Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K191533

B Applicant

Siemens Healthcare Diagnostics Inc.

C Proprietary and Established Names

ADVIA Centaur® Testosterone (TSTII), ADVIA Centaur® SHBG

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CDZ	Class I, reserved	21 CFR 862.1680 - Testosterone Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Testosterone II (TSTII) - Assay re-standardization to align with Center for Disease Control and Prevention (CDC) HoSt Testosterone Reference Measurement Procedure.

Sex hormone-binding globulin (SHBG) - Updated reference intervals and biotin interference testing.

B Measurand:

Testosterone and Sex Hormone Binding Globulin (SHBG)

C Type of Test:

Quantitative, chemiluminescent immunoassays

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
The ADVIA Centaur® Testosterone II (TSTII) assay is for in vitro diagnostic use in the quantitative determination of total testosterone (bound and unbound) in human serum and plasma using the ADVIA Centaur® XP system. 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.

The ADVIA Centaur® SHBG assay is an in vitro diagnostic immunoassay for the quantitative determination of sex hormone-binding globulin (SHBG) in human serum and plasma using the ADVIA Centaur® XP system. The ADVIA Centaur® SHBG assay is intended for use as an aid in the diagnosis of androgen disorders.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

ADVIA Centaur XP System

IV Device/System Characteristics:

A Device Description:

The ADVIA Centaur® Testosterone II (TSTII) consist of the following reagents:

ADVIA Centaur TSTII Primary Reagent ReadyPack (included in assay kit)		
Component	*Volume*	*Ingredients*
ADVIA Centaur TSTII Lite Reagent	10.0 mL/pack	Acridinium ester-labeled hapten (36 µg/mL) in buffered saline with preservatives
ADVIA Centaur TSTII Solid Phase Reagent	17.0 mL/pack	Streptavidin-coated latex particles (0.33 g/L) in buffered saline with preservatives

ADVIA Centaur TSTII Ancillary Reagent ReadyPack (included in assay kit)		
Component	*Volume*	*Ingredients*
ADVIA Centaur TSTII Releasing Agent	10.0 mL/pack	Steroid releasing agent (0.4 µg/mL) and biotinylated sheep monoclonal anti-testosterone antibody (27 µg/L) in buffered saline and preservatives

The ADVIA Centaur® SHBG consist of the following reagents:

ADVIA Centaur SHBG Primary Reagent ReadyPack (included in assay kit)		
Component	*Volume*	*Ingredients*
ADVIA Centaur SHBG Lite Reagent	3.0 mL/pack	Mouse monoclonal anti-SHBG antibody (~130 ng/mL) labeled with acridinium ester in HEPES-buffered saline with bovine serum albumin, mouse serum, sodium azide (< 0.1%), surfactant, and preservatives
ADVIA Centaur SHBG Solid Phase Reagent	11.0 mL/pack	Streptavidin coupled to latex paramagnetic particles (~150 µg/mL) in HEPES buffered saline with bovine serum albumin, mouse serum, sodium azide (< 0.1%), surfactant, and preservatives
ADVIA Centaur SHBG Ancillary Well Reagent	3.0 mL/pack	Biotinylated monoclonal mouse anti-SHBG antibody (~6 µg/mL) in HEPES buffered saline with bovine serum albumin, mouse serum, sodium azide (< 0.1%), surfactant, and preservatives

B Principle of Operation:

ADVIA Centaur® Testosterone (TSTII) assay is a competitive immunoassay using direct chemiluminescent technology. Testosterone in the sample competes with acridinium ester-labeled hapten in the Lite Reagent for binding with the anti-testosterone sheep monoclonal antibody in the ADVIA Centaur TSTII Releasing Agent and streptavidin magnetic latex particles in the Solid Phase Reagent. The ADVIA Centaur TSTII assay uses ADVIA Centaur TSTII Releasing Agent to release bound testosterone from the endogenous binding proteins in the sample.

The ADVIA Centaur® SHBG assay is a sandwich immunoassay that uses three reagent components: Solid Phase, Ancillary Well Reagent, and Lite Reagent. Solid Phase is streptavidin-coupled magnetic latex particles, Ancillary Well Reagent contains biotinylated F(ab)2 monoclonal antibody to SHBG, and Lite Reagent consists of a second F(ab)2 monoclonal antibody to SHBG labeled with acridinium ester (SHBG-AE). The amount of SHBG present in the patient sample is proportional to the amount of relative light units (RLUs) detected by the system. Results are calculated from a master curve adjusted by using high and low calibrators.

V Substantial Equivalence Information:

A Predicate Device Name(s):
ADVIA Centaur Testosterone II (TSTII), ADVIA Centaur SHBG

B Predicate 510(k) Number(s):
K151986

C Comparison with Predicate(s):

TSTII

Device & Predicate Device(s):	K191533	K151986
Device Trade Name	ADVIA Centaur® Testosterone II (TSTII)	ADVIA Centaur Testosterone II (TSTII)
General Device Characteristic Similarities		
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.	Same
Methodology	Chemiluminescence	Same
Assay Protocol	Competitive immunoassay	Same
Traceability/ Standardization	ID-LC-MS/MS	Same
Specimen Type	Human serum and plasma	Same
Sample Volume	20 µL	Same
Measuring Range	7.0–1500 ng/dL	Same
Calibration	2-point calibration	Same
General Device Characteristic Differences		
Reference Interval (ng/dL)	***Adults*** *Males:* <50 yr: 197.44-669.58 ≥50 yr: 187.72-684.19 *Females:* <50 yr: 8.38-35.01 ≥50 yr: <7.00-35.92	***Adults*** *Males:* <50 yr: 123.06-813.86 ≥50 yr: 86.98-780.10 *Females:* <50 yr: 9.01-47.94 ≥50 yr: <7.00-45.62

Device & Predicate Device(s):	K191533	K151986
	Pediatrics *Males:* Tanner Stage 1: <7.00-13.06 Tanner Stage 2: <7.00-79.13 Tanner Stage 3: <7.00-499.18 Tanner Stage 4: 79.10-747.17 Tanner Stage 5: 224.83-669.65 Age 2-10: <7.00-10.50 Age 11: <7.00-478.50 Age 12: <7.00-487.97 Age 13: 8.28-549.79 Age 14: 8.91-535.34 Age 15: 65.96-756.50 Age 16-21: 228.16-710.74 *Females:* Tanner Stage 1: <7.00-10.06 Tanner Stage 2: <7.00-30.11 Tanner Stage 3: <7.00-30.49 Tanner Stage 4: <7.00-35.19 Tanner Stage 5: 11.80-39.30 Age 2-10: <7.00-11.86 Age 11-15: <7.00-27.57 Age 16-21: 11.78-43.34	***Pediatrics*** *Males:* Tanner Stage 1: <7.00-47.43 Tanner Stage 2: <7.00-174.45 Tanner Stage 3: 10.54-802.75 Tanner Stage 4: 63.89-736.20 Tanner Stage 5: 55.69-897.40 Age 2-10: <7.00-29.44 Age 11: <7.00-353.00 Age 12: <7.00-562.42 Age 13: 8.19-528.87 Age 14: 20.35-777.38 Age 15: 127.21-849.36 Age 16-21: 113.19-882.10 *Females:* Tanner Stage 1: <7.00-89.56 Tanner Stage 2: <7.00-38.29 Tanner Stage 3: <7.00-33.86 Tanner Stage 4: <7.00-38.72 Tanner Stage 5: 10.83-50.08 Age 2-10: <7.00-117.76 Age 11-15: <7.00-38.92 Age 16-21: 15.06-42.41

SHBG

Device & Predicate Device(s):	K191533	K151986
Device Trade Name	ADVIA Centaur® SHBG	ADVIA Centaur SHBG
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the quantitative determination of sex hormone-binding globulin (SHBG) in human serum and plasma using the ADVIA Centaur XP system.	Same
Methodology	Chemiluminescence	Same
Assay Protocol	Sandwich immunoassay	Same

Device & Predicate Device(s):	K191533	K151986
Traceability/ Standardization	WHO 2nd International Standard (08/226)	Same
Specimen Type	Human serum and plasma	Same
Sample Volume	20 µL	Same
Measuring Range	1.60–180 nmol/L	Same
Calibration	2-point calibration	Same
General Device Characteristic Differences		
Reference Interval (nmol/L)	***Adults*** *Males:* <50 yr: 11.54-54.49 ≥50 yr: 17.33-71.50 *Females:* <50 yr: 17.69-138.26 ≥50 yr: 23.65-110.61	***Adults*** *Males:* <50 yr: 14.55-94.64 ≥50 yr: 21.63-113.13 *Females:* <50 yr: 10.84->180.00 ≥50 yr: 23.15-159.07

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3, 2004 Evaluation of Precision Performance of Quantitative Measurement Procedures; Approved Guideline – Third Edition
- CLSI EP06-A, 2003 Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline – First Edition
- CLSI EP17-A2, 2013; Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition
- CLSI EP28-A3c, 2010; Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

TSTII: A precision study was performed in accordance with CLSI EP05-A3 guideline. The panel of 9 samples used in the study included 5 human serum pools (Medical Decision Pools MDP), one female human serum sample pool and three controls. Each sample was tested using one reagent lot over 20 days, with 2 runs per testing day and 2 replicates per run. The results of the precision studies are shown below:

Sample	N	Mean (ng/dL)	Within-run		Total	
			SD	%CV	SD	%CV
Control 1	80	257.38	9.06	3.5	14.38	5.6
Control 2	80	636.57	45.14	7.1	53.12	8.3
Control 3	80	1,021.93	62.28	6.1	81.02	7.9
MDP 1	80	20.92	1.3	6.2	1.86	8.9
MDP 2	80	73.57	3.54	4.8	5.24	7.1
MDP 3	80	312.81	13.4	4.3	23.99	7.7
MDP 4	80	776.64	42.59	5.5	58.26	7.5
MDP 5	80	1,123.83	59.22	5.3	109.57	9.7
Female Human Serum	80	15.86	1.84	11.6	2.39	15.1

SHBG: See previous performance in k091867.

2. Linearity:

TSTII: A linearity study was performed in accordance with CLSI EP06-A guideline. A dilution series consisting of 9 levels with concentrations ranging from 6.94 to 1,655.90 ng/dL was prepared by mixing high and low pools of testosterone. For each dilution sample, 3 replicate measurements were made using a single reagent lot, on a single instrument, in a single day. The deviation of the results from the expected linear fit was analyzed. The linear regression formula obtained from the analysis of the results was as follows:

$y = 1.004x - 0.015$

The results from the linearity study support an analytical measuring range from 7 - 1,500 ng/dL.

SHBG: See previous performance in k151986.

3. Analytical Specificity/Interference:

TSTII: Refer to the interference studies reported in k091867.

The sponsor conducted additional testing to evaluate biotin interference on the TSTII assay. Up to 1,500 ng/mL biotin was spiked into two concentrations of TSTII, 83 µg/mL and 289 µg/mL. Triplicate measurements were recorded for each sample (including a negative control without biotin) using a single lot of TSTII assay reagent on the ADVIA Centaur XP Instrument. The sponsor defines no significant interference as <10% change in results, and states that no significant interference was observed at biotin concentrations ≤ 30 ng/mL for both concentrations of TSTII tested.

% Bias for Samples Containing Various Concentration of Biotin							
Testosterone Conc.	**Biotin Concentration (ng/mL)**						
	30	**50**	**100**	**250**	**500**	**1200**	**1500**
83 ng/dL	4	6	23	84	370	3981	6837
289 ng/dL	2	7	19	107	441	>AMR*	>AMR*

* Interference could not be calculated because the results of the biotin spiked samples were above the claimed analytical measuring range of the assay.

The labeling includes the following limitation: "Specimens that contain biotin at a concentration of 30 ng/mL demonstrate a less than or equal to 10% change in results. Biotin concentrations greater than this may lead to falsely elevated results for patient samples. The recommended adult daily dietary intake for biotin is 30 µg/day. Over the counter dietary supplements promoted for use in hair, skin and nail health may contain 5-10 mg of biotin. Pharmacokinetic studies in healthy adults have shown that ingesting 5 mg of biotin can result in serum levels as high as 73 ng/mL. In rare cases, subjects are prescribed up to 300 mg of biotin per day for therapeutic applications, resulting in serum biotin levels as high as 1,160 ng/mL."

SHBG: Refer to the interference studies reported in k091867.

The sponsor conducted additional testing to evaluate biotin interference on the SHBG assay. Up to 1,200 ng/mL biotin was spiked into two concentrations of SHBG, 19.6 and 44.1 nmol/L. Triplicate measurements were recorded for each sample (including a negative control without biotin) using a single lot of SHBG assay reagent on the ADVIA Centaur XP Instrument. The sponsor defines no significant interference as <10% change in results, and states that no significant interference was observed at biotin concentrations ≤ 600 ng/mL for both concentrations of SHBG tested.

% Bias for Samples Containing Various Concentration of Biotin						
SHBG Conc.	**Biotin Concentration (ng/mL)**					
	38	**75**	**150**	**3000**	**600**	**1200**
19.6 nmol/L	-3	-3	-9	-7	-7	-25
44.1 nmol/L	-2	1	-3	-7	-9	-26

The labeling includes the following limitation: "Specimens that contain biotin at a concentration of 300 ng/mL demonstrate a less than or equal to 10% change in results. Biotin concentrations greater than this may lead to falsely depressed results for patient samples. Over the counter dietary supplements promoted for use in hair, skin and nail health may contain 5-10 mg of biotin. Pharmacokinetic studies in healthy adults have shown that ingesting 10 mg of biotin can result in serum levels as high as 141 ng/mL. In rare cases, subjects are prescribed up to 300 mg of biotin per day for therapeutic applications, resulting in serum biotin levels as high as 1,160 ng/mL."

4. Assay Reportable Range:

TSTII: 7.00 - 1,500.00 ng/dL

SHBG: 1.6 - 180.0 nmol/L

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability:

TSTII: The ADVIA Centaur® Testosterone II (TSTII) assay is standardized using internal standards made from USP-grade testosterone, which are traceable to isotope dilution-liquid chromatography-tandem mass spectrometry (ID-LC-MS/MS). The ID-LC-MS/MS is traceable to the primary testosterone standard National Measurement Institute (NMI) M914.

SHBG: The ADVIA Centaur SHBG assay is traceable to the WHO 2nd International Standard for Sex Hormone Binding Globulin (08/226) from National Institute for Biological Standards and Control (NIBSC).

Standardization:
The ADVIA Centaur® Testosterone II (TSTII) assay was re-standardized to more closely align with the CDC HoSt Testosterone Reference Measurement Procedure (RMP). The ADVIA Centaur ® Testosterone II (TSTII) assay is standardized using internal standards manufactured using USP grade testosterone; the assigned values of these standards correlate to the CDC HoSt Testosterone RMP via method comparison. The assigned value of three of the 10 assay gold standards was modified.
The low and high calibrator specifications remain unchanged. Similar to the predicate TSTII assay (K151986), the re-standardized ADVIA Centaur® Testosterone II (TSTII) assay is still standardized using internal standards made from USP-grade testosterone, which are traceable to ID-LC-MS/MS CDC HoST Testosterone RMP. The ADVIA Centaur TSTII Calibrators included in the assay kit for the re-standardized ADVIA Centaur TSTII assay are the same formulation as the calibrators for the predicate ADVIA Centaur TSTII assay.

6. Detection Limit:

TSTII: Limit of blank (LoB) study was performed by testing 5 blank samples of human serum pools using 2 reagent lots over 5 days on a single instrument. Each day, 2 runs were conducted. For each sample, 6 replicate measurements were recorded per run (300 replicates total). LoB was calculated non-parametrically at the 95th percentile for each lot. The LoB for each lot was the result at this rank position. If the rank position was a non-integer, the LoB was determined by interpolation between the bracketing values. The largest LoB for both reagent lots was chosen as the assay's LoB.

Limit of detection (LoD) study was performed by testing 10 low level samples (female human serum pools) using 2 reagent lots over 5 days on a single instrument. Each day, 2 runs were performed and for each sample, 6 replicate measurements were recorded per run (1,200 replicates total). LoD was calculated non-parametrically. The higher LoD of the two lots was the assay's LoD.

Limit of quantitation (LoQ) study was performed using 10 female human sera samples with low levels of analytes and 5 blank male and female human serum pools measured over 5 days using 2 reagent lots on 1 instrument per lot. Each day, 2 runs were performed and for each sample, 6 replicate measurements were recorded. For each reagent lot, the within-laboratory precision (expressed as %CV) was plotted against the mean concentration for each sample. The sponsor defines LoQ as the analyte concentration corresponding to 20% within-lab CV. The largest LoQ for both reagent lots was chosen as the assay's LoQ.

Detection Limits Summary for ADVIA Centaur® Testosterone II (TSTII) assay:

LoB	LoD	LoQ
1.3 ng/dL	3.57 ng/dL	4.57 ng/dL

SHBG: See previous performance in k091867.

7. Assay Cut-Off:
Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

TSTII: The sponsor conducted a method comparison study to verify that the re-standardization of the assay does not have a significant impact on the performance of the device compared to the previous assay (originally cleared in k151986). The study was designed to compare the performance of the TSTII assay to that of the recognized reference method (CDC HoSt Testosterone Reference Measurement Procedure (RMP) ID-LS-MS/MS). The study evaluated a total of 108 individual male and female adult serum samples spanning the assay range. Of these, 72 samples were individual (non-pooled) human sera from single donors obtained by Siemens, with testosterone concentrations assigned by CDC HoSt Testosterone RMP ID-LS-MS/MS. 30 samples were supplied directly by CDC, and were individual human serum obtained from individual blood bank donors, with testosterone concentrations assigned by CDC HoSt Testosterone RMP ID-LS-MS/MS. Less than 5% of the samples were contrived to cover concentrations at the extreme ends of the measuring range. All samples were run singlicate on one ADVIA Centaur XP system using a single reagent lot over 3 days. The results for ADVIA Centaur® Testosterone (TSTII) versus CDC HoSt Testosterone RMP ID-LS-MS/MS were analyzed using Passing-Bablok regression analysis. The results are summarized below:

N	108
Slope	0.97
Intercept	-0.22
R	0.98
Test Range	7.27-1,394 ng/dL

In addition, a method comparison study was performed to evaluate the performance of the re-standardized ADVIA Centaur® Testosterone II (TSTII) assay against the previously cleared assay (k151986). A total of 108 individual male and female adult serum samples spanning the assay range were run on one ADVIA Centaur XP instrument using a single reagent lot. Samples were assayed in singlicate over 3 days. Weighted Deming regression was used for data analysis.

N	108
Slope	1.04
Intercept	-4.14
R	1.00
Test Range	10.93-1,439.77 ng/dL

An additional method comparison study was performed to evaluate the performance of the re-standardized ADVIA Centaur® Testosterone II (TSTII) assay against a commercially available testosterone assay, Dimension Vista LOCI Total Testosterone (k151529). A total of 124 serum samples (79 adults and 45 pediatric subjects) spanning the assay range were run on one ADVIA Centaur XP instrument using a single reagent lot and on one Dimension Vista instrument using one Dimension Vista LOCI TSTT reagent lot. Samples were assayed in singlicate over 3 days. Weighted Deming regression was used for data analysis. The results for all specimens are reported below.

N	124
Slope	1.01
Intercept	-3.32
R	0.99
Test Range	9.00-984 ng/dL

SHBG: See previous performance in k151986.

2. Matrix Comparison:

TSTII: Following a technical risk assessment of the assay performance attributes that may be impacted by re-standardization of the current TSTII assay, the sponsor determined that assay re-standardization is not expected to impact the results dependent on specimen matrix. The sponsor indicated study control is equally affected by the re-standardization, therefore, there is no effect on the result and the claim is unaffected, this is supported by the data showing similar performance to the predicate device. FDA found this justification to be acceptable. Therefore, the matrix comparison study data from the ADVIA Centaur® Testosterone (TSTII) assay cleared in k151986 remains applicable.

SHBG: See previous matrix comparison study in k151986.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

TSTII: A reference interval study was performed for the ADVIA Centaur® Testosterone II (TSTII) assay in accordance with CLSI EP28-A3c guideline. A total of 940 pediatrics and 760 adult samples were collected from apparently healthy individuals. The sample groups tested consisted of:

- 250 adult males under 50 years of age
- 135 adult males ages ≥ 50 years old
- 224 adult females under 50 years of age
- 151 adult females ages ≥ 50 years old
- 460 male pediatrics, ages 2-21 across Tanner Stages 1-5
- 483 female pediatrics, ages 2-21 across Tanner Stages 1-5

Testing was performed using the re-standardized assay. Each sample was assayed in singlicate. For adults, the lower and upper reference limits were estimated as the 5th and the 95th percentiles of the distribution of test results using a non-parametric approach in accordance with the recommendation in CLSI EP28-A3c guideline. Due to the limited availability of pediatric samples, the sample analysis method varied depending on the number of samples in each subgroup. Please see the following descriptions of each subgroup reference intervals determination:

- For groups of 120 or more subjects, the lower and upper reference limits were estimated as the 2.5th and the 97.5th percentiles of the distribution of test results using a non-parametric approach in accordance with the recommendation in CLSI guideline EP28-A3.
- For groups of 40 to 119 subjects, the lower and upper reference limits were estimated as the 2.5th and the 97.5th percentiles of the distribution of test results using a robust measure of location and spread, as developed by Horn and Pesce.
- For groups of less than 40 subjects, the lower and upper reference limits were estimated as the 5th and the 95th percentiles of the distribution of test results.

A summary of the median and reference interval values calculated for adult and pediatrics using the re-standardized ADVIA Centaur® Testosterone II (TSTII) assay is shown below:

	Age	N	ng/dL		
			Median	Central 90th Ref Interval	
				5th	95th
Adult Male	Under 50	250	409.72	197.44	669.58
	50 and Over	135	377.46	187.72	684.19
Adult Female	Under 50	224	18.01	8.38	35.01
	50 and Over	151	14.18	<7.00	35.92
Pediatric Male	Tanner Stage 1	101	<7.00	<7.00	13.06
	Tanner Stage 2	78	<7.00	<7.00	79.13
	Tanner Stage 3	64	59.67	<7.00	499.18
	Tanner Stage 4	88	376.84	79.10	747.17

	Age	N	ng/dL		
			Median	Central 90th Ref Interval	
				5th	95th
	Tanner Stage 5	129	451.17	224.83	669.65
	Age 2-10	147	<7.00	<7.00	10.50
	Age 11	34	10.73	<7.00	478.50
	Age 12	35	132.47	<7.00	487.97
	Age 13	34	199.02	8.28	549.79
	Age 14	34	228.39	8.91	535.34
	Age 15	27	327.89	65.96	756.50
	Age 16-21	149	453.86	228.16	710.74
Pediatric Female	Tanner Stage 1	138	<7.00	<7.00	10.06
	Tanner Stage 2	60	8.17	<7.00	30.11
	Tanner Stage 3	49	12.98	<7.00	30.49
	Tanner Stage 4	98	17.37	<7.00	35.19
	Tanner Stage 5	133	19.76	11.80	39.30
	Age 2-10	159	<7.00	<7.00	11.86
	Age 11-15	174	12.95	<7.00	27.57
	Age 16-21	145	19.81	11.78	43.34

SHBG: A reference interval study was performed for the ADVIA Centaur® SHBG assay in accordance with CLSI EP28-A3c guideline. A total of 760 adult samples were collected from apparently healthy individuals. The sample groups tested consisted of:

- 250 adult males under 50 years of age
- 135 adult males ages ≥ 50 years old
- 224 adult females under 50 years of age
- 151 adult females ages ≥ 50 years old

Each sample was assayed in singlicate. The lower and upper reference limits were estimated as the 5th and the 95th percentiles of the distribution of test results using a non-parametric approach in accordance with the recommendation in CLSI guideline EP28-A3c.

A summary of the median and reference interval values calculated using the re-standardized ADVIA Centaur® SHBG assay is shown below:

	Age	N	nmol/L		
			Median	Central 90th Ref Interval	
				5th	95th
Adult Male	< 50 yrs.	250	23.80	11.54	54.49
	≥ 50 yrs.	135	36.91	17.33	71.50
Adult Female	< 50 yrs.	224	46.72	17.69	138.26
	≥ 50 yrs.	151	47.86	23.65	110.61

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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