



Food and Drug Administration
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November 26, 2014

SIEMENS HEALTHCARE DIAGNOSTICS INC.
FRANCES DILLON
SR. MANAGER, REGULATORY AFFAIRS
PO BOX 6101, M/S 514
NEWARK DE 19714-6101

Re: K140859

Trade/Device Name: Dimension® VISTA Free Thyroxine Flex® Reagent Cartridge, FT4;
Dimension® VISTA Thyroid Stimulating Hormone Flex® Reagent
Cartridge, TSH

Regulation Number: 21 CFR 862.1695

Regulation Name: Free thyroxine test system

Regulatory Class: II

Product Code: CEC, JLW

Dated: November 24, 2014

Received: November 25, 2014

Dear Frances Dillon:

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,


Courtney H. Lias -S

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)
K140859

Device Name
Dimension® Vista Free Thyroxine Flex® reagent cartridge, FT4

Indications for Use (Describe)

The FT4L method is an in vitro diagnostic test for the quantitative measurement of Free Thyroxine in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of free thyroxine are used in the diagnosis and monitoring of thyroid disease.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Indications for Use

510(k) Number (if known)
K140859

Device Name
Dimension Vista® Thyroid Stimulating Hormone Flex® reagent cartridge, TSH

Indications for Use (Describe)

The TSH method is an in vitro diagnostic test for the quantitative measurement of Thyroid Stimulating Hormone in human serum and plasma on the Dimension Vista® System. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

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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Section 6. 510(k) Summary of Safety and Effectiveness

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: K140859

1. **Date Prepared**

November 25, 2014

2. **Applicant Information**

Contact: Frances A. Dillon.
 Senior Manager, Regulatory Affairs

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3. **Regulatory Information**

Table 1. Regulatory Information for Dimension Vista® FT4 and TSH Assays

	FT4	TSH
Trade Name	Dimension Vista® Free Thyroxine Flex® reagent cartridge, FT4	Dimension Vista® Thyroid Stimulating Hormone Flex® reagent cartridge, TSH
Model Numbers	K6410	K6412
Common Name	Radioimmunoassay, free thyroxine	Radioimmunoassay, thyroid stimulating hormone
Classification Name	Free thyroxine test system	Thyroid stimulating hormone test system
FDA Classification	Class II	Class II
Review Panel	Clinical Chemistry	Clinical Chemistry
Product Code	CEC	JLW
Regulation Number	862.1695	862.1690

4. Predicate Device Information

The inclusion of pediatric reference intervals to the labeling (Package Inserts) of the Dimension Vista® FT4 and TSH assays does not require any other device modifications (i.e. no change to design or manufacturing process). No changes were made to the reagents. Therefore, as shown in the table below, the predicate and subject devices are the same.

Table 2. Summary of Predicate Devices for Dimension Vista® FT4 and TSH Assays

	FT4	TSH
Predicate Device	Dimension Vista® Free Thyroxine Flex® reagent cartridge, FT4	Dimension Vista® Thyroid Stimulating Hormone Flex® reagent cartridge, TSH
Subject Device	Same (As above)	Same (As above)
Predicate 510(k)	K053531	K060090

5. Substantial Equivalence Information

The following table demonstrates substantial equivalence between the predicate Dimension Vista® thyroid assays (with unmodified labeling) and Dimension Vista® thyroid assays which have modified Instructions for Use (Package Inserts) including pediatric reference intervals.

Table 3. Summary of Substantial Equivalence for Dimension Vista® FT4 and TSH Assays

Item	Predicate Device (Unmodified Labeling)	Subject Device (With Pediatric Reference Intervals)
Analytes	<u>Dimension Vista® FT4</u> Free Thyroxine (FT4)	<u>Dimension Vista® FT4</u> Same
	<u>Dimension Vista® TSH</u> <u>Thyroid Stimulating Hormone</u>	<u>Dimension Vista® TSH</u> Same
Reagents	<u>Dimension Vista® FT4</u> Dimension Vista® Free Thyroxine Flex® reagent cartridge, FT4	<u>Dimension Vista® FT4</u> Same
	<u>Dimension Vista® TSH</u> Dimension Vista® Thyroid Stimulating Hormone Flex® reagent cartridge, TSH	<u>Dimension Vista® TSH</u> Same
Instruments	Dimension Vista® 500, 1000T, 1500 and 3000T systems	Same
Intended Use Statements	<u>Dimension Vista® FT4</u> The FT4 method is an in vitro diagnostic test for the quantitative measurement of Free Thyroxine in human serum and plasma on the Dimension Vista® System.	<u>Dimension Vista® FT4</u> The FT4 method is an in vitro diagnostic test for the quantitative measurement of Free Thyroxine in human serum and plasma on the Dimension Vista® System. Measurements obtained by this device are used in the diagnosis and treatment of thyroid diseases.*

Table 3. Summary of Substantial Equivalence for Dimension Vista® FT4 and TSH Assays

Item	Predicate Device (Unmodified Labeling)	Subject Device (With Pediatric Reference Intervals)
	<p align="center"><u>Dimension Vista® TSH</u></p> <p>The TSH method is an in vitro diagnostic test for the quantitative measurement of Thyroid Stimulating Hormone in human serum and plasma on the Dimension Vista® System.</p>	<p align="center"><u>Dimension Vista® TSH</u></p> <p>The TSH method is an in vitro diagnostic test for the quantitative measurement of Thyroid Stimulating Hormone in human serum and plasma on the Dimension Vista® System. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.*</p>
Analytical Measuring Range (Assay Range)	<p align="center"><u>Dimension Vista® FT4</u></p> <p>0.1–8.0 ng/dL [1.3–103 pmol/L]</p>	<p align="center"><u>Dimension Vista® FT4</u></p> <p>Same</p>
	<p align="center"><u>Dimension Vista® TSH</u></p> <p>0.005–100 µIU/mL [mIU/L]</p>	<p align="center"><u>Dimension Vista® TSH</u></p> <p>Same</p>
Adult Reference Intervals	<p align="center"><u>Dimension Vista® FT4</u></p> <p>0.76–1.46 ng/dL [9.8–18.8 pmol/L] calculated non-parametrically and represents the central 95% of results determined from a population of 199 apparently healthy adults (140 males and 59 females, 18 – 59 years of age)</p>	<p align="center"><u>Dimension Vista® FT4</u></p> <p>Same</p>
	<p align="center"><u>Dimension Vista® TSH</u></p> <p>0.358–3.74 µIU/mL [mIU/L] calculated non-parametrically and represents the central 95% of results determined from a population of 297 apparently healthy adults (187 males and 110 females, 8–65 years of age).</p>	<p align="center"><u>Dimension Vista® TSH</u></p> <p>Same</p>
Pediatric Reference Intervals	<p align="center"><u>Dimension Vista® FT4</u></p> <p>None</p>	<p align="center"><u>Dimension Vista® FT4</u></p> <p>Infants (01 – 23 months) 0.88 - 1.48 ng/dL Children (02 – 12 years) 0.81 - 1.35 ng/dL Adolescents (13 – 20 years) 0.78 - 1.33 ng/dL</p>
	<p align="center"><u>Dimension Vista® TSH</u></p> <p>None</p>	<p align="center"><u>Dimension Vista® TSH</u></p> <p>Infants (01 – 23 months) 0.816 - 5.91 µIU/mL Children (02 – 12 years) 0.662 - 3.90 µIU/mL Adolescents (13 – 20 years) 0.463 - 3.98 µIU/mL</p>

*Additional text regarding indications added as FDA requested for 510(k) K132249.

6. Standard/Guidance Document Reference

Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline -- Third Edition (CLSI C28-A3c).

7. Pediatric Reference Intervals

Data from a total of 421 patients (82 infants, 191 children, 148 adolescents) were analyzed to establish the Dimension Vista® FT4 and TSH assay reference intervals for the studied pediatric population. Testing was performed on a Dimension Vista® 1500 system. These pediatric reference intervals, as well as the previously-established euthyroid adult reference intervals and analytical measuring ranges, are presented below.

Table 4. Comparison of Pediatric and Adult 95% Reference Intervals

	Dimension Vista® FT4	Dimension Vista® TSH
Infants (01 – 23M)	0.88 - 1.48 ng/dL	0.816 - 5.91 µIU/mL
Children (02 – 12Y)	0.81 - 1.35 ng/dL	0.662 - 3.90 µIU/mL
Adolescents (13 – 20Y)	0.78 - 1.33 ng/dL	0.463 - 3.98 µIU/mL
Euthyroid Adults*	0.76 - 1.46 ng/dL	0.358 - 3.74 µIU/mL
Assay Range*	0.1 - 8.0 ng/dL	0.005 - 100 µIU/mL

* Information taken from existing Instructions for Use (Package Inserts)

A non-parametric approach was used to establish the reference intervals for children and adolescents where the 2.5th and 97.5th percentiles of the distribution of values were calculated. Because fewer than 120 patient samples were included for the infant age group, the reference intervals were calculated by using a robust measure of location and spread, as developed by Horn and Pesce and recommended in CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals.

The robust symmetrical method was used for the Dimension Vista FT4 analysis because the data was normally distributed. The reference interval calculated from the actual data using the robust symmetrical method was confirmed with two simulated reference intervals (nonparametric and robust symmetric). Each simulated reference interval was estimated as the means of the 95% upper and lower bounds from 1000 data sets. In each case, a normal distribution was fitted to the actual results, with either n=120 for the non-parametric analysis, or n=82 for the robust symmetric analysis.

For the Dimension Vista TSH assay, the sample distribution for infant subjects was highly positively skewed. As permitted by CLSI EP28-A3, the actual results were natural log transformed to produce a well-fitted normal distribution. The infant reference intervals were then calculated using the robust symmetric method on the log transformed data. The reference interval was confirmed with two simulated reference intervals (nonparametric and robust symmetric). Each simulated reference interval was estimated as the means of the 95% upper and lower bounds from 1000 data sets. In each case, a normal distribution was fitted to the actual results, with either n=120 for the non-parametric analysis, or n=82 for the robust symmetric analysis.

The 90% confidence intervals for the Infant 95% Reference Intervals are listed below.

Table 5. Infant Reference Interval - 90% Confidence Intervals for Upper and Lower Limits

Infants (01 – 23M)	Dimension® Vista FT4	Dimension® Vista TSH
Calculation Method	Robust Symmetric	Robust Symmetric After Log Transformed
Reference Interval	0.88 – 1.48 ng/dL	0.816 – 5.91 µIU/mL
90% Confidence Interval of Lower Limit	0.82 – 0.95 ng/dL	0.683 – 0.962 µIU/mL
90% Confidence Interval of Upper Limit	1.42 – 1.53 ng/dL	5.06 – 7.09 µIU/mL

8. Performance Characteristics

The inclusion of pediatric reference intervals in the Instructions for Use (Package Inserts) does not necessitate the collection of additional analytical performance data as no changes were made to the reagents. Therefore, all analytical performance data previously reviewed for the Dimension Vista® FT4 and TSH assays continue to apply to these assays. All performance data is cross-referenced to the predicate 510(k) submissions for the FT4 and TSH assays (K053531 and K060090).

Specifically, the following studies are not needed for the purpose of this submission:

- Precision/Reproducibility
- Linearity
- Calibrator/Assay Traceability
- Calibrator/Assay Stability
- Assay Cut-off
- Method Comparison
- Matrix Comparison
- Sensitivity (Detection Limits, LoB, LoD, LoQ)
- Analytical Specificity

9. Shelf-Life

The inclusion of pediatric reference intervals in the Instructions for Use (Package Inserts) does not necessitate the collection of additional stability data as no changes were made to the reagents. Therefore, all stability methods, acceptance criteria and data previously reviewed for the Dimension Vista® FT4 and TSH assays continue to apply to these assays.

Specifically, the following stability studies are not needed for the purpose of this submission:

- Shelf Life Stability
- Onboard Stability
- Open Vial Stability

10. Conclusions

The Dimension Vista® FT4 and TSH assays with pediatric reference intervals are substantially equivalent to the currently marketed Dimension Vista® FT4 and TSH assays.

No changes were made to the reagents. The inclusion of pediatric reference intervals in the Instructions for Use (Package Inserts) does not require a change in the device design or a change in the manufacturing process.

The addition of pediatric reference intervals for the Dimension Vista® FT4 and TSH assays is further supported by the following rationale:

1. Testing of pediatric patients is within the established indications for use (i.e. for use in the diagnosis and treatment of thyroid disease), as described in 21 CFR §862.1695 and 21 CFR §862.1690.
2. The newly-established pediatric reference intervals are either within or are above the previously-established reference intervals for euthyroid (normal thyroid) adult populations and they are within the analytical measuring ranges of the Dimension Vista® FT4 and TSH assays. Therefore, the Dimension Vista® FT4 and TSH assays have appropriate analytical performance to test pediatric patients.