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

May 31, 2016

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

Re: K160647
Trade/Device Name: IMMULITE 2000 Third Generation TSH
IMMULITE 2000 Free T4
Regulation Number: 21 CFR 862.1690
Regulation Name: Thyroid stimulating hormone test system
Regulatory Class: II
Product Code: JLW, CEC
Dated: March 4, 2016
Received: March 7, 2016

Dear Matthew 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 regulation (21 CFR Part 801), 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" (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 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

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 below.

510(k) Number *(if known)* k160647

Device Name
IMMULITE® 2000 Third Generation TSH
IMMULITE® 2000 Free T4

Indications for Use *(Describe)*

For in vitro diagnostic use with the IMMULITE® 2000 Systems Analyzers — for the quantitative measurement of thyrotropin (TSH) in serum. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

For in vitro diagnostic use with the IMMULITE® 2000 Systems Analyzers — for the quantitative measurement of non-protein-bound thyroxine (free T4) in serum and heparinized plasma. Measurements of free thyroxine are used in the diagnosis and treatment 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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

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: k160647

1. Date Prepared

May 3, 2016

2. Applicant Information

Contact: Matthew Gee, M.Sc.
Senior Manager, Regulatory Affairs

Address: Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591-5097

Phone: 914-524-2099

Fax: 914-524-3579

Email: matthew.gee@siemens.com

3. Regulatory Information

Table 1. Regulatory Information for IMMULITE 2000 Third Generation TSH and Free T4

	Third Generation TSH	**Free T4**
Trade Name	IMMULITE® 2000 Third Generation TSH	IMMULITE® 2000 Free T4
Model Numbers	L2KTS2 (200 tests) L2KTS6 (600 tests)	L2KFT42 (200 tests) L2KFT46 (600 tests)
Common Name	Radioimmunoassay, thyroid-stimulating hormone	Radioimmunoassay, free thyroxine
Classification Name	Thyroid stimulating hormone test system	Free thyroxine test system
Product Code	JLW	CEC
Regulation Number	862.1690	862.1695
FDA Classification	Class II	Class II
Review Panel	Clinical Chemistry	Clinical Chemistry

4. Predicate Device Information

The Predicate Device for the modified IMMULITE 2000 Free T4 assay is the unmodified IMMULITE 2000 Free T4 assay (K083373).

The Predicate Device for the modified IMMULITE 2000 Third Generation TSH assay is the unmodified IMMULITE 2000 Third Generation TSH assay (described in K970227).

The modifications to the IMMULITE 2000 Free T4 and Third Generation TSH assays to add pediatric reference intervals to the Package Inserts are limited to changes in labeling. The update of reference intervals does not require modifications to the design or manufacturing processes of the devices. Therefore, the predicate devices and subject devices are the same.

5. Substantial Equivalence Information

The following table demonstrates substantial equivalence between the predicate IMMULITE 2000 Free T4 (K083373) and the IMMULITE 2000 Free T4 which has modified Instructions for Use (Package Inserts) with added pediatric reference intervals.

Table 2. Summary of Substantial Equivalence for IMMULITE 2000 Free T4

Item	Predicate Device (K083373) with Unmodified Labeling	Subject Device with Updated Reference Intervals
Analytes	free thyroxine (T4)	Same
Instruments	IMMULITE 2000 systems	Same
Intended Use Statements	For in vitro diagnostic use with the IMMULITE® 2000 Systems Analyzers — for the quantitative measurement of non-protein-bound thyroxine (free T4) in serum and heparinized plasma, as an aid in the clinical assessment of thyroid status.	For in vitro diagnostic use with the IMMULITE® 2000 Systems Analyzers — for the quantitative measurement of non-protein-bound thyroxine (free T4) in serum and heparinized plasma. Measurements of free thyroxine are used in the diagnosis and treatment of thyroid disease.
Analytical Measuring Range (Assay Range)	0.30 – 6.00 ng/dL (3.9 – 77.2 pmol/L)	Same
Adult Reference Ranges	Euthyroid Hypothyroid Hyperthyroid	Same
Pediatric Reference Intervals	None	Infants: 01 – 23 months Children: 02 – 12 years Adolescents: 13 – 20 years

The following table demonstrates substantial equivalence between the predicate IMMULITE 2000 Third Generation TSH (described in K970227) and the IMMULITE 2000 Third Generation TSH which has modified Instructions for Use (Package Inserts) with updated pediatric reference intervals.

Table 3. Summary of Substantial Equivalence for IMMULITE 2000 Third Generation TSH

Item	Predicate Device (K970227) with Unmodified Labeling	Subject Device with Updated Reference Intervals
Analytes	thyroid stimulating hormone (TSH)	Same
Instruments	IMMULITE 2000 systems	Same
Intended Use Statements	For in vitro diagnostic use with the IMMULITE® 2000 Systems Analyzers — for the quantitative measurement of thyrotropin (TSH) in serum, as an aid in the clinical assessment of thyroid status.	For in vitro diagnostic use with the IMMULITE® 2000 Systems Analyzers — for the quantitative measurement of thyrotropin (TSH) in serum. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.
Analytical Measuring Range (Assay Range)	0.004 – 75 µIU/mL (mIU/L)	Same
Adult Reference Ranges	Euthyroid Hyperthyroid	Same
Pediatric Reference Intervals	Groupings by age (in years) from 1 year to 12 years	Infants: 01 – 23 months Children: 02 – 12 years Adolescents: 13 – 20 years

6. Standard/Guidance Document Reference

Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline -- Third Edition (CLSI EP28-A3c); FDA Recognition Number 7-224.

7. Pediatric Reference Intervals

Free T4

Data from a total of 426 patients (81 infants, 197 children, 148 adolescents) tested with the IMMULITE 2000 Free T4 assay were analyzed to establish the reference intervals for the studied pediatric population. Results are described in the following table.

Table 4. Pediatric 95% Reference Intervals (Free T4)

Group	N	95% Reference Interval	Reference Interval Methodology	90% Confidence Interval for Lower Limit of Reference Interval	90% Confidence Interval for Upper Limit of Reference Interval
Infants (01 – 23 months)	81	0.80 – 1.27 ng/dL (10.3 – 16.3 pmol/L)	Robust Symmetric	0.76 – 0.84 ng/dL (9.8 – 10.8 pmol/L)	1.23 – 1.32 ng/dL (15.8 – 17.0 pmol/L)
Children (02 – 12 years)	197	0.74 – 1.28 ng/dL (9.5 – 16.5 pmol/L)	Non-Parametric	---	---
Adolescents (13 – 20 years)	148	0.75 – 1.27 ng/dL (9.7 – 16.3 pmol/L)	Non-Parametric	---	---

As taken from information in the existing Instructions for Use (Package Insert), the claim for the euthyroid adult reference range is 0.89 – 1.76 ng/dL (11.5 – 22.7 pmol/L), and the

current claim for the assay range is 0.30 – 6.00 ng/dL (3.9 – 77.2 pmol/L). This demonstrates that the new pediatric reference intervals are within the analytical measuring capability of the assay.

Third Generation TSH

Data from a total of 433 patients (90 infants, 195 children, 148 adolescents) tested with the IMMULITE 2000 Third Generation TSH assay were analyzed to establish the reference intervals for the studied pediatric population. These pediatric reference intervals, as well as the previously-established euthyroid adult reference intervals and analytical measuring ranges, are presented below.

Table 5. Pediatric 95% Reference Intervals (Third Generation TSH)

Group	N	95% Reference Interval	Reference Interval Methodology	90% Confidence Interval for Lower Limit of Reference Interval	90% Confidence Interval for Upper Limit of Reference Interval
Infants (01 – 23 months)	90	0.83 – 6.5 µIU/mL (mIU/L)	Robust Symmetric after Log Transform	0.70 – 0.99 µIU/mL (mIU/L)	5.58 – 7.65 µIU/mL (mIU/L)
Children (02 – 12 years)	195	0.58 – 4.1 µIU/mL (mIU/L)	Non-Parametric	---	---
Adolescents (13 – 20 years)	148	0.39 – 4.0 µIU/mL (mIU/L)	Non-Parametric	---	---

As taken from information in the existing Instructions for Use (Package Insert), the claim for the euthyroid adult reference range is 0.40 – 4.0 µIU/mL (mIU/L), and the current claim for the assay range is 0.004 – 75 µIU/mL (mIU/L). This demonstrates that the new pediatric reference intervals are within the analytical measuring capability of the assay.

8. Performance Characteristics

The inclusion of pediatric reference intervals in the Instructions for Use (Package Insert) does not necessitate the collection of additional analytical performance data. Therefore, all analytical performance data currently claimed for the IMMULITE Free T4 and Third Generation TSH assays continue to apply to these devices.

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 Insert) does not necessitate the collection of additional stability data. Therefore, all stability methods, acceptance criteria and data currently claimed for the IMMULITE Free T4 and Third Generation TSH assays continue to apply to these devices.

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 IMMULITE Free T4 and Third Generation TSH assays with updated pediatric reference intervals are substantially equivalent to the currently marketed IMMULITE Free T4 and Third Generation TSH assays.

The modification of the Instructions for Use (Package Insert) to add/update pediatric reference intervals does not require a change in the device design or a change in the manufacturing process.

All analytical data currently claimed for the IMMULITE Free T4 and Third Generation TSH assays continue to apply to these devices.

The modification of pediatric reference intervals for the IMMULITE Free T4 and Third Generation 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 of thyroid or pituitary disorders), as described in 21 CFR §862.1695 and 21 CFR §862.1690.
2. The newly-established pediatric reference intervals are at comparable levels or above the existing reference ranges for euthyroid (normal thyroid) adult populations. In addition, the pediatric reference intervals are well within the analytical measuring ranges of the IMMULITE Free T4 and Third Generation TSH assays. Therefore, the IMMULITE Free T4 and Third Generation TSH assays have appropriate analytical performance to test pediatric patients.