May 6, 2022

Roche Diagnostics
Justin Davis
Regulatory Affairs Manager
9115 Hague Road, PO Box 50416
Indianapolis, Indiana 46250

Re: K211685
Trade/Device Name: Elecsys Testosterone II
Regulation Number: 21 CFR 862.1680
Regulation Name: Testosterone Test System
Regulatory Class: Class I, reserved
Product Code: CDZ
Dated: February 4, 2022
Received: February 7, 2022

Dear Justin Davis:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k211685

Device Name

Elecsys Testosterone II

Indications for Use *(Describe)*

Immunoassay for the in vitro quantitative determination of testosterone in human serum and plasma.
The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 601 immunoassay analyzer.

Measurements of testosterone are used in the diagnosis and treatment of disorders involving the male sex hormones (androgens), including primary and secondary hypogonadism, delayed or precocious puberty, impotence in males and, in females hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries, and adrenogenital syndromes.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Elecsys Testosterone II
510(k) Summary

K211685

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification 510(k).

The purpose of this Traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the Elecsys Testosterone II on the **cobas e** 601.

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Justin Davis Phone: (317) 521-6204 Email: justin.davis@roche.com
Date Prepared	May 27, 2021
Proprietary Name	Elecsys Testosterone II
Common Name	Testosterone II Assay
Classification Name	Radioimmunoassay, Testosterones And Dihydrotestosterone
Product Codes, Regulation Numbers	CDZ 21 CFR 862.1680
Predicate Devices	Elecsys Testosterone II (K093421)
Establishment Registration	Roche Diagnostics GmbH Mannheim, Germany: 9610126 Roche Diagnostics GmbH Penzberg, Germany: 9610529 Roche Diagnostics Indianapolis, IN United States: 1823260

1. DEVICE DESCRIPTION

The Elecsys Testosterone II immunoassay makes use of a competitive test principle using streptavidin-coated microparticles and electrochemiluminescence detection. Results are determined using a calibration curve that is generated specifically on each instrument by a 2-point calibration and master curve provided with the reagent bar code. The Elecsys Testosterone II reagent kit consists of a Reagent Pack (R1, R2, and M (Streptavidin-coated microparticles)).

2. INDICATIONS FOR USE

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

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the **cobas e** 601 immunoassay analyzer.

Measurements of testosterone are used in the diagnosis and treatment of disorders involving the male sex hormones (androgens), including primary and secondary hypogonadism, delayed or precocious puberty, impotence in males and, in females hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries, and adrenogenital syndromes.

3. TECHNOLOGICAL CHARACTERISTICS

The reagent working solutions include:

Rack Pack (kit placed on the analyzer).

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-testosterone-Ab~biotin (gray cap), 1 bottle, 10 mL: Biotinylated monoclonal anti-testosterone antibody (sheep) 40 ng/mL; releasing reagent 2-bromoestradiol; MES buffer 50 mmol/L, pH 6.0; preservative.
- R2 Testosterone-peptide~Ru(bpy)$_3^{2+}$ (black cap), 1 bottle, 9 mL: Testosterone derivative, labeled with ruthenium complex 1.5 ng/mL; MES buffer 50 mmol/L, pH 6.0; preservative.

The following table compares the updated Elecsys Testosterone II with its predicate device, the current Elecsys Testosterone II (K093421).

Table 1: Technical Characteristics Comparison Table between updated Elecsys Testosterone II and current Elecsys Testosterone II

Feature	Candidate Device Elecsys Testosterone II (K211685)	Predicate Device Elecsys Testosterone II (K093421)
Intended Use	Immunoassay for the in vitro quantitative determination of testosterone in human serum and plasma. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the **cobas e** 601 immunoassay analyzer	Same
Indications for Use	Measurements of testosterone are used in the diagnosis and treatment of disorders involving the male sex hormones (androgens), including primary and secondary hypogonadism, delayed or precocious puberty, impotence in males and, in females hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries, and adrenogenital syndromes.	Same
Assay Method	Competitive Principle	Same
Detection Method	Electrochemiluminescence immunoassay (ECLIA)	Same
Instrument Platform	**cobas e** 601	Same
Sample Type/Matrix	Human serum, plasma	Same
Traceability/ Standardization	ID-GC/MS ("Isotope Dilution - Gas Chromatography/Mass Spectrometry").	Same
Sample Anticoagulants	Li-heparin, K2-EDTA and K3-EDTA plasma.	Same
Calibrator	Testosterone II CalSet II Calibrators 1 and 2	Same
Calibration Method	Traceability: This method has been standardized via ID-GC/MS ("Isotope Dilution - Gas Chromatography/Mass Spectrometry"). 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.	Same

Feature	Candidate Device Elecsys Testosterone II (K211685)	Predicate Device Elecsys Testosterone II (K093421)
Calibration Interval	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.	Same
Controls	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.	Same
Reagent Stability	**unopened** at 2-8 °C up to the stated expiration date **after opening** at 2-8 °C 12 weeks **on the analyzer** 8 weeks	Same
Measuring Range	2.50-1500 ng/dL or 0.087-52.0 nmol/L (defined by the Limit of Detection and the maximum of the master curve).	Same

Feature	Candidate Device Elecsys Testosterone II (K211685)	Predicate Device Elecsys Testosterone II (K093421)
Precision	Precision was evaluated on one **cobas e** 601 analyzer according to CLSI guideline EP05-A3. The protocol consisted of testing 5 Aliquots of each control (PreciControl Universal level 1 and PreciControl Universal level 2) and human serum samples (HS1-HS5) per run, 1 run per day for 5 days with 3 lots. Repeatability and intermediate precision (SD and CV values) were calculated according to CLSI EP05-A3. Precision was determined using Elecsys reagents, 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).	Precision was evaluated on one 2010 analyzer according to CLSI guideline EP05-A. The protocol consisted of testing 5 Aliquots of each control (PreciControl Universal level 1 and PreciControl Universal level 2) and human serum samples (HS1-HS5) per run, 1 run per day for 5 days with 3 lots. Repeatability and intermediate precision (SD and CV values) were calculated according to CLSI EP05-A. Precision was determined using Elecsys reagents, pooled human sera and controls in a separate study according to protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84).
LoB	1.50 ng/dL or 0.052 nmol/L	Limit of Blank: 1.2 ng/dL
LoD	2.50 ng/dL or 0.087 nmol/L	Same
LoQ	12.0 ng/dL or 0.416 nmol/L	Same

Feature	Candidate Device Elecsys Testosterone II (K211685)			Predicate Device Elecsys Testosterone II (K093421)		
Cross Reactivity	**Cross-Reactant**	**Concentration (ng/mL)**	**Cross-Reactivity [%]**	**Cross-Reactant**	**Concentration (ng/mL)**	**Cross-Reactivity [%]**
	DHEA-S	50000	0.003	DHEA-S	50000	≤ 0.003
	Androstenedione	100	3.15	Androstenedione	100	≤ 2.50
	Danazol	1000	0.504	Danazol	1000	≤ 0.500
	Estradiol	5000	0.211	Estradiol	1000	≤ 0.160
	Ethisterone	300	3.57	Ethisterone	1000	≤ 2.40
	19-Norethisterone	40	5.51	19-Norethisterone	40	≤ 6.00
	Norgestrel	1000	0.539	Norgestrel	1000	≤ 0.910
	Δ5-Androstene-3ß17ß-diol	1000	0.289	Δ5-Androstene-3ß17ß-diol	1000	≤ 0.290
	Testosterone propionate	100	0.718	Testosterone propionate	100	≤ 2.46
	5α-Androstane-3ß, 17ß-diol	500	2.15	5α-Androstane-3ß, 17ß-diol	1000	≤ 2.11
	5α-Dihydrotestosteron	500	1.30	5α-Dihydrotestosteron	500	≤ 0.860
	11ß-OH-Testosterone	50	20.6	11ß-OH-Testosterone	100	≤ 18.0
	11keto-Testosterone	200	4.87	11keto-Testosterone	1000	≤ 3.22
	Prednisone	5000	n.d.	Prednisone	1000	n.d.
	Prednisolone	5000	n.d.	Prednisolone	1000	n.d.
	Progesterone	5000	0.009	Progesterone	1000	≤ 0.002
	Cortisol	5000	n.d.	Cortisol	1000	≤0.010
	Cortisone	5000	n.d.	Cortisone	2000	n.d.
	Dexamethasone	5000	n.d.	Dexamethasone	2000	n.d.
	Estrone	5000	n.d.	Estrone	1000	≤0.004
	DHEA	5000	0.014	DHEA	1000	≤ 0.016
Biotin	This assay has no biotin interference in serum concentrations up to 1200 ng/mL			< 30 ng/mL		
Special Drug Interference	Testosterone Undecanoate or Nandrolone. Both strongly interfered with Testosterone and produced elevated recovery values.			None		
Method Comparison	Updated Elecsys Testosterone II Biotin assay on the **cobas e** 601 analyzer (y) compared to current Elecsys Testosterone II assay on the **cobas e** 601 analyzer (x).			Elecsys Testosterone II assay on the **cobas e** 801 analyzer (y) with the Elecsys Testosterone II assay on the **cobas e** 601 analyzer (x).		

Feature	Candidate Device Elecsys Testosterone II (K211685)		Predicate Device Elecsys Testosterone II (K093421)	
	Passing/Bablok y = 0.948x + 0.023 T = 0.976	Linear regression y = 0.950x - 0.871 r = 0.998	Passing/Bablok y = 0.961x - 0.015 T = 0.975	Linear regression y = 0.958x - 0.006 r = 0.999

4. NON-CLINICAL PERFORMANCE EVALUATION

The non-clinical performance studies for Elecsys Testosterone II are summarized below. The following performance data are provided in support of the substantial equivalence determination:

- Precision (5-Day and 21-Day) according to CLSI EP5-A3
- Analytical Sensitivity: LoB, LoD and LoQ according to CLSI EP17-A2
- Linearity according to CLSI EP6-A
- Endogenous Interferences – Hemoglobin, Intralipid, Bilirubin, and Rheumatoid Factors
- Biotin Interference (CLSI EP07-A3)
- Common Drug Interferences
- Special Drug Interferences
- Analytical Specificity/ Cross Reactivity (CLSI EP17-A2)
- Matrix Comparison - Anticoagulants
- Method Comparison to Predicate
- Reagent Stability (CLSI EP25-A)
- Lot Calibration Stability (CLSI EP25-A)

All performance specifications were met.

4.1. Precision

4.1.1. 21 Day Precision

Precision was evaluated on one **cobas e** 601 analyzer according to CLSI guideline EP05-A3. The protocol consisted of testing 2 replicates of 2 controls and 5 samples.

Each control and sample underwent 2 runs per day over 21 days using 1 reagent lot. Repeatability and intermediate precision were calculated according to CLSI EP05-A3. Assay calibration was done as specified in the package insert.

4.1.2. 5 Day Precision

Precision was evaluated on one **cobas e** 601 analyzer according to CLSI guideline EP05-A3. The protocol consisted of testing 5 Aliquots of each control (PreciControl Universal Level 1 and Level 2) and human serum samples per run, 1 run per day for 5 days with 3 lots.

Repeatability and intermediate precision were calculated according to CLSI EP05-A3. Assay calibration was done as specified in the package insert.

4.2. Analytical Sensitivity

Analytical Sensitivity limits (LoB, LoD, LoQ) were determined using CLSI EP17-A2.

These studies and acceptance criteria have been reviewed and found to be acceptable. These data support the LoB, LoD, LoQ claims as reported in the package labeling.

4.3. Linearity/Assay Reportable Range

For linearity, one lot was tested on one **cobas e** 601 with one run. One human serum sample with high analyte content above the measuring range was diluted to the lower end of the measuring range with various amounts of human serum sample without analyte content. The dilution series contained 25 steps. Samples were assayed in 3-fold determinations. Data Analysis was determined according to CLSI EP06-A.

4.4. Endogenous Interferences

The effect on quantitation of analyte in the presence of endogenous interfering substances was determined for testosterone concentrations and a dilution set of the added interfering substances.

The endogenous interference study and acceptance criteria have been reviewed and found to be acceptable. These data supports the endogenous interferences claims as reported in the package labeling.

4.5. Biotin Interference

One aliquot of each testosterone sample was spiked with biotin up to 3600 ng/mL. Another aliquot of the sample was spiked with the same volume of the solvent of the interfering endogenous substance (without interfering substance). The recovery (absolute deviation or % recovery) was calculated for each sample compared to the expected value. Data supports the biotin interference claim of to ≤ 1200 ng/mL, as reported in the package labeling.

4.6. Common Drug Interferences

The common drug interference study and acceptance criteria have been reviewed and found to be acceptable. These data supports the common drug interferences claims as reported in the package labeling.

4.7. Special Drug Interferences

The effect on quantitation of analyte in the presence of drugs was determined by comparing values obtained from samples spiked with one special pharmaceutical compound with the reference sample (unspiked). All samples used were Native sample pools. Samples (with testosterone concentrations near 0.5 ng/mL and near 5.0 ng/mL) were divided into aliquots and spiked with the special drug interferents, Testosterone Undecanoate. The reference sample without drug was spiked with the respective amount of solvent.

4.8. Analytical Specificity/Cross-Reactivity

The analytical specificity of the Elecsys Testosterone II assay was determined with one reagent lot on one **cobas e** 601 analyzer using a human serum matrix with one testosterone level (0.5 ng/mL). The sample aliquots were spiked with potential cross-reactants. These data supports the analytical specificity claims as reported in the package labeling.

4.9. Sample Matrix Comparison

The effect on quantitation of analyte in the presence of anticoagulants on the Elecsys Testosterone II assay were determined. All samples used were Native or spiked samples. Values obtained from serum samples (reference) were compared to Li-Heparin, K_2-EDTA and K_3-EDTA plasma. At least 40 serum/plasma pairs were tested in one run on one **cobas e** 601 analyzer. Data was assessed by Passing/Bablok regression analysis.

4.10. Method Comparison to Predicate

Serum samples were measured internally using both the current and updated reagent formulations. One hundred sixty eight (168) samples that span the measuring range were tested with one run per sample (no replicates). To sufficiently cover the measuring range, Native single samples and spiked single samples were used. Equivalence of the current Elecsys Testosterone II (K093421) assay and the updated Elecsys Testosterone II assay were evaluated using:

• Calculation: Scatter-plot of numerical values of the current assay (x-axis) versus the updated assay (y-axis).

• Passing-Bablok analysis for slope and intercept was performed for the updated lot against the current lot.

4.11. Stability Studies

The stability studies and acceptance criteria have been reviewed and found to be acceptable. The stability data supports the claims as reported in the package labeling.

5. CONCLUSIONS

The information provided in this 510(k) Premarket Notification will support a determination of substantial equivalence for the Elecsys Testosterone II. The data from the analytical studies demonstrate that the device is as safe, as effective, and performs as well as or better than the predicate device.