510(k) Summary of Safety and Effectiveness

FEB 2 1 2014

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Device Act of 1990.

The assigned 510(k) Number is: k133491

1. Date Prepared

February 19, 2014

2. Applicant Information

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3. Regulatory Information

Table 1. Regulatory Information for ADVIA Centaur TSTO Assay

Trade Name	ADVIA Centaur® Testosterone (TSTO)
Model Numbers	05476206 (5-pack); 07207660 (1-pack)
Common Name	Radioimmunoassay, testosterones and dihydrotestosterone
Classification Name	Testosterone test system
FDA Classification	Class I (Reserved)
Review Panel	Clinical Chemistry (75)
Product Code	CDZ
Regulation Number	862.1680

4. Predicate Device Information

Predicate Device Name: ADVIA Centaur Testosterone (TSTO) assay

510(k) Number: k934562

5. Intended Use / Indications for Use

For *in vitro* diagnostic use in the quantitative determination of total testosterone (bound and unbound) in serum using the ADVIA Centaur and ADVIA Centaur XP systems.

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.

6. Device Description

The ADVIA Centaur TSTO assay consists of the following:

Table 2. Summary of Ingredients of the ADVIA Centaur TSTO Assay Components

Component	Volume	Ingredients
ADVIA Centaur TSTO Primary Reagent ReadyPack		
ADVIA Centaur TSTO Lite Reagent	2.5 mL/pack	acridinium ester-labeled testosterone in buffered saline with preservatives
ADVIA Centaur TSTO Solid Phase	15.0 mL/pack	polyclonal rabbit antitestosterone antibody bound to monoclonal mouse antirabbit antibody covalently coupled to paramagnetic particles in buffered saline with sodium azide (0.1%) and preservatives
Probe Wash	10.0 mL/pack	buffered saline with sodium azide (0.1%) and preservatives
ADVIA Centaur TSTO Ancillary Reagent ReadyPack		
ADVIA Centaur TSTO Releasing Agent	5.0 mL/pack	steroid releasing agent (~0.1 µg/mL) in buffered saline with sodium azide (0.1%) and preservatives
Calibrator E		
Cal E Low and High Calibrators	2.0 mL/vial	(After reconstitution) low or high levels of cortisol, progesterone and testosterone in human plasma with sodium azide (0.1%) and preservatives

7. Purpose of the Submission

The purpose of this submission is to submit a modification to the ADVIA Centaur TSTO assay. The modification to the assay is due to the qualification of a new polyclonal rabbit anti-testosterone pool.

8. Comparison of Predicate Device and Modified Device

The following table provides a comparison between the predicate ADVIA Centaur TSTO assay (with the current polyclonal antibody pool) and the modified ADVIA Centaur TSTO assay with a Solid Phase antibody derived from a newly-qualified polyclonal antibody pool.

Table 3. Comparison of Modified ADVIA Centaur TSTO Assay to Predicate

Item	Predicate Device (Current Polyclonal Ab Pool for Solid Phase Antibody)	Modified Device (New Polyclonal Ab Pool for Solid Phase Antibody)
Intended Use	For *in vitro* diagnostic use in the quantitative determination of total testosterone (bound and unbound) in serum using the ADVIA Centaur and ADVIA Centaur XP Systems.	Same
Instrument Platforms	ADVIA Centaur ADVIA Centaur XP	Same
Methodology	Competitive immunoassay using direct chemiluminescent technology	Same

Table 3. Comparison of Modified ADVIA Centaur TSTO Assay to Predicate

Item	Predicate Device (Current Polyclonal Ab Pool for Solid Phase Antibody)	Modified Device (New Polyclonal Ab Pool for Solid Phase Antibody)
Capture Antibody (Solid Phase)	Polyclonal rabbit anti-testosterone antibody	Same
Tracer (Lite Reagent)	Acridinium ester-labeled testosterone	Same
Specimen Type	Serum	Same
Sample Volume	15 µL	Same
Measuring Range	10–1500 ng/dL (0.35–52.1 nmol/L)	Same
Calibration	2-point calibration using Calibrator E	Same

9. Standard/Guidance Document References

The following recognized standards from Clinical Laboratory Standards Institute (CLSI) were used as a basis of the study procedures described in this submission:

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition (CLSI EP05-A2, 2004; Recognition Number 7-110)
- Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline (CLSI EP06-A, 2003; Recognition Number 7-193)
- Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition (CLSI EP07-A2, 2005; Recognition Number 7-127)
- Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition (CLSI EP17-A2, 2013; Recognition Number 7-233)
- Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition (CLSI EP28-A3c – formerly C28-A3c, 2010; Recognition Number 7-224)
- Medical devices – Application of risk management to medical devices (ANSI/AAMI/ISO 14971:2007/(R)2010; Recognition Number 5-70)

10. Performance Characteristics

10.1 Precision

A 20-day precision study was performed according to CLSI EP5-A2. Samples included human specimen pools, three levels of controls and one in-house serum control. Each sample was assayed in 2 replicates per run, 2 runs per day for 20 days for a total of 80 replicates. Results from a representative lot are presented below.

Sample	Mean (ng/mL)	Within-Run CV	Total CV
Patient Pool 1	57.8	8.7	13.3
Patient Pool 2	211	4.0	7.9
Patient Pool 3	336	4.5	7.4
Patient Pool 4	574	5.5	7.1
Patient Pool 5	1096	5.1	8.5
Control Level 1	128	6.1	6.8
Control Level 2	487	5.6	8.3
Control Level 3	876	4.4	7.5
Serum Control	1167	5.7	9.1

10.2 Linearity

A linearity study was performed using the modified device according to CLSI EP06-A using 9 serially diluted samples spanning the assay range. The samples were assayed in triplicate and the mean of triplicate results was used for the analyses. As presented below, the mean recovery was between 90% and 110% and the bias from the linear fit estimate was <10%.

Sample	Expected (ng/dL)	Observed (ng/dL)	Recovery	Weighted Linear Fit Estimate	Bias
A	1529.7	1529.7	100.0%	1514.4	1.0%
B	1141.8	1148.0	99.5%	1136.6	0.5%
C	781.2	766.4	101.9%	758.8	3.0%
D	347.2	384.8	90.2%	381.0	-8.9%
E	178.6	194.0	92.1%	192.1	-7.0%
F	98.9	98.6	100.3%	97.7	1.2%
G	53.8	50.9	105.7%	50.4	6.6%
H	27.5	27.0	101.8%	26.8	2.6%
I	3.2	3.2	100.0%	3.2	-0.9%

The weighted linear regression equation is presented below.

Observed = 0.99(Expected) + 0.06 ng/dL (r = 0.999)

10.3 Method Comparison

A method comparison study was performed by comparing the modified device to the currently-marketed predicate device (unmodified ADVIA Centaur TSTO assay) with 120 serum samples distributed over the assay range. The analysis was performed using Deming (Orthagonal) regression. The regression equation from the analysis is presented below.

Modified Device = 0.970(Unmodified Device) + 7.5 ng/dL (r = 0.994)

10.4 Matrix Comparison

Not applicable. Serum is the only claimed sample type for the assay.

10.5 Reference Intervals

Reference intervals ADVIA Centaur TSTO assay were established using the predicate device. The Package Insert claims the following expected values for adult males and females:

Males: 241 to 827 ng/dL

Females: 14 to 76 ng/dL

A reference interval verification study was performed with the modified device according to CLSI EP28-A3c. Results of serum samples from 20 female and 20 male apparently healthy donors tested with the modified device were compared to the published claims in the Package Insert of the currently-marketed predicate device (unmodified ADVIA Centaur TSTO assay). For the male reference interval verification study, 19 specimens were within the range of 241 to 827 ng/dL (1 specimen was below range). For the female reference interval verification study, 18 specimens were within the range of 14 to 76 ng/dL (2 specimens were above range). These results demonstrate that the existing reference intervals for the unmodified predicate device are also applicable to the modified device.

10.6 Detection Limit

The estimations of the Limit of Blank (LoB) and Limit of Detection were performed according to CLSI guideline EP17-A2. Limit of Blank (LoB) is the highest value expected in a series of results on a sample that contains no analyte. The LoB for the modified ADVIA Chemistry TSTO assay is 3 ng/dL. The Limit of Detection (LoD) is the smallest amount that the assay can reliably detect to determine presence or absence of an analyte. The LoD for the modified ADVIA Chemistry TSTO assay is 10 ng/dL.

10.7 Endogenous Interference

Endogenous interference studies were performed according to CLSI EP07-A2. Two sample pools were tested. One sample pool had approximately 90 to 110 ng/dL testosterone. The second sample pool had approximately 360 to 440 ng/dL testosterone. These sample pools were spiked with potential interferents. Control samples were prepared by spiking sample pools with the appropriate diluent at the same volume as the interfering substance stock. Samples were tested in replicates of three (3) using the modified device. Results are presented below.

Endogenous Substance	Dose Without Endogenous Substance (ng/dL)	Dose With Endogenous Substance (ng/dL)	% Interference
Hemoglobin (500 mg/dL)	223	230	3.14
Triglycerides (1000 mg/dL)	218	216	-0.92
Conjugated Bilirubin (20 mg/dL)	223	228	2.24
Unconjugated Bilirubin (20 mg/dL)	211	218	3.32

10.8 Cross-Reactivity

Potential cross-reactants were spiked into one low sample (~ 90-110 ng/dL testosterone) and into one sample consisting only of Multi-Diluent 3 (~ 0 ng/dL). Testing was performed using the modified device in replicates of 6 per sample. Results are presented below.

Cross-Reactant	Cross Reactant Conc. ng/dL	Multi-diluent 3		Test Sample	
		(ng/dL)	% Cross Reactivity (%)	(ng/dL)	% Cross Reactivity (%)
5α-dihydrotestoterone	10000	522.38	5.21	579.62	4.85
	0	1.13		94.97	
Androstenedione	10000	1.26	-0.02	108.39	0.06
	0	3.29		102.54	
Methyltestosterone	10000	13.90	0.14	129.58	0.39
	0	0.00		90.95	
Estradiol-17β	10000	0.21	0.00	89.62	0.00
	0	0.29		91.34	
Androsterone	100000	9.41	0.01	106.72	0.01
	0	1.64		98.36	
Cortisol	100000	18.72	0.01	102.48	0.01
	0	13.46		97.08	
Corticosterone	100000	4.25	0.00	103.54	0.00
	0	1.42		101.10	
Cyproterone	10000	16.10	0.00	98.57	0.00
	0	14.16		103.26	
Danazol	100000	43.07	0.04	160.63	0.07
	0	0.46		92.76	
DHEA-sulfate	100000	0.00	0.00	98.69	-0.01
	0	0.00		105.85	
11-deoxycortisol	100000	1.12	0.00	103.13	0.01
	0	0.70		93.33	
Dexamethasone	100000	0.60	0.00	94.17	0.00
	0	0.00		97.98	
Estrone	10000	2.16	0.02	89.47	-0.01
	0	0.00		96.58	
Oxymetholone	10000	15.45	-0.01	104.59	0.01
	0	16.15		103.28	
Progesterone	100000	92.74	0.09	188.82	0.09
	0	2.23		101.45	

10.9 Stability

The onboard stability of the ADVIA Centaur TSTO reagents is 14 days with a calibration interval of 7 days. The reagents are stable until the date printed on the box label when stored at 2-8°C.

10.10 Clinical Studies

Not applicable.

10.11 Clinical Cut-off

Not applicable.

11. Conclusions

Based on the results of comparative testing, the modified ADVIA Centaur TSTO assay is substantially equivalent in principle and performance to the currently-marketed predicate device, the ADVIA Centaur TSTO assay, cleared under 510(k) k934562.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

SIEMENS HEALTHCARE DIAGNOSTICS INC.
MATTHEW GEE
SENIOR MANAGER, REGULATORY AFFAIRS
511 BENEDICT AVENUE
TARRYTOWN NY 10591-5097

February 21, 2014

Re: K133491
Trade/Device Name: ADVIA Centaur Testosterone (TSTO)
Regulation Number: 21 CFR 862.1680
Regulation Name: Testosterone test system
Regulatory Class: I, reserved
Product Code: CDZ
Dated: December 18, 2013
Received: January 7, 2014

Dear Mr. Gee:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Ruth A. Chesler -S

for
Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
k133491

Device Name
ADVIA Centaur Testosterone (TSTO)

Indications for Use *(Describe)*

For in vitro diagnostic use in the quantitative determination of total testosterone (bound and unbound) in serum using the ADVIA Centaur and ADVIA Centaur XP Systems.

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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yung W. Chan -S

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