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

SYSMEX AMERICA, INC.
MICHELLE PARKER
PROJECT MANAGER, REGULATORY AFFAIRS
577 APTAKISIC ROAD
LINCOLNSHIRE IL 60069

October 21, 2016

Re: K160541
Trade/Device Name: Automated Immunoassay System HISCL -800, HISCL TSH Assay Kit, HISCL TSH Calibrator, HISCL Immuno Multi Control
Regulation Number: 21 CFR 862.1690
Regulation Name: Thyroid stimulating hormone test system
Regulatory Class: II
Product Code: JLW, JIT, JJY, JJE
Dated: September 8, 2016
Received: September 12, 2016

Dear Ms. Parker:

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 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)*
k160541

Device Name
HISCL TSH Assay Kit, Automated Immunoassay System HISCL-800, HISCL TSH Calibrator, and HISCL Immuno Multi Control

Indications for Use *(Describe)*

The Automated Immunoassay System HISCL-800 is a chemiluminescent chemistry analyzer for the determination of analytes in human serum.

The HISCL TSH assay Kit is a magnetic particle chemiluminescent enzyme immunoassay (CLEIA) for the quantitative determination of TSH levels in human serum using the Automated Immunoassay System HISCL-800. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

The HISCL TSH Calibrator is used for calibrating the HISCL TSH Assay Kit on the Automated Immunoassay System HISCL-800.

The HISCL Immuno Multi Control is used for quality control of the HISCL TSH Assay Kit on the Automated Immunoassay System HISCL-800.

Type of Use *(Select one or both, as applicable)*

[X] Prescription Use (Part 21 CFR 801 Subpart D) [ ] Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

# 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K160541.

**807.92 (a)(1):**

**Name:** Sysmex America, Inc.

**Address:** 577 Aptakisic Road
Lincolnshire, IL 60069

**Phone:** 224-543-9639
**FAX:** 224-543-9699
**Contact:** Michelle Parker

**807.92 (a)(2): Device name- trade name and common name, and classification**

**Trade name:**
HISCL TSH Assay Kit
Automated Immunoassay System HISCL-800
HISCL TSH Calibrator
HISCL Immuno Multi Control

**Common Name:**
TSH Assay Kit
Automated Immunoassay System
TSH Calibrator
TSH Control

**Classification:**

| Product Code | Regulation Name | Classification | Regulation Section | Panel |
|---|---|---|---|---|
| JLW | Thyroid stimulating hormone test system | Class II | 21 CFR § 862.1690 | Chemistry (75) |
| JJE | Discrete photometric chemistry analyzer for clinical use | Class I | 21 CFR § 862.2160 | Chemistry (75) |
| JIT | Calibrator, secondary | Class II | 21 CFR§ 862.1150 | Chemistry (75) |
| JJY | Quality control material (assayed and unassayed) | Class I, reserved | 21 CFR §862.1660 | Chemistry (75) |

**807.92 (a)(3): Identification of the legally marketed predicate devices**

The Sysmex TSH assay kit is substantially equivalent to the ADVIA Centaur TSH3-Ultra (TSH3-UL, Siemens Medical Solutions, Inc., Malvern, PA) cleared under K083844 on May 8, 2009.

**807.92 (a)(4): Device Description**

The HISCL-800 is a fully automated floor model random access immunoassay system that can quantitatively or qualitatively analyze samples for minute traces of a variety of chemistry analytes. The HISCL-800 has a maximum through-put of 100 tests / hour with an analysis time per analyte of 17 minutes and has capacity for 24 on board reagent sets in the cooled reagent storage. Reagent tracking utilizes RFID technology. Using six 5-sample racks, the HISCL-800 has a walk-away capacity for 30 specimens and one STAT sample loading position. An onboard mixer automatically mixes the magnetic particle reagent as needed. The analyzer has a dedicated sample arm which uses disposable tips and three reagent dispensing arms. The HISCL-800 employs chemiluminescent enzyme technology based on CDP-Star™ chemiluminescent substrate. The analyzer has the capacity to run both one-step and two-step sandwich immunoassays.

The HISCL TSH Assay Kit measures TSH based on the chemiluminescent enzyme immunoassay method with CDP-*Star*® chemiluminescent substrate. The assay utilizes a 1-step sandwich immunoassay, as follows:

1. ALP (alkaline phosphatase)-labeled anti-TSH monoclonal antibodies (mouse) in R1 reagent specifically react with TSH in the sample. Biotinylated anti-TSH monoclonal antibodies (mouse) in R3 reagent specifically bind to TSH, and bind to streptavidin-coated MP (magnetic particles) in R2 reagent.

2. After bound/free (B/F) separation, ALP on MP decomposes CDP-*Star*® substrate in R5 to an excited intermediate, which produces a luminescent signal.

Because the light production increases in proportion to TSH concentration, sample TSH concentration can be obtained with a calibration curve prepared with calibrators.

<u>Description of Reagents</u>

*HISCL TSH Assay Kit* - All assay reagents contain sodium azide as a preservative.

1) R1 reagent: contains ALP-labeled anti-TSH monoclonal antibodies (mouse) 0.4 U/mL
2) R2 reagent: contains streptavidin coated with magnetic particles
3) R3 reagent: contains biotinylated anti-TSH monoclonal antibodies (mouse) 9µg/mL

*HISCL Substrate Reagent Set*

1) R4 Reagent (contains sodium azide as a preservative): used for dispersing the magnetic particles before starting the chemiluminescence reaction. The reproducibility of chemiluminescence is improved by dispersing the magnetic particles. Futhermore, the R4 reagent contains inhibitors of endogenous alkaline phosphatase, which helps reduce the background.

2) R5 Reagent (alkaline solution with pH 9.6): contains the chemiluminescent substrate (CDP-*Star*®): Disodium 2-e-chloro-5-(4-methoxyspiro {1,2-dioxetane-3,2'-(5'-chloro)-tricyclo [3.3.1.13,7] decan}-4-yl)-1-phenyl phosphate 0.48mM

*HISCL TSH Calibrators*- All calibrators contain sodium azide as a preservative.

1) HISCL TSH C0 (0 µIU/mL)
2) HISCL TSH C1 (2 µIU/mL)
3) HISCL TSH C2 (10 µIU/mL)
4) HISCL TSH C3 (50 µIU/mL)
5) HISCL TSH C4 (120 µIU/mL)
6) HISCL TSH C5 (200 µIU/mL)

HISCL TSH C1-C5 have been adjusted by in-house standard materials based on WHO Standard 80/558. The calibrators contain recombinant TSH, and no components contain human-derived materials.

*HISCL Immuno Multi Control*

1) HISCL Immuno Multi Control Level 1 (targeted at 2.006 µIU/mL)
2) HISCL Immuno Multi Control Level 2 (targeted at 6.340 µIU/mL)

HISCL Immuno Multi Control Level 1 and Level 2 contain human-derived materials.
HISCL Immuno Multi Controls are lyophilized and are reconstituted using distilled water.

*HISCL Diluent*

1) HISCL Diluent: contains Bovine Serum Albumin

Diluent contain sodium azide as a preservative.

*HISCL Probe Washing Solution*

1) HISCL Probe Washing Solution: contains sodium hypochlorite

*HISCL Line Washing Solution*

1) HISCL Line Washing Solution: contains Tris(hydroxymethyl)aminomethane

*HISCL Washing Solution*

1) HISCL Washing Solution: contains Tris-(hyroxymethyl)aminomethane

**807.92 (a)(5): Intended Use**

The Automated Immunoassay System HISCL-800 is a chemiluminescent chemistry analyzer for the determination of analytes in human serum.

The HISCL TSH Assay Kit is a magnetic particle chemiluminescent enzyme immunoassay (CLEIA) for the quantitative determination of TSH levels in human serum using the Automated Immunoassay System HISCL-800. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

The HISCL TSH Calibrator is used for calibrating the HISCL TSH Assay Kit on the Automated Immunoassay System HISCL- 800.

The HISCL Immuno Multi Control is used for quality control of the HISCL TSH Assay Kit on the Automated Immunoassay System HISCL-800.

**807.92 (a)(6): Technological Similarities and Differences to the Predicate**

The HISCL TSH Assay Kit is substantially equivalent to the ADVIA Centaur TSH3-Ultra (TSH3-UL, Siemens Medical Solutions, Inc., Malvern, PA) cleared under K083844. The following summary (Table 1) describes similarities and differences between the ADVIA Centaur XP Immunoassay System and the Automated Immunoassay System HISCL-800. Table 2 describes the similarities and differences between the ADVIA Centaur TSH3-Ultra Assay Kit and the Sysmex HISCL TSH Assay Kit.

## Table 1- Instrument Comparisons

| Feature | Automated Immunoassay System HISCL-800 | Siemens ADVIA Centaur XP Immunoassay System K083844 |
|---|---|---|
| **Overview** | | |
| Intended Use | The Automated Immunoassay System HISCL-800 is a chemiluminescent chemistry analyzer for the determination of analytes in human serum. | This system is intended for professional use in a laboratory environment only. Tests performed using this system are intended for *in vitro* diagnostic use. As with all diagnostic tests, a definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated. |
| System Description | Random access immunoassay system | Random access immunoassay system |
| Throughput | 100 tests per hour | Up to 240 tests per hour |
| Assay Technology | Alkaline phosphatase for the enzyme and CDP-*Star*®, which shows a strong emission intensity with chemiluminescent substrates to achieve high sensitivity | Direct chemiluninescence using acridinium ester technology |
| **Sample Handling** | | |
| Sampler | Universal 5-position rack holds multiple tube types. 6 position rack adapter for sample cups.<br><br>No pause load and unloading | Universal 5-position rack holds multiple tube types.<br><br>No pause loading and unloading |
| STAT Handling | An urgent sample is given priority over regular samples. A sample can be placed in the urgent sample holder. | Dedicated STAT port accepts samples any time |
| Automatic Dilutions | Not Available | Available |
| Sample Barcodes | EAN/UPC/JAN,ITF, Codabar /NW7,Code39,Code 128 | Code 128, Code 39, Codabar, Interleaved 2 of 5 |
| **Reagent Handling** | | |
| Reagent Cooling | 24 position on the reagent disk cooled 2°C to 15°C | 30-position reagent tray cooled 4°C to 8°C |
| Reagent Integrity Control | Tracked using the RFID label<br>・Reagent item<br>・Reagent type<br>・test counts flag<br>・expired date flag (Lot/onboard) | Barcode reagent identification, automatic inventory tracking and flagging, calibration validity tracked and flagged, reagent on board stability tracked and flagged, reagent expired/reagent low flagging |
| Reagent Mixing | Automatically mixes the magnetic particle reagent (R2) on board. | ReadyPacks automatically rocked onboard |
| **User Interface** | | |
| Monitor | 21.5 inch LCD screen<br>Touch panel | 19-inch diagonal high-resolution LCD touch screen with adjustable height |

## Table 1- Instrument Comparisons (continued)

| **General Specifications** | | |
|---|---|---|
| Dimensions | Approximately<br>51.0 (h) X 40.1 (w) X 42.9 (d) in | Approximately<br>51.5 (h) X 72.4 (w) X 41.0 (d) in |
| Weight | Approximately 320 kg (704 lbs) | Approximately 545 kg (1200 lbs) |

## Table 2: Assay Comparisons

| **Feature** | **Sysmex HISCL TSH Assay Kit** | **Siemens ADVIA Centaur XP TSH Assay Kit- K083844** |
|---|---|---|
| Intended Use | The HISCL TSH assay Kit is a magnetic particle chemiluminescent enzyme immunoassay (CLEIA) for the quantitative determination of TSH levels in human serum using the Automated Immunoassay System HISCL-800. 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 in the quantitative determination of thyroid stimulating hormone (TSH, thyrotropin) in serum, heparinized plasma, and EDTA plasma using the ADVIA Centaur and the ADVIA Centaur XP systems. |
| Sample Type | Serum | Serum, Heparinized Plasma, EDTA Plasma |
| Sample Volume | 200 µL | 200 µL |
| Reportable Range | 0.008 µIU/mL to 75 µIU/mL | 0.008 µIU/mL to 150 µIU/mL |

## Table 3: Calibrator Comparisons

| Similarities | | |
|---|---|---|
| Item | HISCL TSH Calibrator (New Device) | ADVIA Centaur® Calibrator B (K920372) |
| Intended Use | The HISCL TSH Calibrator is used for calibrating the HISCL TSH Assay Kit on the Automated Immunoassay System HISCL-800. | For *in vitro* diagnostic use in calibrating the following assays using ADVIA Centaur® or ACIS:180® Systems: Digoxin; FSH; Total IgE; LH, LH2, Prolactin; Total hCG; **TSH**. |
| Number of Levels | 6 | 10 standard calibrators<br>2 adjusters |
| Form | Liquid | Lyophilized |
| Matrix | Triethanolamine hydrochloride buffer | Equine serum |
| Calibrator Concentrations | Target Concentrations<br>1. HISCL TSH C0 = 0 µlU/mL<br>2. HISCL TSH C1 = 2 µlU/mL mL<br>3. HISCL TSH C2 = 10 µlU/mL<br>4. HISCL TSH C3 = 50 µlU/mL<br>5. HISCL TSH C4 = 120 µlU/mL<br>6. HISCL TSH C5 = 200 µlU/mL | Lot Specific<br>Standard Calibrators<br>Lot Number: 114290<br>7. 0 µlU/mL<br>8. 0.125 µlU/mL<br>9. 0.742 µlU/mL<br>10. 1.99 µlU/mL<br>11. 4.51 µlU/mL<br>12. 9.26 µlU/mL<br>13. 20.2 µlU/mL<br>14. 51 µlU/mL<br>15. 114 µlU/mL<br>16. 191 µlU/mL<br>Adjuster<br>Lot Number: CH90<br>1. 0.033 µlU/mL<br>2. 102 µlU/mL |
| Storage Temperature | 2 - 8°C | Same |
| Special instruments | HISCL-800 instrument | ADVIA Centaur® or ACIS:180® Systems |
| Differences | | |
| Item | HISCL TSH Calibrator (New Device) | ADVIA Centaur® Calibrator B (Predicate Device) |
| Analytes | TSH | Multi Analyte:<br>Digoxin, FSH, Total IgE, LH LH2, Prolactin, Total hCG, **TSH** |

## Table 4: Control Comparisons

| Similarities | | |
|---|---|---|
| Item | HISCL TSH Control (New Device) | BioRad Liquichek Immunoassay Plus Controls (K122838) |
| Intended Use | The HISCL Immuno Multi Control is used for quality control of the HISCL TSH Assay Kit on the Automated Immunoassay System HISCL-800. | For in vitro diagnostic use to monitor the precision and the accuracy of laboratory tests as specified in the package insert |
| Matrix | Human-derived material | Human serum |
| Control Concentrations | Level 1: Targeted at 2.006 µlU/mL<br><br>Level 2: Targeted at 6.340 µlU/mL | Lot Specific<br><u>Standard Controls</u><br>Lot Number: 40900<br><br>Level 1:<br>Mean = 0.689 µlU/mL<br>Range = 0.555 to 0.824 µlU/mL<br><br>Level 2:<br>Mean = 4.77 µlU/mL<br>Range = 3.79 to 5.75 lU/mL<br><br>Level 3:<br>Mean = 24.6 µlU/mL<br>Range = 19.7 to 29.5 µlU/mL |
| Storage Temperature | 2 - 8°C before reconstitution | 2 - 8°C |
| Special instruments | HISCL-800 instrument | Various, including the ADVIA Centaur® |
| Differences | | |
| Item | HISCL Immuno Multi Control (New Device) | BioRad Liquichek Immunoassay Plus Controls (K122838) |
| Analytes | TSH | Multi-analytes, including TSH |
| Number of Levels | 2 | 3 |
| Form | Lyophilized | Liquid |

**807.92 (b)(1): Brief Description of Nonclinical Data**

A series of studies were performed that evaluated traditional laboratory performance characteristics; a summary of each study follows.

*20-Day Precision*

Five samples (2 controls and 3 serum samples) were each assayed in- house according to CLSI EP5-A3, meaning testing was performed over 20 days, in duplicate, two runs per day, for a total of 80 results per sample. The study included four reagent lots and three instruments.

| Sample ID | Mean (µIU/mL) | Repeatability (Within-run) | | Between-Run Precision | | Between-Day Precision | | Within- Laboratory Precision | |
|---|---|---|---|---|---|---|---|---|---|
| | | SD | %CV | SD | %CV | SD | %CV | SD | %CV |
| Sample 2 | 0.138 | 0.003 | 2.2% | 0.000 | 0.0% | 0.002 | 1.4% | 0.004 | 2.9% |
| Control 1 | 1.984 | 0.045 | 2.3% | 0.020 | 1.0% | 0.021 | 1.1% | 0.054 | 2.7% |
| Control 2 | 5.991 | 0.122 | 2.0% | 0.088 | 1.5% | 0.069 | 1.2% | 0.165 | 2.8% |
| Sample 1 | 5.044 | 0.122 | 2.4% | 0.040 | 0.8% | 0.046 | 0.9% | 0.137 | 2.7% |
| Sample 3 | 23.260 | 0.461 | 2.0% | 0.193 | 0.8% | 0.447 | 1.9% | 0.670 | 2.9% |

*Limit of Blank, Limit of Detection*

Limit of Blank

Four zero TSH samples were obtained from four distinct lots of HISCL Diluent; these were the blank samples. The samples were assayed in replicates of five over four days (n = 80) with each of two lots of test kits on two different instruments (total of four combinations). LoBs (for each lot/instrument combination) were calculated according to CLSI EP17-A2. The LoB with the highest concentration of the four combinations was selected to describe the LoB for the test system. The LoB was determined to be 0.0007µIU/mL, but the measuring range is 0.008 to 75 µIU/mL.

Limit of Detection

Five low samples were prepared by adding varying amounts of TSH to the diluent so that the values ranged from the LoB, to five-times (5x) the LoB. Each sample was assayed by each of two reagent lots and one instrument (two combinations) 8x/day for five days (n = 40/sample with each lot/instrument combination). From this testing, the LoDs were calculated per the CLSI EP17-A2, and the LoD with the highest concentration of the two combinations was selected to describe the LoD for the test system. The LoD was determined to be 0.001µIU/mL, but the measuring range is 0.008 to 75 µIU/mL.

*Limit of Quantitation (Functional Sensitivity)*

The limit of quantitation was described by a functional sensitivity study. Functional sensitivity was defined as the lowest TSH concentration that may be measured with reasonable precision. The target for the LoQ was at, or lower than, 0.002 µIU/mL. The study included seven (7) low TSH samples. Four of the samples were human pools where 10 discrete, native serum samples were combined and TSH was stripped; the three remaining samples were serial dilutions of the TSH low control.

The samples were tested twice a day for 20 days (n = 40 results per level), and means, standard deviations, and %CVs were calculated. The study employed two lots of reagents and two lots of calibrators (4 combinations). For each combination, the TSH values (x-axis) were plotted against %CVs (y-axis). A cutoff of 20% was chosen to represent the highest allowable %CV, and the concentrations of TSH meeting this criterion ranged from 0.0010 to 0.0014µIU/mL. All values were lower than the target of 0.002µIU/mL, and therefore the 0.002µIU/mL functional sensitivity has been validated. The measuring range is 0.008 to 75 µIU/mL.

*Interference*

Two serum samples with low and high TSH levels targeted at 0.3µIU/mL and 8µIU/mL, respectively, were used. Moderate and high levels of various biological and pharmaceutical substances were added to the neat samples, and all samples were tested in triplicate. The impact of HAMA-positive samples was also evaluated. The differences and percent differences of the means between samples with the potential interferents and without the potential interferents (neat) were calculated.

The data demonstrated that the TSH system was not affected (all differences within 10% of the neat control) for the following substances at the following levels:

- Hemoglobin up to 500 mg/dL
- Conjugated and unconjugated bilirubin up to 40 mg/dL
- HAMA up to 138 ng/mL
- Rheumatoid factor up to 500 mg/dL
- Triglycerides up to 750 mg/dL
- Biotin up to 10 ng/mL
- Total protein up to 12 g/dL
- Acetaminophen up to 20 mg/dL
- Ibuprofen up to 50 mg/dL
- Aspirin up to 65 mg/dL

*Cross-reactivity*

Two serum samples with low and high TSH levels targeted at 0.3µIU/mL and 8µIU/mL, respectively, were used. High levels of hCG, FSH, and LH were added to the neat samples, and all samples were tested in triplicate.

Representative data is shown in the following table:

| Sample TSH Concentration (Containing cross-reactant) (µIU/mL) | Reference TSH Concentration (No cross-reactant) (µIU/mL) | Interferent | Material added (mIU/mL) | %Cross Reactivity |
|---|---|---|---|---|
| 0.298 | 0.299 | hCG | 300,000 | $-3.33 \times 10^{-10}$ |
| 0.301 | 0.299 | FSH | 1,000 | $2.00 \times 10^{-7}$ |
| 0.305 | 0.299 | LH | 1,000 | $6.00 \times 10^{-7}$ |
| 7.427 | 7.091 | hCG | 300,000 | $1.12 \times 10^{-7}$ |
| 7.297 | 7.091 | FSH | 1,000 | $2.06 \times 10^{-5}$ |
| 7.422 | 7.091 | LH | 1,000 | $3.31 \times 10^{-5}$ |

*High Dose Hook Effect*

Five high concentration TSH samples (~2,000 µIU/mL) were prepared. From each sample, three, five-fold serial dilutions were created with the HISCL Diluent to achieve the following TSH levels: 400 µIU/mL, 80 µIU/mL, and 16 µIU/mL. Each serial dilution, plus the neat, high sample, was assayed in triplicate.

The data demonstrated that the diluted samples quantitated at their respective levels, and the undiluted sample (~2,000 µIU/mL) and the 400 µIU/mL samples reported >200 µIU/mL. Therefore, no hook effect was observed.

*Spike Recovery*

Four native low TSH serum level samples, with TSH concentrations between 0.002 to 4.22 µIU/mL, were identified and measured. Two solutions of high TSH, with levels of 100 and 1,000 µIU/mL, were prepared from WHO standards, and these prepared samples were spiked into the four native samples in the ratio of 1:9 and were tested in triplicate, along with non- spiked samples, in the same run. Performance was targeted to demonstrate that recoveries were such that the native samples would reflect a 10x increase with the 100 µIU/mL spike, and a 100x increase with the 1,000 µIU/mL spike, within a 20% tolerance.

The means were calculated for each sample at each concentration. Also, the expected TSH levels, based on the mathematical calculations from the spikes, were calculated, and then the difference and percent difference between the mean observed concentration and expected concentration were compared. All data was found to be acceptable.

*Sample Storage Stability*

Fourteen (14) serum samples were collected from donors. Ten (10) serum samples were neat and the other four (4) serum samples were spiked with TSH values ranging from approximately 5 µIU/mL to 120 µIU/mL TSH and processed and aliquoted within 8 hours of collection. This was considered the Time 0 timepoint. Samples were retained at the following conditions and time points, and were tested in replicates of three at each timepoint/condition, and then compared back to the Time 0 quantitations.

- refrigerated (2-8ºC) Days 3, 5, 7, and 8
- multiple freeze thaws (-20 ºC) 1x, 3x, 5x
- long-term storage at -20 ºC 1month, 2 months, 3 months.

The data was found to be acceptable. The samples were stable for every sample, at each condition, and at each time point.

*Sample On-board Stability*

Fourteen (14) serum samples were collected from donors. Ten (10) serum samples were neat and the other four (4) serum samples were spiked with TSH values ranging from approximately 5 µIU/mL to 120 µIU/mL TSH and processed and aliquoted within 8 hours of collection. Samples were tested upon aliquoting and this was considered the Time 0 timepoint. The samples were placed on the instrument and tested in replicates of three at the time intervals of 1, 2, 4, 6, and 8 hours past Time 0. The data demonstrated that percent differences were all within 10% of the Time 0 time point.

*Reagent, Calibrator, and Control Stability*

The results of real time stability for open and closed vials for the HISCL TSH Assay Kit reagents, HISCL TSH Calibrators, and HISCL Immuno Multi Controls are shown below:

HISCL TSH Assay Kit

| Storage Temperature | Shelf LIfe |
|---|---|
| Storage at 2-8°C before opening | Expiration Date |
| Storage at 2-8°C/on board after opening | 30 days |

HISCL TSH Calibrators

| Storage Temperature | Shelf LIfe |
|---|---|
| Storage at 2-8°C before opening | Expiration Date |
| Storage at 2-8°C after opening | 60 days |

HISCL Immuno Multi Control

| Storage Temperature | Shelf LIfe |
|---|---|
| Storage at 2-8°C before reconstitution | Expiration date |
| After reconstitution at -20°C or lower | 60 days |
| After reconstitution at 2-8°C | 7days |
| After reconstitution at 8-30°C | 8 hours |

*Sample Carryover*

Three levels of contrived TSH serum pools (low [L], middle [M] and high [H]) were prepared and measured in the following order: of M, H, L, M, M, L, L, H, H, and M in accordance with CLSI EP-10-A3. Four sets of carryover sequences were assayed per day for five days. The data were found to be acceptable and no carryover was observed.

*Linearity/Reportable Range:*

A contrived high serum sample was mixed with a low contrived sample to create 39 intermediate samples with concentrations that are known relative to one another. The samples tested in this study ranged from 0.001 to 257.887 µIU/mL. The expected values were plotted against the observed values and the following regression equation was obtained:

- $y = 0.994x + 8.115 \times 10^{-5}$
- correlation coefficient: $R^2 = 1.00$

**807.92 (b)(2): Brief Description of Clinical Data**

Clinical performance of the Automated Immunoassay System HISCL 800 and HISCL TSH Assay was assessed via two studies where testing was performed by an external clinical laboratory with clinical specimens. The first study was a reference range study to identify the HISCL reference range according to CLSI EP28-A3c, and the second study was a method comparison study where TSH quantitations obtained with the Automated Immunoassay System HISCL 800 and HISCL TSH Assay were directly compared to the clinical site's reference method, the Siemens ADVIA Centaur TSH3-Ultra Assay (and Centaur instrument), using paired samples.

For the reference range study, the data demonstrated the following:

- N = 127 (65 males, 62 females)
- Age range 21 and 70 years
- Central 95% interval 0.446 µIU/mL and 4.780 µIU/mL

For the method comparison study, the data demonstrated the following:

- N = 165
- TSH range = 0.009 µIU/mL to 74.604 µIU/mL
- Deming regression analysis (95% confidence interval)
  - slope 0.950 (0.936 to 0.964)
  - y-intercept -0.0019 (-0.0056 to 0.0018)
  - correlation coefficient 0.993 (0.991 to 0.995)

**807.92 (b)(3): Conclusions from Nonclinical and Clinical Testing**

The data from the nonclinical and clinical testing indicate that the test system is safe and effective for its intended use.