0.490 to 0.660 on the E170. The sponsor set the LoQ claim as 2.0 nmol/L.

The measuring range of the assay was set at 0.800 – 200 nmol/L. The low end of the measuring range was determined based on the limit of detection.

e. Analytical specificity:

Previously established in k031717

f. Assay cut-off:

See expected values/reference ranges in M(5) below

2. Comparison studies:

a. Method comparison with predicate device:

Previously tested in k031717

b. Matrix comparison:

Previously tested in k031717

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:

Reference range studies were performed to obtain expected human sex hormone-binding globulin (SHBG) and testosterone values for healthy males and females using the Elecsys® SHBG and Elecsys® Testosterone II (K093421) assays.

Testosterone and SHBG concentrations were measured in apparently healthy males (n=214) and females (n=160) using the Elecsys® SHBG and Elecsys® Testosterone II (K093421) assays on the Elecsys® E170 Immunoassay Analyzer. The health status of the apparently healthy group was confirmed by a standard clinical chemistry and hematology profile and health examination. The expected values are presented in the table below:

	N	SHBG (nmol/L)			Testosterone (nmol/L)		
		Median	5 th %	95 th %	Median	5 th %	95 th %
Males 20-49 yrs	136	33.5	16.5	55.9	18.6	8.64	29.0
Males ≥50 yrs	78	40.8	19.3	76.4	16.5	6.68	25.7
Females 21-49 yrs	89	64.3	24.6	122	0.941	0.290	1.67
Females ≥50 yrs	71	57.4	17.3	125	0.563	0.101	1.42

The free testosterone index (FTI) or free androgen index (FAI) was obtained as follows: % FTI or FAI = ((Testosterone (nmol/L) ÷ SHBG (nmol/L)) x 100. The results are presented in the table below:

	Free Testosterone Index (FTI)/Free Androgen Index (FAI) (nmol/L)			
	N	Median	5 th %	95 th %
Males 20-49 yrs	136	57.2	35.0	92.6
Males ≥50 yrs	78	38.2	24.3	72.1
Females 21-49 yrs	89	1.53	0.297	5.62
Females ≥50 yrs	71	1.15	0.187	3.63

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.