510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K251543

B Applicant

Siemens Healthcare Diagnostics, Inc.

C Proprietary and Established Names

Atellica® IM TSH3-Ultra II (TSH3ULII)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JLW	Class II	862.1690 - Thyroid Stimulating Hormone Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification of existing device

B Measurand:

Thyroid Stimulating Hormone (TSH)

C Type of Test:

Quantitative, chemiluminescence immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Atellica® IM TSH3-Ultra II (TSH3ULII) 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 Atellica® IM Analyzer. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the diagnosis of thyroid or pituitary disorders.

C Special Conditions for Use Statement(s):

Rx-For Prescription Use Only

D Special Instrument Requirements:

Atellica® IM Analyzer

IV Device/System Characteristics:

A Device Description:

The Atellica® IM TSH3ULII assay kit consists of the following reagents:

Ultra-Lite Reagent- bovine serum albumin (BSA) conjugated to monoclonal anti- TSH (~0.3 µg/mL) labeled with acridinium ester in buffer, mouse IgG, BSA, goat serum, sodium azide (< 0.1%); surfactant, and preservatives.

Solid Phase Reagent - anti-fluorescein monoclonal mouse antibody covalently linked to paramagnetic particles (PMP) (~85 µg/mL) in buffer, BSA, goat serum, sodium azide (< 0.1%); surfactant, and preservatives.

Ancillary Well Reagent – Fluorescein isothiocyanate conjugated to monoclonal anti-TSH antibody (~3 µg/mL), BSA, BCG, goat serum, sodium azide (< 0.1%); surfactant, and preservatives.

The Atellica® IM TSH3ULII assay kit is comprised of the following components:

- Ready Pack primary reagent packs containing TSH3ULII Lite Reagent, Solid Phase, and Ancillary Well Reagent
- Atellica® IM TSH3ULII master curve and test definition.
- CAL 3A low calibrator.

- CAL 3A high calibrator.
- Atellica® IM CAL 3A calibrator assigned value sheet.

Materials Required but Not Provided
Atellica® IM Analyzer and system fluids including Atellica® IM Wash, Atellica® IM Acid, Atellica® IM Base and Atellica® IM Cleaner.

B Principle of Operation:

The Atellica® IM TSH3ULII is a homogeneous, sandwich chemiluminescent immunoassay. 75 µL of sample is incubated with FITC-labeled mouse monoclonal anti-TSH antibody and mouse monoclonal anti-TSH antibody conjugated to BSA. Then FITC-labeled mouse monoclonal anti-TSH antibody and mouse monoclonal anti-fluorescein antibody linked to paramagnetic particles are added and incubated. After washing the immunocomplex with the Atellica® IM wash, Atellica® IM Acid Reagent and Atellica® IM Base Reagent are added to initiate the chemiluminescent reaction. 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.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ADVIA Centaur® TSH3-Ultra II (TSH3ULII)

B Predicate 510(k) Number(s):

K233050

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251543	K233050
Device Trade Name	Atellica® IM TSH3-Ultra II	ADVIA Centaur® TSH3-Ultra II
General Device Characteristic Similarities		
Intended Use/Indications For Use	Quantitative determination of thyroid-stimulating hormone (TSH, thyrotropin) in human serum and plasma. Measurements of thyroid stimulating hormone produced by the anterior pituitary are used in the	Same

Device & Predicate Device(s):	K251543	K233050
	diagnosis of thyroid or pituitary disorders.	
Test principle and technology	Chemiluminescence immunoassay	Same
Sample Type	Human serum and plasma	Same
General Device Characteristic Differences		
Instrument	Atellica® IM Analyzer	ADVIA Centaur® XP system
Sample volume	75 µL	100 µL
Assay Measuring Interval	0.008–150 µIU/mL (mIU/L)	0.01–150 µIU/mL (mIU/L)
LoQ	0.004 µIU/L	0.010 µIU/L

VI Standards/Guidance Documents Referenced:

Clinical Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition

CLSI EP09c: Measurement Procedure Comparison and Bias Estimation Using Patient Samples – Third Edition

CLSI EPI7-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline - Second Edition

CLSI EP06: Evaluation of the Linearity of Quantitative Measurement – Second Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:
   Precision studies were conducted following the recommendations in CLSI EP05-A3 to estimate repeatability, within-laboratory precision, and reproducibility.

   Repeatability and Within-Lab Precision:
   The study was conducted using 3 reagent lots of the candidate assay on one Atellica IM analyzer. Six human serum samples, five lithium heparin plasma samples and five controls were tested in duplicate over twenty days, 2 runs per day, 2 replicates per run with for a total of 80 replicates per sample using 3 lots of reagents and one instrument. Repeatability and within laboratory precision were calculated. The within-laboratory SD and %CV includes

within-run, between-run, and between-day variance components. Results were similar between lots. The results from a representative lot are summarized below.

			Repeatability		Within-Laboratory Precision	
Sample	N	Mean µIU/ml	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)
Serum 1	80	0.091	0.0020	2.2	0.0038	4.2
Serum 2	80	0.205	0.0047	2.3	0.0084	4.1
Serum 3	80	0.519	0.0106	2.0	0.0269	5.2
Serum 4	80	4.846	0.1010	2.1	0.2343	4.8
Serum 5	80	47.864	1.4013	2.9	2.4523	5.1
Serum 6	80	96.779	2.9121	3.0	5.0733	5.2
Plasma1	80	0.102	0.0018	1.8	0.0046	4.5
Plasma 2	80	0.531	0.0097	1.8	0.0293	5.5
Plasma 3	80	4.894	0.1173	2.4	0.2730	5.6
Plasma 4	80	52.592	1.3057	2.5	2.4539	4.7
Plasma 5	80	91.668	4.1801	4.6	6.5350	7.1
Control 1	80	0.110	0.0021	1.9	0.0040	3.6
Control 2	80	0.544	0.0080	1.5	0.0244	4.5
Control 3	80	4.903	0.0619	1.3	0.2364	4.8
Control 4	80	47.588	0.7170	1.5	2.0892	4.4
Control 5	80	100.16	1.5253	1.5	5.0022	5.0

Reproducibility:

Six human serum samples, five lithium heparin plasma samples, and controls were tested in replicates of five with one run per day over five days for a total of 225 replicates per sample. Testing was performed using three instruments and three reagent lots. Repeatability, between-day, between-lot, between-instrument, and reproducibility were calculated. The results are summarized below.

		Repeatability		Between-Day		Between-Lot		Between-Instrument		Reproducibility	
Sample	Mean µIU/ml	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)
Serum 1	0.087	0.002	2.12	0.001	1.30	0.003	3.44	0.001	1.26	0.004	4.43
Serum 2	0.172	0.004	2.12	0.002	1.42	0.005	2.82	0.002	0.92	0.007	3.93
Serum 3	0.449	0.009	2.04	0.004	0.92	0.011	2.52	0.003	0.58	0.015	3.42
Serum 4	4.450	0.094	2.12	0.054	1.21	0.067	1.50	0.044	0.98	0.135	3.03
Serum 5	53.797	1.160	2.15	0.672	1.25	1.042	1.94	0.614	1.14	1.805	3.36
Serum 6	100.021	2.250	2.25	1.789	1.79	3.066	3.06	0.590	0.59	4.244	4.24
Plasma 1	0.090	0.002	2.23	0.001	1.07	0.003	3.54	0.002	1.86	0.004	4.70
Plasma 2	0.422	0.009	2.13	0.004	1.06	0.010	2.42	0.007	1.54	0.016	3.73
Plasma 3	4.293	0.080	1.86	0.082	1.91	0.065	1.52	0.023	0.54	0.134	3.12

		Repeatability		Between-Day		Between-Lot		Between-Instrument		Reproducibility	
Sample	Mean µIU/ml	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)	SD µIU/ml	CV (%)
Plasma 4	47.836	1.052	2.20	0.789	1.65	0.768	1.61	0.731	1.53	1.689	3.53
Plasma 5	98.087	2.139	2.18	2.522	2.56	2.877	2.93	1.824	1.86	4.743	4.84
Control 1	0.102	0.002	2.06	0.001	1.12	0.004	3.71	0.001	0.69	0.005	4.44
Control 2	0.506	0.008	1.63	0.005	1.08	0.013	2.57	0.003	0.59	0.017	3.28
Control 3	4.627	0.082	1.78	0.045	0.96	0.079	1.70	0.024	0.52	0.125	2.69
Control 4	45.957	0.854	1.86	0.586	1.28	0.725	1.58	0.000	0.00	1.264	2.75
Control 5	95.579	2.007	2.06	1.228	1.26	2.508	2.57	0.000	0.00	3.439	3.52

2. Linearity:

   A linearity study was performed following CLSI EP06-2nd edition. A total of 15 levels of serum samples ranging from 0.004 to 158.0 µIU/ml were prepared by mixing different proportions of a serum sample containing a high concentration of TSH with a serum sample containing a low concentration of TSH. Five replicates of each sample were tested on one Atellica IM Analyzer using 3 reagent lots. The maximum observed deviation within the claimed analytical measuring interval was ±6.5%. The results support the claimed measuring interval of 0.008–150 µIU/mL.

   High-Dose Hook Effect: The sponsor evaluated susceptibility to high-dose hook effect. Results are similar to K233050.

3. Analytical Specificity/Interference:

   The sponsor provided information to support that analytical specificity is unchanged from what was established in K233050.

4. Detection Limit and Assay Reportable Range:

   Detection capability was determined in accordance with CLSI EP17-A2. The studies supported the following detection limit claims:

   Limit of Blank (LoB) 0.001 µIU/mL (mIU/L)
   Limit of Detection (LoD) 0.003 µIU/mL (mIU/L)
   Limit of Quantitation (LoQ) 0.004 µIU/mL (mIU/L)

   The LoQ corresponds to the lowest analyte concentration at which the within laboratory CV is ≤ 20%.

   The assay reportable range is 0.008 to 150 µIU/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Traceability is unchanged since it was established in K233050.

Stability: Onboard stability, pack calibration interval, and lot calibration interval studies were completed; the results support the claimed onboard stability, pack calibration interval, lot calibration interval and onboard stability of 63 days.

6. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A method comparison study was conducted in accordance with CLSI EP09C-Ed3 using 323 human serum samples. Samples were tested in singlicate using 3 reagent lots of the candidate device on the Atellica IM analyzer and tested in singlicate using a single reagent lot of the legally marketed comparator device.

   Data were analyzed using Passing-Bablok regression analyses and the differences between the two test systems were evaluated. Results were similar between lots. The results from a representative lot are summarized below.

N	Sample range* (µIU/ml)		Slope	Intercept	r
	Low	High			
323	0.011	147.2	0.97	-0.006	0.998

   *as determined by the comparator method

2. Matrix Comparison:

   Matrix equivalency between serum and plasma (Lithium Heparin and K2-EDTA) is unchanged since it was established in K233050.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Clinical Cut-Off:

   Not applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Expected Values/Reference Range:

Expected values are unchanged from when they were established in K233050.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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