



Food and Drug Administration  
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SIEMENS HEALTHCARE DIAGNOSTICS, INC.  
JULIE WARREN  
REGULATORY TECHNICAL SPECIALIST  
500 GBC DR. P.O. BOX 6101 M/S 514  
NEWARK DE 19714

February 11, 2016

Re: K151529

Trade/Device Name: Dimension Vista® LOCI Total Testosterone Flex® Reagent Cartridge  
Dimension Vista® Testosterone Calibrator

Regulation Number: 21 CFR 862.1680

Regulation Name: Testosterone test system

Regulatory Class: I, Reserved

Product Code: CDZ, JIT

Dated: February 08, 2016

Received: February 09, 2016

Dear Julie Warren:

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 Industry and Consumer Education 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” (21 CFR 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 Industry and Consumer Education 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,

  
**Katherine Serrano -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

## Indications for Use

510(k) Number (if known)

k151529

Device Name

Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge

Indications for Use (Describe)

The Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge is an in vitro diagnostic test for the quantitative measurement of total testosterone in human serum and plasma on the Dimension Vista® 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.

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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## Indications for Use

510(k) Number (if known)

k151529

Device Name

Dimension Vista® Testosterone Calibrator

Indications for Use (Describe)

The Dimension Vista® Testosterone Calibrator is an in vitro diagnostic product for the calibration of the Total Testosterone (TTST) assay on the Dimension Vista® System.

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)

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## 510(k) Summary

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

The assigned 510(k) number is: K151529

### 1. Submitter

Siemens Healthcare Diagnostics, Inc.  
500 GBC Dr.  
Newark, DE 19714

Contact Person: Julie Warren  
Tel: 302-631-8722  
Fax: 302-631-6299  
Email: julie.warren@siemens.com

Date of Preparation: February 5, 2016

### 2. Device Information

Name of Device: Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge  
Common Name: Testosterone test system  
Regulatory Class: I (21 CFR §862.1680, Testosterone test system)  
Product Code: CDZ  
Panel: Clinical Chemistry

Name of Device: Dimension Vista® Testosterone Calibrator  
Common Name: Testosterone Calibrator  
Regulatory Class: II (21 CFR §862.1150, Calibrator)  
Product Code: JIT  
Panel: Clinical Chemistry

### 3. Predicate Device

Assay:

Roche Diagnostics Corp.

Device Name: Elecsys® Testosterone II Immunoassay

510(k) Number: K093421

Regulatory Class: I (21 CFR §862.1680, Testosterone test system)

Classification Product Code: CDZ

Panel: Clinical Chemistry

Calibrator:

Roche Diagnostics Corp.

Device Name: Elecsys® Testosterone Calset II

510(k) Number: K003411

Regulatory Class: II (21 CFR §862.1150, Calibrator)

Classification Product Code: JIT

Panel: Clinical Chemistry

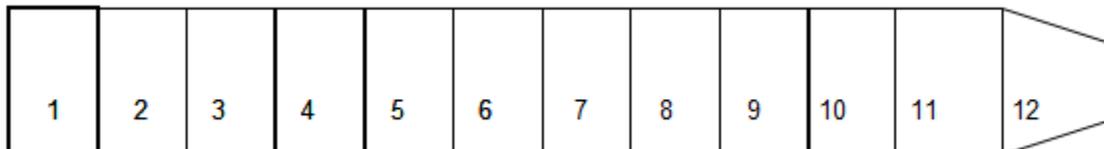
### 4. Device Description

#### Dimension Vista® LOCI Total Testosterone Flex® Reagent Cartridge

The Dimension Vista® LOCI Total Testosterone Flex® Reagent Cartridge (TTST) method is a homogeneous, competitive chemiluminescent immunoassay based on LOCI® technology. LOCI reagents include two synthetic bead reagents and labeled testosterone antibody. The first bead reagent (Chemibeads) is coated with a testosterone analog and contains a chemiluminescent dye. The second bead reagent (Sensibeads) is coated with streptavidin and contains photosensitive dye. Chemibeads and labeled testosterone antibody are added sequentially to the reaction vessel. Testosterone from the patient sample competes with the testosterone-analog-chemibead for a limited amount of labeled testosterone antibody. Sensibeads are then added and bind to the biotinylated portion of the labeled testosterone antibody to form bead pair immunocomplexes. Illumination of the complex by light at 680 nm generates singlet oxygen from the Sensibeads which diffuses to the Chemibeads triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is an inverse function of the concentration of total testosterone in the sample.

Dimension Vista® LOCI Total Testosterone reagents are liquid and contained in reagent wells of a Flex® reagent cartridge. There are twelve (12) wells in each Flex® reagent cartridge. A barcode label on the Flex® reagent cartridge identifies the test method, lot number, expiration date, and fixed number of tests for which the Flex® reagent cartridge can supply reagent. There are eighty (80) tests per Flex® reagent cartridge and four (4) Flex® reagent cartridges per carton. The reagents for this assay are assigned to wells as per the table below.

## Example Flex® Reagent Cartridge Well Configuration



Wells	Form	Name	Concentration
1-4	Liquid	Testosterone Biotinylated Antibody Reagent <sup>c, d</sup> (Sheep monoclonal);  Displacer	31.3 ng/mL;  1200 ng/mL
5-8	Liquid	Testosterone Chemibead Reagent <sup>d</sup>	100 µg/mL
9-12	Liquid	Testosterone Sensibead Reagent <sup>d</sup>	400 µg/mL

- Wells are numbered consecutively from the wide end of the cartridge.
- Nominal value per well in a cartridge.
- Antibody titer and conjugate activity may vary from lot to lot.
- Contain buffers, stabilizers and preservatives.

### Calibrator

The Dimension Vista® Testosterone Calibrator (TTST CAL) is a lyophilized human serum based calibrator set containing testosterone and preservatives. Within each set of twelve (12) vials there are two (2) 1.0 mL amber glass vials for each calibrator level. There are six (6) calibrator levels labeled A, B, C, D, E, and F, which span the assay range. Each glass vial is closed with a plug and a color coded plastic cap. Vials are stored at 2-8°C. Lyophilized calibrators are reconstituted with reagent grade water using the steps listed in the instructions for use (IFU).

### **5. Intended Use/Indications for Use**

#### Assay

The Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge is an *in vitro* diagnostic test for the quantitative measurement of total testosterone in human serum and plasma on the Dimension Vista® 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.

## Calibrator

The Dimension Vista® Testosterone Calibrator is an *in vitro* diagnostic product for the calibration of the Total Testosterone (TTST) assay on the Dimension Vista® System.

### **7a. Standards Referenced**

1. *CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents, Approved Guideline*; September 23, 2009
2. *CLSI EP05-A2 Evaluation of Precision Performance of Clinical Chemistry Devices, Approved Guideline, Second Edition*; August 2004
3. *CLSI EP6-A: Evaluation of the Linearity of Quantitative Analytical Measurement Procedure: A Statistical Approach, Approved Guideline*; April 2003.
4. *CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, Approved Guideline, Second Edition*; June 18, 2012
5. *CLSI EP07-A2 Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition*; November 23, 2005
6. *CLSI EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples, Approved Guideline, Third Edition*; August 30, 2013
7. *CLSI EP28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, Approved Guideline, Third Edition*; October 19, 2010
8. *CLSI EP32-R Metrological Traceability and Its Implementation, A Report*; February 17, 2006

### **7b. Guidance Documents Referenced**

- Guidance for Industry and FDA Staff: Bundling Multiple Devices or Multiple Indications in a Single Submission - June 22, 2007
- *In Vitro* Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions – Jan. 1997
- Format for Traditional and Abbreviated 510(k)'s – Guidance for Industry and Staff – Nov. 17, 2005
- Administrative Procedures for CLIA Categorization - Guidance for Industry and Food and Drug Administration Staff – March 12, 2014
- Guidance for Industry and Food and Drug Administration Staff - eCopy Program for Medical Device Submissions - October 10, 2013
- Refuse to Accept Policy for 510(k)s - Guidance for Industry and Food and Drug Administration Staff – December 31, 2012

### **8. Medical Device to Which Equivalence is Claimed**

The Siemens Healthcare Diagnostics Inc. Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge and the Roche Diagnostics Elecsys Testosterone II Assay (K093421) are *in vitro* diagnostic devices intended to be used for the quantitation of testosterone in human serum and plasma. The Siemens Healthcare Diagnostics Inc.

Dimension Vista® Testosterone Calibrator and the Roche Diagnostics Cal II Set (K003411) are *in vitro* diagnostic devices intended to be used for calibrating quantitative testosterone assays on automated clinical chemistry analyzers. The proposed and predicate devices support the use in quantitating testosterone in human serum and plasma. The proposed devices were compared side by side via the following tables to examine their similarities and differences. The predicate labeling is enclosed in Attachment 12.

The intended usage and observed performance characteristics between the proposed devices and their predicates are substantially equivalent. Any differences in performance based on experimental data do not raise any questions of safety and effectiveness of the assay and calibrator. Siemens Healthcare Diagnostics Inc. claims substantial equivalence to the currently marketed Roche Diagnostics Elecsys® Testosterone II Assay (K093421) and Roche Diagnostics Testosterone CalSet II (K003411).

**Substantial Equivalence Comparison of Technological Characteristics with the Predicate Device**

Attribute	Predicate Device Roche Elecsys® Testosterone II Assay (K093421)	Proposed Device Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge
<b>Similarities</b>		
Intended Use	Immunoassay for the <i>in vitro</i> quantitative determination of testosterone in human serum and plasma.	The TTST assay is an <i>in vitro</i> diagnostic test for the quantitative measurement of total testosterone in human serum and plasma.
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
Measurand	Testosterone	Same

Attribute	Predicate Device Roche Elecsys® Testosterone II Assay (K093421)	Proposed Device Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge
<b>Similarities</b>		
Measurement Method	Immunoassay	Same
Test Principle	Competitive assay with sheep monoclonal antibody	Same
Reagent Form	Ready to use, in a unit that cannot be separated	Same
<b>Differences</b>		
Technology	electrochemiluminescence “ECLIA”	chemiluminescent “LOCI®”
Instrument	Elecsys® 2010 and Cobas e Immunoassay analyzers	Dimension Vista® System
Sample Size	20 µL	10 µL
Sample Type	Human Serum and Li-heparin, K2- and K3-EDTA plasma.	Human Serum, Li and Na Heparin, K2 EDTA
Detection	Electrochemiluminescence (ECLIA)	Chemiluminescence LOCI® technology
Measuring Range	2.5 -1500 ng/dL (0.087 – 52.0 nmol/L)	8-1000 ng/dL (0.278 – 34.7 nmol/L)
High Samples	Generally not necessary due to the broad measuring range.	Samples outside the assay range are diluted with MULTI 2 SDIL 1:2 dilution
Limits of Detection	Limit of Blank: 1.2 ng/dL Limit of Detection: 2.5 ng/dL	Limit of Blank: 4 ng/dL Limit of Detection: 5 ng/dL
Limit of Quantitation	12.0 ng/dL	8 ng/dL

Attribute	Roche Elecsys Testosterone Calset II (K003411)	Dimension Vista® Testosterone Calibrator
<b>Similarities</b>		
Intended Use	Elecsys Testosterone CalSet II is used for calibrating the quantitative Testosterone assay.	The TTST CAL is an <i>in vitro</i> diagnostic product for the calibration of the Total Testosterone (TTST) assay.
Measurand	Testosterone	Same
Calibrator Form	Lyophilized	Same
Calibrator Matrix	Human Serum	Same

Attribute	Roche Elecsys Testosterone Calset II (K003411)	Dimension Vista® Testosterone Calibrator
<b>Differences</b>		
Instrument	Elecsys and Cobas e immunoassay analyzers	Dimension Vista® System
Traceability/Standardization	ID-GC/MS (Isotope Dilution Gas Chromatography/Mass Spectrometry)	ID-LC/MS/MS (Isotope dilution liquid chromatography/tandem mass spectrometry)
Calibrator	Two levels Cal 1: <1.0 ng/mL Cal 2: 13.0 ng/mL	Six levels at the approximate concentrations listed below. Calibrator A: 0 ng/dL Calibrator B: 20 ng/dL Calibrator C: 50 ng/dL Calibrator D: 100 ng/dL Calibrator E: 200 ng/dL Calibrator F: 1100 ng/dL

## 9. Performance Characteristics

The Siemens Healthcare Diagnostics Inc. Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge calibrated with Dimension Vista® Testosterone Calibrator and the predicate Roche Testosterone II Assay calibrated with Roche Testosterone CalSet II are *in vitro* diagnostic immunoassay systems intended for the measurement of Testosterone in human serum and plasma. Performance of the Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge was evaluated at Siemens Healthcare Diagnostics' Newark, DE site on the Dimension Vista® 1500 System.

### a. Method Comparison

A method comparison study was performed to demonstrate the accuracy of the Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge following *CLSI/EP09-A3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples, Approved Guideline, Third Edition*.

Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge was tested versus the reference method, CDC Isotope dilution/liquid chromatographic-tandem mass spectrometry (CDC ID/LC-MS/MS).

One hundred twenty (120) serum samples across the assay range were measured. Six (6) samples were removed because they measured below the Dimension Vista® TTST assay range and one (1) sample was removed for being above the assay range. A Passing & Bablok regression analysis was done on results within the reportable range of 8 ng/dL to 1000 ng/dL, for a total of 113 samples. Correlation coefficient is based on least squares regression statistics.

#### Regression Summary

N	113
Range	7.3 -1033 ng/dL CDC ID-LC-MS/MS 8-949 ng/dL Vista TTST
Slope	0.93
y-intercept	4.0
Correlation coefficient (r)	0.994
95% confidence interval	Slope: 0.92 to 0.95 Intercept: 0.4 to 5.7

#### b. Precision

Reproducibility testing was conducted in accordance with *CLSI EP05-A2 Evaluation of Precision Performance of Clinical Chemistry Devices, Approved Guideline, Second Edition*. Serum pools, a plasma pool, and commercial controls were run in singlicate from two independent cups twice a day for twenty (20) days. The repeatability and within lab standard deviation and %CV were calculated by analysis of variance method.

Observed performance on the Dimension Vista® LOCI Total Testosterone assay is summarized below.

Sample	Mean Vista TTST (ng/dL)	Repeatability		Within-Lab	
		Standard Deviation	%CV	Standard Deviation	%CV
Serum Pool 1	13	0.7	5.2	1.0	7.3
Serum Pool 2	75	1.4	1.9	1.6	2.1
Serum Pool 3	767	13.8	1.8	18.2	2.4
Li Heparin Plasma Pool	384	14.3	3.7	15.8	4.1
Bio-Rad Liquichek™ Level 1*	71	1.2	1.7	1.8	2.6
Bio-Rad Liquichek™ Level 2*	441	4.1	0.9	5.6	1.3
Bio-Rad Liquichek™ Level 3*	855	13.2	1.6	16.9	2.0

\*Bio-Rad® is a registered trademark of Bio-Rad Laboratories, Irvine, CA 92618, USA.  
Liquichek™ is a trademark of Bio-Rad Laboratories, Irvine, CA 92618, USA.  
Bio-Rad Liquichek™ Immunoassay Plus Controls, Bio-Rad Laboratories, Irvine, CA.

c. Analytical Measuring Range/Linearity

Linearity was evaluated to determine the upper limit of the assay range according to *CLSI EP6-A: Evaluation of the Linearity of Quantitative Analytical Measurement Procedure: A Statistical Approach, Approved Guideline*. For each sample type tested, a high pool (greater than the assay range) and low pool were combined in varying ratios to produce dilutions covering the measuring interval, 8 to 1,000 ng/dL. Each level was assayed N=5 replicates.

Polynomial regression analysis was performed for the mean observed value vs. the expected value. The method is statistically linear across the analytical measuring range (AMR) of 8 to 1,000 ng/dL for serum and the following plasma sample types: lithium heparin, sodium heparin, and EDTA. The p-values observed were not significant; all sample types tested have p value >0.05.

Sample Type	Deming Regression	Correlation Coefficient	R <sup>2</sup>
Serum	0.97x + 0.1	0.999	0.998
Sodium Heparin	0.98x + 0.1	0.998	0.996
Lithium Heparin	0.98x + 0.0	0.999	0.999
EDTA	0.96x + 0.1	0.999	0.999

d. Limits of Detection and Quantitation

Limits of Blank (LoB) and Limit of Detection (LoD) were determined experimentally following *CLSI EP 17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline; Second Edition*. The limit of blank was claimed as 4 ng/dL based on data using testosterone free serum samples. The limit of detection was claimed as 5 ng/dL based on data obtained from low testosterone serum samples.

Limit of Quantitation (LoQ) was determined experimentally following *CLSI EP05-A2 Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline; Second Edition*. The limit of quantitation, 8 ng/dL, is based on the lowest analyte concentration that can be reproducibly measured with a total precision of ≤20%.

e. Interferences

Interference testing was evaluated according to *CLSI EP07-A2 Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition*. Hemolysate, Icterus, Bilirubin and Lipemia and several method specific interferences were tested using a paired-difference approach. Results are summarized below.

<b>Substance</b>	<b>Substance Concentration</b>	<b>TTST Bias (%) @ 50 ng/dL</b>	<b>TTST Bias (%) @ 300 ng/dL</b>
Hemoglobin	1000 mg/dL	2%	-7%
Bilirubin (unconjugated)	60 mg/dL	2%	-8%
Bilirubin (conjugated)	60 mg/dL	-2%	6%
Lipemia (Intralipid)	1000 mg/dL	2%	0%

Non-Interfering substances were tested according to *CLSI EP07-A2 Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition*. Results are as follows. Albumin at 6 g/dL increases TTST results by 19% at a testosterone concentration of 50 ng/dL. Immunoglobulin G at 5 g/dL decreases TTST results 27% at a testosterone concentration of 300 ng/dL. Nandrolone decanoate (19-nortestosterone) shows significant cross-reactivity with the TTST assay at 1,000 ng/mL. Do not use samples from patients under Nandrolone treatment. The following compounds at the specified concentrations tested did not show significant interference.

<b>Substance</b>	<b>Concentration Tested</b>
Acetaminophen	20 mg/dL
Acetylcysteine	150 mg/L
Amikacin	8 mg/dL
Ampicillin	5.3 mg/dL
Ascorbic Acid	6 mg/dL
Biotin	100 ng/mL
Calcium Dobesilate	200 mg/L
Caffeine	6 mg/dL
Carbamazepine	3 mg/dL
Cefoxitin	2500 mg/L
Chloramphenicol	5 mg/dL
Chlordiazepoxide	1 mg/dL
Chlorpromazine	0.2 mg/dL
Cholesterol	503 mg/dL
Cimetidine	2 mg/dL
Creatinine	30 mg/dL
Cyclosporine	5 mg/L
Dextran 40	5000 mg/dL
Diazepam	0.51 mg/dL
Digoxin	6.1 ng/mL
Doxycycline	50 mg/L
Enoxaparin Sodium	60 mg/L
Erythromycin	6 mg/dL
Ethanol	400 mg/dL

Substance	Concentration Tested
Ethosuximide	25 mg/dL
Furosemide	6 mg/dL
Gentamicin	1 mg/dL
Heparin	3 U/mL
Ibuprofen	50 mg/dL
Immunoglobulin G	4 g/dL
Levodopa	20 mg/L
Lidocaine	1.2 mg/dL
Lithium	2.2 mg/dL
Leuprolide	200 ng/mL
Methyldopa	20 mg/L
Metronidazole	200 mg/L
Nicotine	0.1 mg/dL
Penicillin G	25 U/mL
Pentobarbital	10 mg/dL
Phenobarbital	15 mg/dL
Phenylbutazone	400 mg/L
Phenytoin	5 mg/dL
Primidone	4 mg/dL
Propoxyphene	0.16 mg/dL
Protein: Albumin	5 g/dL
Protein: Total	10.5 g/dL
Rheumatoid Factor	1110 IU/mL
Rifampicin	60 mg/L
Salicylic Acid	60 mg/dL
Theophylline	4 mg/dL
Triglycerides	900 mg/dL
Urea	500 mg/dL
Uric Acid	20 mg/dL
Valproic Acid	50 mg/dL
Vancomycin	10 mg/dL

f. Heterophilic Antibody Interference

Heterophilic antibody interference was evaluated and reagent was designed with blockers based on the efficacy in minimizing the extent of potential interference. Human anti-mouse antibodies (HAMA) interference was evaluated according to *CLSI EP07-A2 Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition*. Samples were individual human serum samples with low and high endogenous HAMA. Two levels of testosterone were tested, approximately 150 ng/dL testosterone and ~700-800 ng/dL. Less than 10% interference was observed for HAMA at 285ng/mL and 1248 ng/mL in the presence of ~150 ng/dL and ~700-800 ng/dL testosterone.

HAMA Concentration	Testosterone Level	% Interference
1248 ng/mL	149 ng/dL	-4%
285 ng/mL	156 ng/dL	-2%
1248 ng/mL	887 ng/dL	-6%
285 ng/mL	746 ng/dL	-5%

g. Cross-reactivity

Cross-reactivity of multiple compounds was evaluated in two concentrations of testosterone, at a 0 ng/mL and 300 ng/mL. Spiked test samples were assayed and compared to control samples. Percent cross-reactivity was calculated between the means, where ND denotes not detected. Observed results are shown below.

Cross Reactant	Conc. Tested	Testosterone 0 ng/dL	Testosterone 300 ng/dL
5 $\alpha$ -dihydrotestosterone	500 ng/mL	0.3%	-0.1%
5 $\alpha$ -androstane-3-beta,17-beta-diol	1000 ng/mL	0.02%	-0.03%
5-androstene-3b,17b-diol	1000 ng/mL	0.2%	0.1%
5 $\beta$ -androstane-3b,17b-diol	100 ng/mL	ND	-0.2%
11b-hydroxytestosterone	100 ng/mL	1.9%	1.0%
11-deoxycortisol	1000 ng/mL	ND	0.01%
11-ketotestosterone	1000 ng/mL	0.2%	1.6%
17 $\alpha$ -methyltestosterone	100 ng/mL	4.2%	1.7%
17 $\beta$ -Estradiol	1000 ng/mL	0.01%	-0.02%
Androstenedione	100 ng/mL	0.2%	-0.1%
Androsterone	1000 ng/mL	ND	0.004%
Corticosterone	1000 ng/mL	ND	0.001%
Cortisol	1000 ng/mL	ND	0.01%
Danazol	1000 ng/mL	0.1%	0.04%
Dehydroepiandrosterone (DHEA)	1000 ng/mL	ND	-0.01%
Dehydroepiandrosterone sulfate (DHEA-S)	50,000 ng/mL	0.02%	0.03%
Dexamethasone	2000 ng/mL	ND	0%
Estrone	1000 ng/mL	ND	-0.01%
Ethisterone	1000 ng/mL	0.1%	-0.003%
Norethindrone	50 ng/mL	0.4%	0.5%
Norgestrel	1000 ng/mL	0.1%	-0.02%
Oxymetholone	100 ng/mL	ND	0.02%
Progesterone	1000 ng/mL	ND	0%
Testosterone Propionate	100 ng/mL	ND	0%
Prednisone	1000 ng/mL	ND	0.01%
Prednisolone	1000 ng/mL	ND	-0.002%
Cortisone	2000 ng/mL	ND	0.003%

h. Serum and Plasma Equivalency

The recommended tube types for use with the Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge are serum, lithium heparin plasma, sodium heparin plasma, and K2 EDTA. Sixty (60) matched sets were freshly drawn and tested. Samples included in the regression spanned the assay range. One sample was removed from analysis because it quantitated below the assay range. Regression analysis was performed on each sample type versus serum.

Comparative Specimen	Slope	Intercept	Correlation Coefficient	Number of Samples
Li Hep Plasma	0.98	-1.6 ng/dL	0.998	59
Na Hep Plasma	0.99	-1.4 ng/dL	0.996	59
K2 EDTA Plasma	1.00	-1.1 ng/dL	0.995	59

i. Expected Values (Reference Interval)

The following patient populations were tested to determine the reference interval for the Dimension Vista® Testosterone Assay following *CLSI EP28-A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, Approved Guideline, Third Edition*.

The reference intervals were calculated non-parametrically and represent the central 95% of results determined from healthy males ≤50 years old, males >50 years of, normal cycling females and postmenopausal females.

Reference Range Category	Observed TTST Value (ng/dL)	Sample Range TTST (ng/dL)	Number of Samples
Adult Males ≤50 years old	2.5% = 113 ng/dL; 97.5% = 1065 ng/dL	41-1465 ng/dL	174
Adult Males >50 years old	2.5% = 95 ng/dL; 97.5% = 948 ng/dL	24-1053 ng/dL	146
Pre-menopausal females	2.5% = 9 ng/dL; 97.5% = 53 ng/dL	3-64 ng/dL	189
Post-menopausal females	2.5% = <8 ng/dL; 97.5% = 48 ng/dL	0-61 ng/dL	146

The reference intervals for pediatric ranges were calculated either non-parametrically or using the "Robust" method of Horn & Pesce, depending on the number of samples per age group.

Number of Samples	Percentile Reported	Calculation Method
19 ≤ N ≤ 38	5 <sup>th</sup> and 95 <sup>th</sup> (Central 90 <sup>th</sup> )	Non-parametric
N = 39	2.5 <sup>th</sup> and 97.5 <sup>th</sup> (Central 95 <sup>th</sup> )	Non-parametric
40 ≤ N ≤ 119	2.5 <sup>th</sup> and 97.5 <sup>th</sup> (Central 95 <sup>th</sup> )	“Robust” method of Horn & Pesce
N ≥ 120	2.5 <sup>th</sup> and 97.5 <sup>th</sup> (Central 95 <sup>th</sup> )	Non-parametric

The reference intervals represent females ages 2-10 years, 11-15 years, and 16-21 years and males 2-10 years, 16-21 years, and individual ages 11,12,13, 14, and 15. In addition, the Tanner stages I-V were evaluated for both males and females.

Stages/Age	Gender	N	Median (ng/dL)	Median (nmol/L)	Lower Limit (ng/dL)	Upper Limit (ng/dL)	Lower Limit (nmol/L)	Upper Limit (nmol/L)
Ages 2-10	Male	44	< 8	< 0.278	< 8	31	< 0.278	1.08
Ages 11	Male	21	12	0.416	< 8	321	< 0.278	11.1
Ages 12	Male	24	84	2.91	< 8	531	< 0.278	18.4
Ages 13	Male	20	107	3.71	< 8	609	< 0.278	21.1
Ages 14	Male	30	275	9.54	23	652	0.798	22.6
Ages 15	Male	20	298	10.3	126	792	4.37	27.5
Ages 16-21	Male	44	424	14.7	116	779	4.03	27.0
Ages 2-10	Female	40	< 8	< 0.278	< 8	80	< 0.278	2.78
Ages 11-15	Female	125	21	0.729	< 8	49	< 0.278	1.70
Ages 16-21	Female	35	34	1.18	20	56	0.694	1.94

Stages/Age	Gender	N	Median (ng/dL)	Median (nmol/L)	Lower Limit (ng/dL)	Upper Limit (ng/dL)	Lower Limit (nmol/L)	Upper Limit (nmol/L)
Tanner Stage I	Male	39	< 8	< 0.278	< 8	64	< 0.278	2.22
Tanner Stage II	Male	41	13	0.451	< 8	166	< 0.278	5.76
Tanner Stage III	Male	42	208	7.22	< 8	609	< 0.278	21.1
Tanner Stage IV	Male	42	308	10.7	43	756	1.49	26.2
Tanner Stage V	Male	42	422	14.6	66	841	2.29	29.2
Tanner Stage I	Female	45	< 8	< 0.278	< 8	79	< 0.278	2.74
Tanner Stage II	Female	41	17	0.59	< 8	45	< 0.278	1.56
Tanner Stage III	Female	39	23	0.798	< 8	49	< 0.278	1.70
Tanner Stage IV	Female	40	25	0.868	8	54	0.278	1.87
Tanner Stage V	Female	41	30	1.04	14	71	0.486	2.46

## 10. Conclusion

The Siemens Healthcare Diagnostics Inc. Dimension Vista® LOCI Total Testosterone Flex® reagent cartridge is considered substantially equivalent to the Roche Diagnostics Elecsys® Testosterone II Assay (K093421) based on their substantially equivalent intended use. Feature comparison and assay comparative testing described in the submission demonstrates substantially equivalent performance.

Dimension Vista® Testosterone Calibrator is considered substantially equivalent to the Roche Diagnostics Testosterone Cal II Set (K003411) based on their substantially equivalent intended use. Feature comparison and comparative testing described in the submission demonstrates substantially equivalent performance.

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