510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k151792

B. Purpose for Submission:

Adding previously cleared assay on a new instrument

C. Measurand:

Thyroid Stimulating Hormone (TSH)

D. Type of Test:

Quantitative, chemiluminescence immunoassay

E. Applicant:

Siemens Healthcare Diagnostics Inc.

F. Proprietary and Established Names:

Trinidad IM Thyroid Stimulating Hormone (TSH) Assay

Trinidad IM TSH Calibrators

Trinidad Immunoassay (IM) System

G. Regulatory Information:

Product Code	Regulation Name	Classification	Regulation Section	Panel
JLW	Thyroid stimulating hormone test system	Class II	21 CFR § 862.1690	Chemistry 75
JIT	Calibrator, secondary	Class II	21 CFR§ 862.1150	Chemistry 75
JJE	Discrete photometric chemistry analyzer for clinical use	Class I	21 CFR § 862.2160	Chemistry 75

H. Intended Use:

1. Intended use(s):

   See indication(s) for use below

2. Indication(s) for use:

   The Trinidad Immunoassay (IM) system is an automated, immunoassay analyzer designed to perform in vitro diagnostic tests on clinical specimens. The Trinidad IM system's assay application utilizes chemiluminescents technology for clinical use.

   The Trinidad IM Thyroid Stimulating Hormone (TSH) assay is for in vitro diagnostic use in the quantitative determination of thyroid-stimulating hormone (TSH, thyrotropin) in human serum, and plasma (EDTA and lithium heparin) using the Trinidad IM system. Measurements of the thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

   The Trinidad IM TSH Calibrators are for in vitro diagnostic use in calibrating the Trinidad IM system TSH assay.

3. Special conditions for use statement(s):

   For prescription use.

4. Special instrument requirements:

   The Trinidad Immunoassay (IM) system

I. Device Description:

The Trinidad Immunoassay (IM) system is an automated, immunoassay analyzer that utilizes chemiluminescent technology. The analyzer is a floor model; fully automated, microprocessor-controlled, integrated instrument system that utilizes chemiluminescent technology and uses pre-packaged reagent packs to measure a variety of analytes in human body fluids.

The Trinidad IM TSH assay Ready Pack consists of the following reagents:

- Lite Reagent: 6.0 mL reagent pack contains bovine serum albumin (BSA) conjugated to murine monoclonal anti-TSH (~0.3 µg/mL) labeled with acridinium ester, buffer, stabilizers (murine, bovine, caprine), surfactant, and preservatives.
- Solid Phase Reagent: 21.0 mL reagent pack contains anti-fluorescein murine monoclonal antibody covalently linked to paramagenetic particles (~85 µg/mL), buffer, stabilizers (bovine, caprine), surfactant, and preservatives.
- Ancillary Reagent: 6.0 mL reagent pack contains fluorescein label (FITC)

conjugated to murine monoclonal anti-TSH (~0.3 µg/mL), buffer, stabilizers (murine, bovine, caprine), surfactant, and preservatives.

- Wash 3.0 L pack phosphate-buffered saline with sodium azide (<0.1%) and surfactant.
- Trinidad IM TSH calibrator: The Trinidad Calibrators consists of 1 (2mL) vial of lyophilized low calibrator and 1 (2mL) vial of lyophilized high calibrator. After reconstitution, the calibrators contain low and high levels of TSH, buffer, equine serum, sodium azide (0.1%), and preservatives. The low and high calibrators are targeted at ~0.032 and 97.5 µIU/mL.

The Trinidad IM TSH reagents and Trinidad IM TSH calibrator are the same reagents and calibrators as the reagents and calibrators cleared in the predicate device (k150403). The packaging is identical and the only difference is the labeling.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   ADVIA Centaur Thyroid Stimulating Hormone (TSH) assay, including calibrators
   ADVIA Centaur XP system

2. Predicate 510(k) number(s):
   k150403, k041133

3. Comparison with predicate:

Instrument

Similarities and Differences		
Item	Candidate Device Trinidad IM System	Predicate Device Advia Centaur XP system k041133
Intended Use	An automated immunoassay analyzer designed to perform in vitro diagnostic immunochemical assay analysis on clinical specimens	Same
Type of system	Random access and batch	Same
Throughput rate	250 to 450 tests/hour	120 to 240 tests/hour
External connectivity to LIS	Yes	Same
Sample container	sample cups or primary tubes	Same

Similarities and Differences		
Item	Candidate Device Trinidad IM System	Predicate Device Advia Centaur XP system k041133
Dispense system	Automated pipetting of samples using precision syringe	Same
Sample probe	Air pressure fluid sensing and disposable tip sensing; clog detection mechanism to alert operator to clogged sample probe.	Same
Sample size	10 to 100 µL	10 to 200 µL
Dilutions	Allowed on per-assay basis; capability of dilution of samples requiring pretreatment	Same
Reagent storage temp.	4 °C to 8 °C	Same

TSH Assay Reagent

Similarities and Differences		
Item	Candidate Device Trinidad IM Thyroid Stimulating Hormone (TSH) Assay	Predicate Device Advia Centaur TSH assay k150403
Intended Use	For in vitro diagnostic use in the quantitative determination of thyroid stimulating hormone (TSH, thyrotropin) in serum, heparinized plasma, and EDTA plasma	Same
Measured analyte	thyroid stimulating hormone (TSH) also known as thyrotropin	Same
Principle of assay	Chemiluminescence using magnetic particle solid phase and chemiluminescents label	Same

Similarities and Differences		
Item	Candidate Device Trinidad IM Thyroid Stimulating Hormone (TSH) Assay	Predicate Device Advia Centaur TSH assay k150403
Analytical measuring range	0.008-150 µIU/mL	Same
Sample type	serum, heparinized plasma, and EDTA plasma	Same

TSH Calibrator

Similarities and Differences		
Item	Candidate Device Trinidad IM Thyroid Stimulating Hormone (TSH) Calibrator	Predicate Device Advia Centaur TSH Calibrator k150403
Intended Use	In vitro diagnostic use in calibrating the TSH assay.	Same
Calibration	Two-point user run calibration	Same
Matrix	Lyophilized buffered equine serum	Same
Traceability	Standardized to internal standards and is traceable to the WHO 3rd International standard for human TSH (IRP 81/565)	Same

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP05-A3: Evaluation of Precision of Qualitative Measurement Methods Procedures; Approved Guideline

CLSI Guideline EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline

CLSI Guideline EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline- Third Edition

CLSI Guideline EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline

L. Test Principle:

The Trinidad IM TSH assay employs anti-FITC monoclonal antibody covalently bound to paramagnetic particles, a FITC-labeled anti-TSH capture monoclonal antibody, and a tracer consisting of a proprietary acridinum ester and an anti-TSH monoclonal antibody conjugated to bovine serum albumin (BSA) for chemiluminescents detection.

A direct relationship exists between the amount of TSH present in the patient sample and the amount of relative light units (RLUs) detected by the system.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision was performed on 20 days on 2 Trinidad IM systems with 2 reagent lots in accordance with CLSI EP05-A2 as a guideline. Repeatability and within-lab imprecision was evaluated by testing four serum-based controls, six human serum pools and six human plasma pools (three EDTA and three lithium heparin). The samples were run in 2 replicates per run, 2 runs per day for 20 days for a total of 80 replicates. The following precision results were obtained:

Specimen Type	Mean (µIU/mL)	Repeatability		Within-Lab	
		SD (µIU/mL)	CV (%)	SD (µIU/mL)	CV (%)
Control 1	0.034	0.001	2.356	0.002	4.448
Control 2	0.404	0.008	1.956	0.017	4.205
Control 3	5.257	0.091	1.735	0.233	4.439
Control 4	32.826	0.599	1.824	1.624	4.946
Plasma Pool 1	3.378	0.079	2.345	0.152	4.448
Plasma Pool 2	37.894	1.258	3.321	2.253	5.947
Plasma Pool 3	143.658	3.681	2.562	7.671	5.339
Plasma Pool 4	0.724	0.010	1.448	0.029	4.003
Plasma Pool 5	4.992	0.106	2.119	0.209	4.194
Plasma Pool 6	79.946	1.792	2.241	3.855	4.822
Serum Pool 1	1.106	0.016	1.459	0.041	3.665
Serum Pool 2	5.827	0.086	1.474	0.242	4.150
Serum Pool 3	11.440	0.213	1.858	0.425	3.713
Serum Pool 4	34.709	0.626	1.804	1.247	3.592
Serum Pool 5	59.879	1.056	1.764	2.266	3.784
Serum Pool 6	131.895	2.657	2.014	6.226	4.720

b. *Linearity/assay reportable range:*

The Trinidad IM TSH linearity was evaluated by using a high TSH serum sample (151.4 µIU/mL) mixed with a low equine serum pool (0.001 µIU/mL) to prepare intermixed samples ranging in various different TSH levels. All nine samples were assayed in triplicate using one reagent lot on one Trinidad IM system.

The weighted Deming regression equation is:

y = 0.957x + 0.0000; R = 1.000

The sponsor claimed that the TSH assay has a measuring range of 0.008 to 150 µIU/L.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The Trinidad IM TSH assay is standardized to internal standards, which are traceable to the World Health Organization (WHO) 3rd International Standard for Human TSH (IRP 81/565).

The Trinidad IM Thyroid Stimulating Hormone (TSH) assay utilizes a factory set master curve standards (10 levels) that have fixed TSH doses and corresponding relative light units (RLU) signals that are reagent dependent. The master curve values are contained on the master curve card provided with each kit. The barcode reader or keyboard is used to enter the master curve values on the system. The 2 calibrators in the kit are run when the lot is first used or after expiration of the calibration interval. If the calibration run is valid as determined by prearranged parameters, the values are stored and used to "normalize" test values to the master curve.

The sponsor has a statement in the package insert: Do not mix calibrator lots with different lots of reagent packs.

The Trinidad IM TSH calibrators were previously cleared under k041133.

Trinidad IM Thyroid Stimulating Hormone (TSH) Calibrators are stable at 2-8 °C for 12 months unopened. The open vial stability (reconstituted) is stable for 28 days and the on-system stability is 4 hours. The stability study protocol and acceptance criteria have been provided and found to be adequated.

d. *Detection limit:*

The Limit of Blank (LoB) for the Trinidad IM TSH assay was determined as recommended in CLSI guideline EP17-A2 (Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures). Five blank samples with no detectable

levels of TSH were assayed for a minimum of two runs per day, two replicates per run, using three lots of reagent on two Trinidad IM systems over five days for a total of 200 replicates. The LoB was established as the TSH value corresponding to the 95th rank position in each dataset. LoB was calculated to be 0.001 µIU/mL.

The Limit of Detection (LoD) was determined as recommended in CLSI guideline EP17-A2 by using five serum samples with TSH levels ranging from 0 to 0.0073 µIU/mL. All samples were assayed in duplicate in each of a minimum of 20 runs using three lots of reagents on two Trinidad IM systems over a minimum of 10 days (n=80). The LoD was calculated to be 0.005 µIU/mL using the following equation $LoD = LoB + c_pSD_{L.}$

The Limit of Quantitation (LoQ), using functional sensitivity, was determined by using five (5) low-level TSH serum sample. TSH levels ranging from 0.0078 to 0.0208µIU/mL were used. All samples were assayed in duplicate in each of 10 runs, on two Trinidad IM systems, using three reagent lots, and over a period of at least 10 days (n=80).

The functional sensitivity was based on the within lab precision of 20% CV and was determined to be 0.008 µIU/mL.

The claimed measuring range of the assay is 0.008 to 150 µIU/mL.

e. *Analytical specificity:*

An interference study was conducted to evaluate the effect of endogenous interfering substances (hemoglobin, triglycerides, bilirubin, conjugated and unconjugated) using 4 serum samples on the Trinidad IM TSH assay. All samples were tested in triplicate with one reagent lot on one Trinidad IM system. Based on the sponsors definition of non-significant interference (≤10 % recovery of the control value), no significant interference for the substances and concentrations listed below:

Potential interfering endogenous substances	Highest interferent concentration tested at which no significant interference was observed
Hemoglobin	600 mg/dL
Triglycerides (Intralipid)	2000 mg/dL
Bilirubin, conjugated	60 mg/dL
Bilirubin, unconjugated	60 mg/dL

In addition, to determine the cross reactivity of related proteins in the Trinidad TSH assay, four human samples with TSH levels of 0.37, 3.74-3.83, 44.1-45.8 and 120-125 µIU/mL were spiked with the following levels of cross-reactants:

- hCG at 200, 000 µIU/mL
- FSH at 1500µIU/mL
- LH at 600 µIU/mL

The control samples and the spiked samples were assayed in triplicate using one reagent lot on one Trinidad IM system.

Based on the sponsor's definition of non-significant interference (≤5% of the control value), no significant interference for the compounds and concentrations below:

Compound Tested	Concentration
hCG	200, 000 µIU/mL
FSH	1500µIU/mL
LH	600 µIU/mL

Hook effect: To evaluate the potential for high dose hook effect in the Trinidad IM TSH assay a high TSH sample (~9200 µIU/mL) was prepared. The sample was serially diluted 2-fold. The neat sample and the dilutions were assayed in triplicate with one lot of reagent on one Trinidad IM system. There was no high dose effect observed at TSH concentrations up to 3,000 µIU/mL.

The sponsor included the following statement in the Trinidad IM TSH assay package insert:

"High TSH levels can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, TSH levels as high as 3000 µIU/mL (mIU/L) will assay greater than 150 µIU/mL."

f. Assay cut-off:

Not applicable)

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed to compare TSH on the Trinidad IM TSH assay with the Advia Centaur TSH3-Ultra assay (predicate). A total of 347 samples ranging from 0.008-148.8 µIU/mL were tested. A total of 24 samples were contrived (7% contrived). Samples were assayed in duplicate using one reagent lot on two Trinidad IM systems and one Advia Centaur XP system. Testing was performed over multiple days. Deming regression analysis was performed using the first replicate of each data set. The data is summarized in the table below:

n	Weighted Deming Regression	Correlation Coefficient	Sample Range (µIU/mL)
347	y = 1.069x – 0.003	0.994	0.008 – 148.787

b. Matrix comparison:

A matrix comparison study was conducted utilizing ninety matched lithium heparin, EDTA plasma and serum samples. Seven sets were spiked with TSH to cover the upper range of the assay. The TSH values ranged from 0.014 to 135 µIU/mL. All samples were assayed in duplicate with one reagent lot on one Trinidad IM system. The statistical results using the Deming regression was performed on plasma verses serum samples. The first replicate of each data set was used for the analysis. Results are summarized in the table below:

Sample	n	Weighted Deming Regression	Correlation Coefficent	Sample range (µIU/mL)
Lithium Heparin	90	1.01x – 0.001	0.999	0.014-134.530
EDTA Plasma	90	1.00x – 0.0001	1.000	0.014-134.530

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The reference interval was previously established on the Advia Centaur System using the predicate device (in k0150403); including the pediatric reference intervals. To verify the reference range, a transferability and verification study was conducted according to CLSI

Guideline EP28-A3c. The study results support the original reference range established with the predicate device. The expected values are as follows:

Age Range	Reference Range
Infants (01 – 23 months)	0.87 – 6.15 µIU/mL
Children (02 – 12 years)	0.67 – 4.16 µIU/mL
Adolescents (13-20 years)	0.48 – 4.17 µIU/mL
Adults (≥ 21 years)	0.55 – 4.78 µIU/mL

N. Instrument Name:

Trinidad Immunoassay (IM) System

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes ___X_____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No ___X_____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes ___X_____ or No _____

3. Specimen Identification:

   Manual entry, Barcode, or LIS

4. Specimen Sampling and Handling:

   Automated or manual sample dilution, automated sample handling

5. Calibration:

   The Trinidad IM TSH Calibrators are provided with each kit. Calibration is required at

the end of the 14-day pack calibration interval, for calibrated reagent packs on the system.

6. Quality Control:

   The sponsor recommends analyzing two levels of quality control material with a known TSH concentration at least once each day.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

A carry over study has been performed and found to be acceptable.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.