



April 25, 2025

Siemens Healthcare Diagnostics Inc.  
Yevgenia Sarkisian  
Regulatory Affairs Professional  
500 GBC Drive  
Newark, Delaware 19714

Re: K243570

Trade/Device Name: Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL); Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)  
Regulation Number: 21 CFR 862.1690  
Regulation Name: Thyroid Stimulating Hormone Test System  
Regulatory Class: Class II  
Product Code: JLW, CEC  
Dated: March 13, 2025  
Received: March 14, 2025

Dear Yevgenia Sarkisian:

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 (the 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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system>.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory->

[assistance/contact-us-division-industry-and-consumer-education-dice](#)) for more information or contact DICE by email ([DICE@fda.hhs.gov](mailto:DICE@fda.hhs.gov)) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Paula V. Caposino -S

Paula Caposino, Ph.D.  
Deputy Director  
Division of Chemistry and  
Toxicology Devices  
OHT7: Office of In Vitro Diagnostics  
Office of Product Evaluation and Quality  
Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)

K243570

Device Name

Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL)

Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)

Indications for Use (Describe)

The TSHL method is an in vitro diagnostic test for the quantitative measurement of Thyroid Stimulating Hormone (TSH, thyrotropin) in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of TSH are used in the diagnosis and monitoring of thyroid disease.

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.

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## 510(k) Summary

This 510(k) summary of safety and effectiveness information is submitted in accordance with the requirements of 21 CFR 807.92 and SMDA 1990.

The assigned 510(k) number is: K243570

### I. Applicant Information

Contact Person: Yevgenia Jenny Sarkisian  
Address: Siemens Healthcare Diagnostics Inc.  
500 GBC Drive, M/S 514  
Newark, DE 19714  
E-mail: yevgenia.sarkisian@siemens-healthineers.com  
Phone: 302-437-5949  
Date of Preparation: March 13, 2025

### II. Regulatory Information

|                      |                                                                             |                                                                |
|----------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------|
| Proprietary Name     | Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL) | Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L) |
| Common Name:         | Radioimmunoassay, thyroid-stimulating hormone                               | Radioimmunoassay, free thyroxine                               |
| Classification Name: | Thyroid-stimulating hormone test system                                     | Free thyroxine test system                                     |
| Regulation Number:   | 21 CFR 862.1690                                                             | 21 CFR 862.1695                                                |
| Classification:      | Class II                                                                    | Class II                                                       |
| Product Code:        | JLW                                                                         | CEC                                                            |
| Review Panel:        | Clinical Chemistry                                                          | Clinical Chemistry                                             |

### III. Predicate Device Information

The predicate devices, Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL) and Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L) are manufactured by Siemens Healthcare Diagnostics Inc., Newark, DE, USA, and were cleared by the FDA under the following K numbers.

| Name                                                                        | Predicate 510(k) |
|-----------------------------------------------------------------------------|------------------|
| Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL) | K081074          |
| Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)              | K073604          |

### IV. Device Description

The Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL) and Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L) assays were cleared under K081074 and K073604, respectively. The components of the cleared assays were modified to reduce biotin interference.

The modified Assays are comprised of the following components:

Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL)

The modified Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL) consists of prepackaged liquid reagents in a plastic eight-well cartridge. The components of each well are listed in the below table:

| Wells <sup>a,b</sup> | Form   | Ingredient                     | Concentration <sup>c</sup> | Source                     |
|----------------------|--------|--------------------------------|----------------------------|----------------------------|
| 1 – 2                | Liquid | Biotinylated TSH antibody      | 7.5 µg/mL                  | Mouse monoclonal           |
| 3 – 4                | Liquid | TSH antibody coated Chemibeads | 200 µg/mL                  | Mouse monoclonal           |
| 5 – 6                | Liquid | Streptavidin Sensibeads        | 1400 µg/mL                 | Recombinant <i>E. coli</i> |
| 7 – 8                | Empty  |                                |                            |                            |

a. Wells are numbered consecutively from the wide end of the cartridge.

b. Wells 1 – 6 contain buffers, stabilizers and preservatives.

c. Nominal value per well in a cartridge.

#### Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)

The modified Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L) consists of prepackaged liquid reagents in a plastic eight-well cartridge. The components of each well are listed in the below table:

| Wells <sup>a,b</sup> | Form   | Ingredient                | Concentration <sup>c</sup> | Source                     |
|----------------------|--------|---------------------------|----------------------------|----------------------------|
| 1 – 2                | Liquid | Streptavidin Sensibeads   | 225 µg/mL                  | Recombinant <i>E. coli</i> |
| 3 – 4                | Liquid | T3 Chemibeads             | 200 µg/mL                  |                            |
| 5 – 6                | Liquid | FT4 Biotinylated antibody | 50 ng/mL                   | Mouse monoclonal           |
| 7 – 8                | Empty  |                           |                            |                            |

a. Wells are numbered consecutively from the wide end of the cartridge.

b. Wells 1 – 6 contain buffers, stabilizers and preservatives.

c. Nominal value per well in a cartridge.

## Test Principle

#### Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL)

The Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge method is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI® technology. The LOCI® reagents include two synthetic bead reagents and a biotinylated anti-TSH monoclonal fragment. The first bead reagent (Sensibeads) is coated with streptavidin and contains a photosensitizer dye. The second bead reagent (Chemibeads) is coated with second anti-TSH monoclonal antibody and contains chemiluminescent dye. Sample is incubated with biotinylated antibody and Chemibeads to form bead-TSH-biotinylated antibody sandwiches. Sensibeads are added and bind to the biotin to form bead-pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is a direction function of the TSH concentration in the sample.

#### Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)

The Dimension LOCI Free Thyroxine Flex reagent cartridge method is a homogeneous, sequential, chemiluminescent immunoassay based on LOCI® technology. The LOCI® reagents include two synthetic bead reagents and a biotinylated anti-T4 mouse monoclonal antibody. The first bead reagent (Chemibeads) is coated with triiodothyronine (T3), a naturally occurring, weaker binding analog of T4, and contains chemiluminescent dye. The second bead reagent (Sensibeads) is coated with streptavidin and contains a photosensitizer dye. In a first step, sample is incubated with biotinylated antibody which allows T4 from the sample to saturate a fraction of the biotinylated antibody that is directly related to the free thyroxine (FT4) concentration. In a second step, T3 Chemibeads are added and form bead/biotinylated antibody immunocomplexes with the non-saturated fraction of the biotinylated antibody.

Sensibeads are then added and bind to the biotin to form bead pair immunocomplexes. Illumination of the complex at 680 nm generates singlet oxygen from Sensibeads which diffuses into the Chemibeads, triggering a chemiluminescent reaction. The resulting signal is measured at 612 nm and is an inverse function of the FT4 concentration in the sample.

## V. Intended Use / Indications for Use

### Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL)

The TSHL method is an *in vitro* diagnostic test for the quantitative measurement of Thyroid Stimulating Hormone (TSH, thyrotropin) in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of TSH are used in the diagnosis and monitoring of thyroid disease.

### Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)

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.

## VI. Comparison to Predicate Device

Table 1. Comparison Table of Candidate and Predicate Device

| Attribute                          | Candidate Device:<br>Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL),<br><br>Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Predicate Device:<br>Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL) (K081074)<br><br>Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L) (K073604) |
|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Intended Use / Indications for Use | <p><u>TSHL</u>:<br/>The TSHL method is an <i>in vitro</i> diagnostic test for the quantitative measurement of Thyroid Stimulating Hormone (TSH, thyrotropin) in human serum and plasma on the Dimension® EXL™ integrated chemistry system with LOCI® Module. Measurements of TSH are used in the diagnosis and monitoring of thyroid disease.</p> <p><u>FT4L</u>:<br/>The FT4L method is an <i>in vitro</i> 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.</p> | Same                                                                                                                                                                                       |
| Analyte                            | <p><u>TSHL</u>: Thyroid Stimulating Hormone</p> <p><u>FT4L</u>: Free Thyroxine (FT4)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Same                                                                                                                                                                                       |
| Automated                          | Automated assay                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Same                                                                                                                                                                                       |
| Measurement                        | Quantitative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Same                                                                                                                                                                                       |
| Sample Type                        | Serum, lithium and sodium heparin, or EDTA plasma                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Same                                                                                                                                                                                       |

| Detection Limit                     | <p><b>TSHL:</b><br/>Limit of Blank (LoB) = 0.003 µIU/mL (0.003 mIU/L)<br/>Limit of Detection (LoD) = 0.005 µIU/mL (0.005 mIU/L)<br/>Limit of Quantitation (LoQ) = 0.007 µIU/mL (0.007 mIU/L)</p> <p><b>FT4L:</b><br/>Limit of Blank (LoB) = 0.03 ng/dL (0.4 pmol/L)<br/>Limit of Detection (LoD) = 0.05 ng/dL (0.6 pmol/L)<br/>Limit of Quantitation (LoQ) = 0.06 ng/dL (0.8 pmol/L)</p> | <p><b>TSHL:</b><br/>Limit of Blank (LoB) = 0.0025 µIU/mL [mIU/L]<br/>Limit of Detection (LoD) = 0.004 µIU/mL [mIU/L]</p> <p><b>FT4L:</b><br/>Limit of Blank (LoB) = 0.03 ng/dL (0.39 pmol/L)<br/>Limit of Detection (LoD) = 0.06 ng/dL (0.77 pmol/L)</p> |                    |          |        |            |             |     |
|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------|--------|------------|-------------|-----|
| Assay Measuring Interval            | <p><b>TSHL:</b> 0.007 – 100 µIU/mL (mIU/L)</p> <p><b>FT4L:</b> 0.1 – 8.0 ng/dL (1.3 – 103 pmol/L)</p>                                                                                                                                                                                                                                                                                    | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Operating Principle                 | Immunologic sandwich                                                                                                                                                                                                                                                                                                                                                                     | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Technology                          | Direct chemiluminescent                                                                                                                                                                                                                                                                                                                                                                  | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Instrument                          | Dimension® EXL™ integrated chemistry system with LOCI® Module                                                                                                                                                                                                                                                                                                                            | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Sample Volume                       | <p><b>TSHL:</b> 12 µL</p> <p><b>FT4L:</b> 10 µL</p>                                                                                                                                                                                                                                                                                                                                      | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Calibrator                          | LOCI Thyroid Calibrator                                                                                                                                                                                                                                                                                                                                                                  | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Controls                            | Commercially available                                                                                                                                                                                                                                                                                                                                                                   | Same                                                                                                                                                                                                                                                     |                    |          |        |            |             |     |
| Interfering Substances - Biotin     | <p><b>TSHL and FT4L:</b><br/>Specimens that contain biotin at a concentration of 1200 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.</p>                                                                                                                             | <p><b>TSHL:</b> Biotin concentration of 250 ng/mL demonstrate a less than or equal to 10% change in results.</p> <p><b>FT4L:</b> Biotin concentration of 100 ng/mL demonstrate a less than or equal to 10% change in results.</p>                        |                    |          |        |            |             |     |
| Non-Interfering Substances - Biotin | <p><b>TSHL and FT4L:</b></p> <table border="1"> <thead> <tr> <th>Substance</th><th>Test Concentration</th><th>SI Units</th></tr> </thead> <tbody> <tr> <td>Biotin</td><td>1200 ng/mL</td><td>4908 mmol/L</td></tr> </tbody> </table>                                                                                                                                                     | Substance                                                                                                                                                                                                                                                | Test Concentration | SI Units | Biotin | 1200 ng/mL | 4908 mmol/L | N/A |
| Substance                           | Test Concentration                                                                                                                                                                                                                                                                                                                                                                       | SI Units                                                                                                                                                                                                                                                 |                    |          |        |            |             |     |
| Biotin                              | 1200 ng/mL                                                                                                                                                                                                                                                                                                                                                                               | 4908 mmol/L                                                                                                                                                                                                                                              |                    |          |        |            |             |     |

## VII. Summary of Performance Testing

Substantial equivalence of the modified Dimension® LOCI® Thyroid Stimulating Hormone Flex® reagent cartridge (TSHL) and Dimension® LOCI® Free Thyroxine Flex® reagent cartridge (FT4L) assays was demonstrated by testing performance characteristics including detection capability, linearity, method comparison, precision, recovery, interference, hook effect, reference range and matrix comparison.

The following performance data are provided in support of a substantial equivalence determination.

### i. Detection Limits

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were determined in

accordance with CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition*. The LoB, LoD, and LoQ estimates are summarized in the table below:

Table 2. Detection Capability

|     | Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L) | Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL) |
|-----|-------------------------------------------------------------|--------------------------------------------------------------------------|
| LoB | 0.03 ng/dL (0.4 pmol/L)                                     | 0.003 $\mu$ IU/L (0.003 mIU/L)                                           |
| LoD | 0.05 ng/dL (0.6 pmol/L)                                     | 0.005 $\mu$ IU/L (0.005 mIU/L)                                           |
| LoQ | 0.06 ng/dL (0.8 pmol/L)                                     | 0.007 $\mu$ IU/L (0.007 mIU/L)                                           |

## ii. Measuring Interval / Linearity

Linearity studies were conducted with one (1) reagent lot consistent with the governing standard CLSI EP06-ED2: *Evaluation of the Linearity of Quantitative Measurement Procedures*.

Low and high human serum pools were used for the linearity study. A dilution series composed of 12 levels for Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge and 10 levels for Dimension LOCI Free Thyroxine Flex reagent cartridge was prepared by mixing the low and high pools. Measurements were made with N=5 replicates per level. Expected low and high sample values were assigned as the mean of the 5 replicates from one reagent lot. The expected values for the middle levels were calculated from high and low pool values and the dilution factors. Bias was calculated for each sample as the difference between the mean observed value and the value predicted by the linear regression model. These were converted into % Bias values, with respect to the predicted value for each sample, as appropriate and compared to the acceptance criteria.

Linearity was confirmed across the assay range by acceptable ADL at each individual level and supports the measuring interval of:

Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL): 0.007 – 100  $\mu$ IU/mL (mIU/L)

Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L): 0.1 – 8.0 ng/dL (1.3 – 103 pmol/L)

## iii. Method Comparison: Quantitative Assay

The method comparison study was run according to the guidance from *CLSI EP09c, 3rd ed Measurement Procedure Comparison and Bias Estimation Using Patient Samples*.

The method comparison study was performed comparing the modified device to the currently marketed device. A single replicate was processed for each sample. Two replicates were processed for each sample and the first replicate was analyzed. Slope and Y-intercept and Correlation (r) results were generated using Deming regression.

Table 3. Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL): A total of 145 patient samples covering the full range of the assay were analyzed and included in the final analysis.

| Lot | Specimen Type | Comparison Assay (x)        | N   | Regression Equation                 |
|-----|---------------|-----------------------------|-----|-------------------------------------|
| 1   | Serum         | TSHL commercial formulation | 145 | $y = 0.99x + 0.039 \mu\text{IU/mL}$ |

Table 4. Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L): A total of 146 patient samples covering the full range of the assay were analyzed and included in the final analysis.

| Lot | Specimen Type | Comparison Assay (x)        | N   | Regression Equation              |
|-----|---------------|-----------------------------|-----|----------------------------------|
| 1   | Serum         | FT4L commercial formulation | 146 | $y = 1.02x + 0.03 \text{ ng/dL}$ |

#### iv. Verification of Assay Precision

Repeatability studies were conducted on three (3) reagent lots on one (1) Dimension EXL analyzer in accordance with CLSI EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures*. Testing was performed on five (5) serum samples for Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge and three (3) serum samples for Dimension LOCI Free Thyroxine Flex reagent cartridge, spanning the range of the assay. Each sample was tested in duplicate over a period of 20 days, two runs per day.

Table 5. Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL): Repeatability

| Level | Mean (μIU/mL) | Within-Run  |      | Total       |      |
|-------|---------------|-------------|------|-------------|------|
|       |               | SD (μIU/mL) | %CV  | SD (μIU/mL) | %CV  |
| 1     | 0.110         | 0.0040      | 3.6% | 0.0029      | 2.6% |
| 2     | 0.372         | 0.0116      | 3.1% | 0.0069      | 1.9% |
| 3     | 3.765         | 0.1209      | 3.2% | 0.0802      | 2.1% |
| 4     | 15.208        | 0.3936      | 2.6% | 0.3108      | 2.0% |
| 5     | 88.676        | 3.9406      | 4.4% | 2.6218      | 3.0% |

Table 6. Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L): Repeatability

| Level | Mean (ng/dL) | Within-Run |      | Total      |      |
|-------|--------------|------------|------|------------|------|
|       |              | SD (ng/dL) | %CV  | SD (ng/dL) | %CV  |
| 1     | 0.81         | 0.021      | 2.6% | 0.009      | 1.1% |
| 2     | 1.50         | 0.033      | 2.2% | 0.014      | 0.9% |
| 3     | 6.41         | 0.168      | 2.6% | 0.055      | 0.9% |

Reproducibility studies were conducted on three (3) reagent lots on three Dimension EXL analyzers in accordance with CLSI EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures*. Testing was performed on five (5) serum samples for Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL) and three (3) serum samples for Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L), spanning the range of the assay. Each sample was tested over a period of five (5) days, five (5) replicates per day.

Table 7. Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL): Reproducibility

| Level | Mean<br>(ng/dL) | Repeatability        |        | Between-Day          |        | Between-Lot          |        | Between-System       |        | Reproducibility      |        |
|-------|-----------------|----------------------|--------|----------------------|--------|----------------------|--------|----------------------|--------|----------------------|--------|
|       |                 | SD<br>( $\mu$ IU/mL) | CV (%) | SD<br>( $\mu$ IU/mL) | CV (%) | SD<br>( $\mu$ IU/mL) | CV (%) | SD<br>( $\mu$ IU/mL) | CV (%) | SD<br>( $\mu$ IU/mL) | CV (%) |
| 1     | 0.094           | 0.0025               | 2.7%   | 0.0049               | 5.2%   | 0.0022               | 2.3%   | 0.0040               | 4.3%   | 0.0071               | 7.6%   |
| 2     | 0.358           | 0.0088               | 2.5%   | 0.0089               | 2.5%   | 0.0051               | 1.4%   | 0.0163               | 4.6%   | 0.0211               | 5.9%   |
| 3     | 3.855           | 0.1082               | 2.8%   | 0.1193               | 3.1%   | 0.0000               | 0.0%   | 0.0755               | 2.0%   | 0.1778               | 4.6%   |
| 4     | 14.425          | 0.3358               | 2.3%   | 0.4980               | 3.5%   | 0.0117               | 0.1%   | 0.3037               | 2.1%   | 0.6732               | 4.7%   |
| 5     | 81.372          | 2.4293               | 3.0%   | 2.8811               | 3.5%   | 1.1456               | 1.4%   | 0.0000               | 0.0%   | 3.9389               | 4.8%   |

Table 8. Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L): Reproducibility

| Level | Mean<br>(ng/dL) | Repeatability |        | Between-Day   |        | Between-Lot   |        | Between-System |        | Reproducibility |        |
|-------|-----------------|---------------|--------|---------------|--------|---------------|--------|----------------|--------|-----------------|--------|
|       |                 | SD<br>(ng/dL) | CV (%) | SD<br>(ng/dL) | CV (%) | SD<br>(ng/dL) | CV (%) | SD<br>(ng/dL)  | CV (%) | SD<br>(ng/dL)   | CV (%) |
| 1     | 0.70            | 0.008         | 1.1%   | 0.013         | 1.9%   | 0.002         | 0.3%   | 0.008          | 1.1%   | 0.017           | 2.4%   |
| 2     | 1.49            | 0.014         | 0.9%   | 0.019         | 1.3%   | 0.005         | 0.3%   | 0.028          | 1.9%   | 0.036           | 2.4%   |
| 3     | 6.49            | 0.058         | 0.9%   | 0.103         | 1.6%   | 0.000         | 0.0%   | 0.009          | 0.1%   | 0.119           | 1.8%   |

#### v. Recovery

Dilution recovery was conducted with 1 reagent lot consistent with CLSI EP34-ED1:2018 Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking for Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge. Manual dilution of 5x increases the upper end of the measuring interval from 100.000  $\mu$ IU/mL to 500.000  $\mu$ IU/mL.

See Table 9 below.

Table 9. Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL) Dilution Recovery

| Operator                                                                | Dilution | Replicate | Sample value (μIU/mL) |          |          |          |          |          |          |
|-------------------------------------------------------------------------|----------|-----------|-----------------------|----------|----------|----------|----------|----------|----------|
|                                                                         |          |           | Sample 1              | Sample 2 | Sample 3 | Sample 4 | Sample 5 | Sample 6 | Sample 7 |
| 1                                                                       | 1        | 1         | 28.952                | 92.725   | 35.653   | 34.008   | 24.694   | 38.264   | 31.634   |
|                                                                         |          | 2         | 28.922                | 90.896   | 36.832   | 34.361   | 22.559   | 37.912   | 30.315   |
|                                                                         |          | 3         | 29.980                | 95.951   | 36.287   | 34.746   | 24.076   | 38.750   | 31.700   |
|                                                                         | 2        | 1         | 28.041                | 95.940   | 35.531   | 35.037   | 25.489   | 37.942   | 30.767   |
|                                                                         |          | 2         | 28.853                | 96.417   | 32.648   | 34.582   | 24.532   | 38.484   | 32.629   |
|                                                                         |          | 3         | 29.072                | 95.794   | 34.895   | 34.712   | 24.176   | 37.376   | 31.437   |
| 2                                                                       | 1        | 1         | 27.513                | 98.611   | 35.685   | 35.336   | 23.533   | 36.042   | 29.336   |
|                                                                         |          | 2         | 28.388                | 99.592   | 34.653   | 35.052   | 23.346   | 35.748   | 28.785   |
|                                                                         |          | 3         | 28.791                | 92.230   | 34.932   | 34.754   | 23.692   | 35.552   | 26.989   |
|                                                                         | 2        | 1         | 26.165                | 88.588   | 35.973   | 34.436   | 23.747   | 34.676   | 29.743   |
|                                                                         |          | 2         | 28.224                | 92.116   | 35.585   | 34.959   | 22.339   | 33.752   | 28.819   |
|                                                                         |          | 3         | 28.639                | 93.167   | 35.373   | 35.248   | 23.823   | 35.097   | 28.220   |
| Average Value (μIU/mL)                                                  |          |           | 28.462                | 94.336   | 35.337   | 34.769   | 23.834   | 36.633   | 30.031   |
| Dilution Factor                                                         |          |           | 5                     | 5        | 5        | 5        | 5        | 5        | 5        |
| Estimated Value (μIU/mL)                                                |          |           | 142.308               | 471.678  | 176.686  | 173.846  | 119.169  | 183.165  | 150.156  |
| Dimension LOCI TSHL Reagent Cartridge (Predicate Device) Value (μIU/mL) |          |           | 137.211               | 470.077  | 167.028  | 165.169  | 119.141  | 174.674  | 147.087  |
| %Recovery                                                               |          |           | 104%                  | 100%     | 106%     | 105%     | 100%     | 105%     | 102%     |

#### vi. Interferences

Hemolysis, Icterus, and Lipemia (HIL) – Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL)

Interference testing for the Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL) method was performed in accordance with *CLSI EP07-ED3: Interference Testing in Clinical Chemistry, third edition*.

The following substances tested were determined to have no significant interference:

Table 10. Interference HIL Claims – Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL):

| Compound                          | Interferent test Concentration | TSH Level                    |
|-----------------------------------|--------------------------------|------------------------------|
| Hemolysis (Hemoglobin)            | 500 mg/dL                      | 0.300 μIU/mL                 |
| Hemolysis (Hemoglobin)            | 750 mg/dL                      | 8.000 μIU/mL                 |
| Icterus, Bilirubin (unconjugated) | 60 mg/dL                       | 0.300 μIU/mL<br>8.000 μIU/mL |
| Icterus, Bilirubin (conjugated)   | 40 mg/dL                       | 0.300 μIU/mL                 |
| Icterus, Bilirubin (conjugated)   | 60 mg/dL                       | 8.000 μIU/mL                 |
| Lipemia (Intralipid®)             | 3000 mg/dL                     | 8.000 μIU/mL                 |

#### Interfering Substances – Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL)

Interference testing was performed in accordance with *CLSI EP07-ED3: Interference Testing in Clinical Chemistry, third edition*. Specimens that contain biotin at a concentration of 1200 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.

Table 11. Non-Interfering Substances Claims – Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL):

| Compound | Interferent test Concentration | TSH Level    |
|----------|--------------------------------|--------------|
| Biotin   | 1200 ng/mL                     | 0.300 µIU/mL |

#### Non-Interfering Substances – Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL)

The modifications to the assay to reduce biotin interference does not impact the specificity of the assay to the analyte or to the interferents other than biotin. All non-interfering substances referenced in the Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge Instructions for Use were previously verified and cleared under K081074.

#### Hemolysis, Icterus, and Lipemia (HIL) – Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L)

Interference testing for the Dimension LOCI Free Thyroxine Flex reagent cartridge method was performed in accordance with *CLSI EP07-ED3: Interference Testing in Clinical Chemistry, third edition*.

The following substances tested were determined to have no significant interference:

Table 12. Interference HIL Claims – Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L):

| Compound                          | Interferent test Concentration | FT4 Level                |
|-----------------------------------|--------------------------------|--------------------------|
| Hemolysis (Hemoglobin)            | 750 mg/dL                      | 1.10 ng/dL<br>3.00 ng/dL |
| Icterus, Bilirubin (unconjugated) | 30 mg/dL                       | 1.10 ng/dL<br>3.00 ng/dL |
| Icterus, Bilirubin (conjugated)   | 26 mg/dL                       | 1.10 ng/dL<br>3.00 ng/dL |
| Lipemia (Intralipid®)             | 3000 mg/dL                     | 1.10 ng/dL<br>3.00 ng/dL |

#### Interfering Substances – Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L)

Interference testing was performed in accordance with *CLSI EP07-ED3: Interference Testing in Clinical Chemistry, third edition*. Specimens that contain biotin at a concentration of 1200 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.

Table 13. Non-Interfering Substances Claims – Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L):

| Compound | Interferent test Concentration | FT4 Level                |
|----------|--------------------------------|--------------------------|
| Biotin   | 1200 ng/mL                     | 1.10 ng/dL<br>3.00 ng/dL |

#### Non-Interfering Substances – Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L)

The modifications to the assay to reduce biotin interference does not impact the specificity of the assay to the analyte or to the interferents other than biotin. All non-interfering substances referenced in the Dimension LOCI Free Thyroxine Flex reagent cartridge Instructions for Use were previously verified and cleared under K073604.

#### vii. Hook Effect

No hook effect was observed up to 30,000  $\mu$ IU/mL for Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge.

#### viii. Verification of Reference Range

The reference range was verified by assaying apparently healthy samples according to *CLSI EP28-A3C: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory*. The existing reference ranges were verified:

#### Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (TSHL):

Adults (age 21-65): 0.358 - 3.74  $\mu$ IU/mL

Pediatric populations:

Infants (01-23 months): 0.867 - 6.43  $\mu$ IU/mL

Children (02-12 years): 0.704 - 4.01  $\mu$ IU/mL

Adolescents (13-20 years): 0.516 - 4.13  $\mu$ IU/mL

#### Dimension LOCI Free Thyroxine Flex reagent cartridge (FT4L):

Adults (age 21-65): 0.76 – 1.46 ng/dL

Pediatric populations:

Infants (01-23 months): 0.93 – 1.45 ng/dL

Children (02-12 years): 0.82 – 1.40 ng/dL

Adolescents (13-20 years): 0.78 – 1.34 ng/dL

Siemens provides this information for reference. As with all in vitro diagnostic assays, each laboratory should determine its own reference ranges for the diagnostic evaluation of patient results. Consider these values as a guideline only.

#### ix. Matrix Comparison

The matrix comparison/specimen equivalence study was performed to evaluate the performance using different tube types (Serum, lithium heparin, sodium heparin and K2-EDTA) comparing plasma to serum. The study demonstrated comparable values to serum samples.

### VIII. Conclusion

These performance studies support that the modified Candidate Devices, Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge and Dimension LOCI Free Thyroxine Flex reagent cartridge are substantially equivalent to the currently marketed Predicate Devices, Dimension LOCI Thyroid Stimulating Hormone Flex reagent cartridge (K081074) and Dimension LOCI Free Thyroxine Flex reagent cartridge (K073604).