510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k122793

B. Purpose for Submission:

New Device

C. Measurand:

Testosterone

D. Type of Test:

Quantitative Chemiluminescent Immunoassay

E. Applicant:

DiaSorin Inc.

F. Proprietary and Established Names:
LIAISON® Testosterone
LIAISON® Testosterone Control Set

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CDZ	Class I, reserved	21 CFR 862.1680 Testosterone Test System	Clinical Chemistry (75)
JJX	Class I, reserved	21 CFR 862.1660 Quality Control Material	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

The DiaSorin LIAISON® Testosterone is a direct, competitive,

chemiluminescence immunoassay (CLIA) intended for the quantitative determination of testosterone in human serum and EDTA plasma on the LIAISON® Analyzer. The assay is intended for in vitro diagnostic use. Measurement of testosterone is 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 male subjects and, in female subjects hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries, and adrenogenital syndromes.

The DiaSorin LIAISON® Testosterone Control Set is intended for use as assayed quality control samples to monitor the accuracy and precision of the DiaSorin LIAISON® Testosterone immunoassay.

2. Indication(s) for use:

   Same as intended use.

3. Special conditions for use statement(s):

   For in vitro diagnostic use only
   For prescription use only

4. Special instrument requirements:

   For use on the DiaSorin LIAISON® Analyzer

I. Device Description:

1. Reagent Integral contains: Magnetic particles - coated with monoclonal antibody, stabilizers and preservatives; 2.4 mL

Conjugate - Testosterone conjugated to an isoluminol derivative, with PBS, BSA and preservatives; 12 mL

Assay Buffer – containing BSA, surfactant, and preservatives, 12 mL

2 Levels calibrators containing steroid free human serum, Testosterone at 2 different concentrations, stabilizers and preservatives; 2 vials each level, 2 mL. Calibrators are provided ready to use and provided with the reagent kit (not to be sold separately).

2. Control set contains: 2 levels controls containing steroid free human serum, spiked with testosterone, stabilizers and preservatives; 2 vials each level, 3.5 mL. Controls are provided ready to use.

Each serum/plasma donor unit used in the preparation of this product has been tested by an U.S. FDA approved method and found non-reactive for the presence of the

antibody to Human Immunodeficiency Virus 1 and 2 (HIV 1/2), the Hepatitis B surface antigen (HBV), and the antibody to Hepatitis C (HCV).

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Cobas® Testosterone II Test
Roche PreciControl Universal 1 and 2

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

k093421, k090541

3. Comparison with predicate:

Reagent Similarities and Differences		
Item	New Device LIAISON® Testosterone	Predicate Device Roche Cobas® Testosterone II
Intended Use/Indications for Use	For the quantitative determination of testosterone in human serum and plasma. Measurement of testosterone is 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 male subjects and, in female subjects hirsutism (excessive hair) and virilization (masculinization) due to tumors, polycystic ovaries, and adrenogenital syndromes.	Same
Sample size	100 uL	20 uL
Capture Antibody	Mouse monoclonal antibodies to testosterone	Biotinylated sheep monoclonal antibodies to testosterone

Reagent Integral Storage	In refrigerator @ 2-8°C	On analyzer or in refrigerator @ 2-8°C
Open storage 2-8°C	4 weeks	12 weeks
Sample Matrix	Serum and EDTA plasma	Serum and Plasma (Li-heparin, K2-EDTA, and K3 –EDTA)
Calibration	Two-point verification of stored master curve.	Two-point verification of stored master curve.
Sample Handling/Processing	Automated	Automated
Measurement System	Photomultiplier (flash chemiluminescence reader)	Photomultiplier (flash chemiluminescence reader)

Control similarity and differences table:

Item	The DiaSorin **LIAISON® Testosterone Control Set**	Roche PreciControl Universal
Intended Use	It is intended for use as assayed quality control samples to monitor the accuracy and precision of the DiaSorin LIAISON® Testosterone immunoassay.	Intended for use as quality control of Elecsys® immunoassays on the Elecsys® and Cobas® immunoassay analyzers
Matrix	Human Serum	Human Serum
Levels	Two concentrations: High and Low	Two concentrations: High and Low
Reagent Format	Liquid, ready to use	Lyophilized
Storage conditions	2-8°C	2-8°C

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

- CLSI Guideline EP5-A2, Vol.24, No.25; Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition 2004
- CLSI Guideline EP6-A, Vol.23, No.16; Evaluation of Linearity of Quantitative Analytical Methods; Approved Guideline 2003
- CLSI Guideline EP7-A2, Vol.25, No.27; Interference Testing in Clinical Chemistry; 2005 Approved Guideline - Second Edition
- CLSI Guideline EP9-A2-IR, Vol.30, No.17; Method Comparison and Bias Estimation Using Patient Samples; 2010 Approved Guideline Approved Guideline - Second Edition
- CLSI Guideline EP17-A, Vol.24, No.34; Protocols for Determination of Limits of Detection and Limits of Quantitation; 2004 Approved Guideline
- CLSI Guideline C28-A3, Vol.28, No.30; How to Define and Determine Ref.

Intervals in the Clinical Laboratory; 2008 Approved Guideline

L. Test Principle:

The method for quantitative determination of the LIAISON® Testosterone assay is a direct, competitive, chemiluminescence immunoassay (CLIA). Specific antibody to testosterone is bound to magnetic particles (solid phase) and testosterone is linked to an isoluminol derivative. During the incubation, testosterone is dissociated from its binding protein and competes with labeled testosterone for binding sites on the antibody. After the incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is inversely proportional to the concentration of testosterone present in calibrators, controls, or samples.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Following CLSI document EP5-A2, the sponsor evaluated the precision using 8 samples (2 serum controls and 6 patient serum samples) with concentrations spanning the working range of the assay. The samples were run at several test sites, using multiple LIAISON® Testosterone kit lots, and 2 runs per day for 20 days (N=480 measurements per sample). Results of within-run and total precision are summarized in the table below.

Sample ID#	N	Mean ng/dL	Within Run		Total/Across Lots/Across Sites	
			SD	%CV	SD	%CV
QC Level 1	480	219	8.0	3.4%	20.0	9.1%
QC Level 2	480	781	22.0	2.8%	55.0	7.1%
Sample 1	480	37.0	3.0	7.3%	5.0	14.0%
Sample 2	480	83.0	5.0	5.5%	9.0	10.5%
Sample 3	480	237	11.0	4.5%	20.0	8.6%
Sample 4	480	418	18.0	4.3%	38.0	9.2%
Sample 5	480	1048	37.0	3.5%	94.0	9.0%
Sample 6	480	1325	42.0	3.2%	105	7.9%

b. *Linearity/assay reportable range:*

The sponsor performed linearity studies in accordance with CLSI EP6-A guidelines using three high samples of each tube type (serum, SST serum, and EDTA plasma). High endogenous or spiked samples were diluted to span the working range of the assay. A total of 9 samples (1 high and 8 diluted) for each linearity sample set were tested in duplicate on the LIAISON® analyzer. Samples tested ranged from 15 to 1528 ng/dL. The observed values were plotted against the expected values and linear regression was performed. All three samples tested with each tube type yielded similar linear regressions. A representative of each tube types are summarized below.

Serum: $y = 0.9944x – 16.12$, $R^2 = 0.9959$,

SST Serum: $y = 1.0189x – 14.59$, $R^2 = 0.9965$

EDTA Plasma:, $y = 1.0057x – 13.19$, $R^2 = 0.9913$.

The data support the claimed measuring range of this device, 16 to 1500 ng/dL.

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

Traceability: The LIAISON® Testosterone Calibrators and Controls are traceable to testosterone USP reference material.

Stability: Shelf life stability studies were performed with assay reagents, calibrators, and controls and demonstrated that they are stable until the expiration date shown on the product labeling when stored as instructed. Calibrators and controls are stable until the expiration date printed on the label when stored as directed and for 28 days once opened when stored as instructed.

Calibration curve stability and reagent open vial stability were performed by the sponsor and demonstrated that the calibration curve is stable for 7 days and open reagent vials are stable for 28 days when stored at 2-8°C.

Value assignment: Kit calibrators and controls concentrations are assigned through an internal procedure. Master calibrators are prepared from a stock solution made from reference material whose concentration is determined spectrophotometrically by the sponsor. The master calibrators are then used to assign values to the kit calibrators and controls using multiple LIASON analyzers with several kit calibrator and control vials over several run and the mean results are used to determine the target values. The mean of the results + 2SD are used for establishing the control ranges.

Testosterone Calibrators have the following target values:

Level 1= 30 -50 ng/dL

Level 2= 680 – 920 ng/dL

Testosterone Controls have the following target ranges:

Level 1= 150- 250 ng/dL

Level 2= 560 -840 ng/dL

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were determined in accordance with CLSI document EP17-A. LoB was calculated using 5 blank samples tested on 2 LIAISON® analyzers over three days using 6 runs with two reagent lots. LoD was calculated using 4 low concentration samples, at and above the mean LoB, tested on 2 LIAISON® analyzers over 3 days using 6 runs and 2 reagent lots. LoQ was calculated using 8 samples tested on 2 LIAISON® analyzers over 3 days using 6 runs and 2 reagent lots.

The LoB was determined to be 3.1 ng/dL and the LoD was determined to be 9.8 ng/dL. The LoQ, which was defined as the lowest concentration for which the CV is less than 20%., was calculated to be 16 ng/dL.

The claimed measuring range of the device is 16 to 1500 ng/dL.

e. Analytical specificity:

Interference:

Following CLSI guidance document EP7-A2, interference studies were performed using two different concentrations of testosterone samples spiked with a single concentration of 5 different endogenous substances (see below chart) and compared to unspiked control samples. The two sets of matched spiked and control samples containing each interferent were tested in the LIAISON® Testosterone assay using multiple replicates (24 replicates for 80 ng/mL testosterone and 15 replicates for 200 ng/dL testosterone) with 1 reagent lot. HAMA (Human anti-mouse antibodies) interference was performed using 5 HAMA samples with testosterone concentrations ranging from 15 to 795 ng/dL. The sponsor defines non-significant interference as bias within 10% between the spiked and the control samples. Results of non-significant interference are summarized in the table below.

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Substance	Concentration Tested
Hemoglobin	600 mg/dL
Bilirubin (unconjugated)	20 mg/dL
Triglycerides	1000 mg/dL
Cholesterol	500 mg/dL
HAMA	1753 ng/mL

In addition, common pharmaceutical compounds were spiked into native human serum samples and tested with the LIAISON ® Testosterone assay. Two serum samples pools containing approximately 80 ng/dL and 200 ng/dL testosterone were spiked with potential interferents. The reference sample (control) without interferent was spiked with the respective amount of solvent. Based on the sponsor's definition of non-significant interference (greater than ± 10% of control value), the sponsor claims no interference for the compounds and concentrations listed in the table below:

Compounds tested	Concentration
Acetylcystein	150 mg/L
Ampicillin	1000 mg/L
Ascorbic acid	300 mg/L
Ca-Dobesilate	200 mg/L
Cyclosporine	5 mg/L
Cefoxitin	2500 mg/L
Heparin	5000 U
Levodopa	20 mg/L
Methyldopa	20 mg/L
Metronidazole	200 mg/L
Phenylbutazone	400 mg/L
Doxycyclin	50 mg/L
Acetylsalicylic Acid	1000 mg/L
Rifampicin	60 mg/L
Acetaminophen	200 mg/L
Ibuprofen	50 mg/L
Theophilline	100 mg/L
Heparin Clexane	5000 U
Dexamethasone	20 mg/L

Cross Reactivity:

A cross-reactivity study was performed using pooled human serum samples, representing 3 testosterone concentrations, each spiked with various testosterone metabolites or similar compounds. Spiked and non-spiked

samples were tested in triplicate using 1 lot of LIAISON® Testosterone assay and 1 LIAISON® analyzer.

The highest observed cross reactivity is summarized below:

Cross reactant	Concentration ng/mL	% Cross reactivity
Androstenedione	100	≤4.27
Cortisol	1000	≤0.03
Cortisone	2000	≤0.01
Danazol	1000	≤0.02
Dexamethasone	2000	≤0.01
DHEA	1000	≤0.02
DHEA-S	50000	≤0.01
D-5-Androstene-3B-17B-diol	1000	≤0.06
Estrone	1000	≤0.03
Ethisterone	1000	≤0.43
Nandrolone	100	≤3.33
Norgesterel	1000	≤0.02
Testosterone propionate	50	≤7.48
5-a-Androstane-3B,17B-diol	500	≤0.81
5-a-Dihydrotestosterone	500	≤2.37
11-B-Hydroxytestosterone	50	≤15.28
11-Keto-testosterone	10	<37.70
Prednisone	1000	<0.03
Prednisolone	1000	<0.04
Progesterone	1000	<0.12
17-a-Estradiol	1000	<0.02

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Following the CLSI EP9-A2 guidance document, the sponsor performed a method comparison study of the LIAISON® Testosterone assay versus the predicate device. A total of 162 serum samples (66 females and 89 males) and 8 testosterone spiked samples were compared across methods, following the manufacturers' instructions (samples ranged from 17 ng/dL to 1393 ng/dL).

Singlicate results were used for the linear regression analysis. Passing-Bablock linear regression analysis resulted the following: Y = 0.9458x – 1.49; R^2 = 0.9809 (95% CI for the slope is 0.92 to 0.96 and CI for the intercept is -2 to 2 ng/dL).

b. Matrix comparison:

The sponsor performed a matrix comparison using 51 matched patient sets of serum, SST serum, and EDTA plasma samples. Samples ranging from 16 to 1500 ng/dL were analyzed in singlicate using one lot of LIAISON® Testosterone reagents.

Passing-Bablok linear regression analysis reported the following results:

1. SST-Serum (Y) to Serum (X): y=1.02x + 1.6, R^2=1

2. EDTA Plasma (Y) to Serum (X): y=1.04x + 1.6, R^2=1

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:

Human serum samples from 622 apparently healthy adults were tested to determine the reference range for the LIAISON® Testosterone assay. The observed central 95% reference intervals for males and females are listed below.

Population	N	Median (ng/dL)	Central 95% Interval (ng/dL)
Males 18-49 years	161	439	120 - 1019
Males ≥ 50 years	132	453	195 - 895
Females 18-49 years	202	24.0	<16.0 - 73.0
Females ≥ 50 years	127	22.0	<16.0 - 51.0

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.