510(k) SUMMARY

Lumipulse® ***G*** TSH-III
K171103

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Device Name: Lumipulse ***G*** TSH-III Immunoreaction Cartridges
Classification: Class II
JLW
75, Clinical Chemistry
21 CFR § 862.1690

Predicate Device: k983442
Abbott Laboratories
ARCHITECT TSH

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Device Description:

Lumipulse ***G*** TSH-III is an assay system, including a set of immunoassay reagents, for the quantitative measurement of TSH in specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE ***G*** System. TSH in specimens specifically binds to anti-human TSH monoclonal antibody (mouse) on the particles, and antigen-antibody immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Alkaline phosphatase (ALP: calf)-labeled anti-human TSH monoclonal antibody (mouse) specifically binds to TSH of the immunocomplexes on the particles, and additional immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Substrate Solution is added and mixed with the particles. AMPPD contained in the Substrate Solution is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of TSH.

Lumipulse ***G*** TSH-III:

Lumipulse ***G*** TSH-III Immunoreaction Cartridges REF 235294

The Lumipulse ***G*** TSH-III Immunoreaction Cartridges consists of 3 × 14 tests. Each kit contains the following:

1) Antibody-Coated Particle Solution
(Liquid when used, 250 µL/Immunoreaction Cartridge)
Contains 200 µg/mL anti-human TSH monoclonal antibody (mouse)-coated particles, protein stabilizers (bovine and mouse) and chemical stabilizers in 0.15 M sodium chloride/Tris buffer. This solution contains gelatin and turns into gel at 15 °C or lower. Preservative: sodium azide.

2) Enzyme-Labeled Antibody Solution
(Liquid, 350 µL/Immunoreaction Cartridge)
Contains 0.3 µg/mL alkaline phosphatase (ALP:calf)-labeled anti-TSH monoclonal antibody (mouse), protein stabilizers (bovine and calf) and chemical stabilizers in 0.15 M sodium chloride/MES buffer. Preservative: sodium azide.

Lumipulse ***G*** TSH-III Calibrators CAL 231135, Liquid 1x3 concentrations
Each calibrator kit contains one bottle each of Calibrators 1 – 3. The calibrator kit is packaged separately.

CAL 1 0 µIU/mL TSH calibrator (1 × 1.5 mL)
CAL 2 5 µIU/mL TSH calibrator (1 × 1.5 mL)
CAL 3 200 µIU/mL TSH calibrator (1 × 1.5 mL)
Contains thyroid stimulating hormone (TSH) in 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: sodium azide

Device Intended Use:

Lumipulse ***G*** TSH-III Immunoreaction Cartridges

For in vitro diagnostic use.

Lumipulse ***G*** TSH-III is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of thyroid stimulation hormone (TSH) in human serum on the LUMIPULSE ***G*** System.

Lumipulse ***G*** TSH-III is to be used as an aid in the diagnosis of thyroid or pituitary disorders.

Device Indications for Use:
Same as Intended Use

Substantial Equivalence:

Comparison between the Lumipulse *G* TSH-III assay and Abbott ARCHITECT TSH assay

Similarities and Difference		
	Lumipulse® *G* TSH-III (Proposed Device)	**Abbott ARCHITECT TSH (Predicate Device) K983442**
Device Type	*In vitro* diagnostic	same
Classification	Class II	same
Regulation Number	21CFR § 862.1690 Thyroid stimulating hormone test system	same
Product Usage	Clinical and Hospital laboratories	same
Principle of Operation	Automated Quantitative Chemiluminscent Enzyme Immunoassay (CLEIA)	Chemiluminescent Microparticle Immunoassay (CMIA)
Specimen Collection Method	Routine Phlebotomy Techniques	same
Intended Use	For in vitro diagnostic use. Lumipulse ***G*** TSH-III is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative determination of thyroid stimulation hormone (TSH) in human serum on the LUMIPULSE ***G*** System. Lumipulse ***G*** TSH-III is to be used as an aid in the diagnosis of thyroid or pituitary disorders.	The ARCHITECT TSH assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of human Thyroid Stimulating Hormone (TSH) in human serum and plasma.
Instrument System	LUMIPULSE ***G*** System	ARCHITECT
Assay Type	Two-step sandwich immunoassay based on chemiluminescent technology	same
Sample Volume	60 µL	200 µL
Type of Specimen	Human serum	Human serum or plasma (lithium heparin, sodium heparin or potassium EDTA)
Assay Range	0.02 – 100 µIU/mL	0.000 – 100.00 µIU/mL

Performance Characteristics

Data were generated using the LUMIPULSE ***G***1200 System.

1. Analytical performance:

a. *Precision/Reproducibility:*

20 Day

The Lumipulse ***G*** TSH-III demonstrated Within-Laboratory (Total) precision of ≤6.4% CV in a study run according to the Clinical and Laboratory Standards Institute (CLSI) Protocol EP5-A3. Five human serum-based panels were assayed in replicates of two at two separate times of the day for 20 days (n=80 for each sample) using one LUMIPULSE ***G***1200 System. Within-Laboratory (Total) precision combines Within-run, Between-run and Between-day precision data. Data from this study are summarized below.

		Within-Run (Repeatability)		Between Run		Between-Day		Within-Laboratory (Total)	
Sample	**Mean (µIU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 1	0.365	0.012	3.3%	0.000	0.0%	0.001	0.2%	0.012	3.3%
Panel 2	1.029	0.018	1.8%	0.044	4.3%	0.042	4.1%	0.063	6.2%
Panel 3	4.533	0.086	1.9%	0.018	0.4%	0.000	0.0%	0.088	1.9%
Panel 4	8.773	0.098	1.1%	0.261	3.0%	0.427	4.9%	0.510	5.8%
Panel 5	73.991	1.585	2.1%	2.125	2.9%	3.950	5.3%	4.757	6.4%

Lot-To-Lot Reproducibility for Combined Data

The precision analyses for the combined lot-to-lot analysis determined the total precision for Lumipulse ***G*** TSH-III to be ≤ 4.6% for the 3 panels in this study. The total precision of Lumipulse ***G*** TSH-III for the 3 panels ranged from 3.1% to 4.6%. The between-lot precision for Lumipulse ***G*** TSH-III was ≤ 4.0%.

Data from this study are summarized below.

		Between-Lot		Between Day		Between Run		Within-Run (Repeatability)		Within-Laboratory (Total)	
Sample	**Mean (µIU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 2	1.046	0.029	2.8%	0.000	0.0%	0.005	0.5%	0.020	1.9%	0.036	3.4%
Panel 4	8.895	0.209	2.3%	0.000	0.0%	0.041	0.5%	0.177	2.0%	0.277	3.1%

		Between-Lot		Between Day		Between Run		Within-Run (Repeatability)		Within-Laboratory (Total)	
Sample	**Mean (µIU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 5	77.333	3.071	4.0%	1.044	1.3%	0.712	0.9%	1.181	1.5%	3.525	4.6%

Site to Site Reproducibility for Combined Data

The precision analyses for the combined site-to-site analysis for Lot A determined the total precision for Lumipulse ***G*** TSH-III to be ≤ 4.3% for the 3 panels in this study. The total precision of Lumipulse ***G*** TSH-III in the study ranged from 2.9% to 4.3%. The between-site precision for Lumipulse ***G*** TSH-III was ≤ 2.4%.

Data from this study are summarized below.

		Between Site		Between Day		Between Run		Within-Run (Repeatability)		Reproducibility (Total)	
Sample	**Mean (µIU/mL)**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Panel 2	1.049	0.025	2.4%	0.010	0.9%	0.019	1.8%	0.032	3.0%	0.046	4.3%
Panel 4	9.015	0.095	1.1%	0.087	1.0%	0.112	1.2%	0.200	2.2%	0.263	2.9%
Panel 5	76.043	0.662	0.9%	0.000	0.0%	1.888	2.5%	1.757	2.3%	2.662	3.5%

b. Linearity/assay reportable range:

Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System demonstrated linearity in a study consistent with the guidelines in the CLSI Protocol EP6-A. High and low sample pools were created using patient samples that contained naturally expressed TSH. The linearity was found in the range of 0.001 to 227.804 µIU/mL. Lumipulse ***G*** TSH-III correlated with expected concentrations according to the linear regression formulas:

Serum: $y = 1.03(x) + 0.001$; R-squared: 0.9962

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System, no high dose hook effect was observed for samples containing up to ~5,000 µIU/mL of TSH.

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

The calibrators for use with the Lumipulse ***G*** TSH-III are prepared gravimetrically and are traceable to in-house reference calibrators, whose values have been assigned to the 3rd International Standard, 2003 (code: 81/565) by the National Institute for Biological Standards and Control (NIBSC).

3 Bottles (1.5 mL each) are supplied for the Lumipulse ***G*** TSH-III Calibrators. Preservative: Sodium azide. The calibrators are at the following concentrations:

Calibrator Level	TSH Concentration (µIU/mL)
CAL 1	0
CAL 2	5
CAL 3	200

Master calibration data are recorded in a two-dimensional bar code on the Immunoreaction Cartridge case. The calibration curve is created based on the recorded master calibration data and the calibration data. The TSH concentration of a specimen is automatically calculated from the calibration curve. The result of the calculation is reported in µIU/mL.

Shelf life

The shelf life for Lumipulse ***G*** TSH-III Immunoreaction Cartridges and the Lumipulse ***G*** TSH-III Calibrators is 12 months at 2–10°C.

On board the LUMIPULSE ***G***1200

The Lumipulse ***G*** TSH-III Immunoreaction Cartridges are stored at 12°C. To reduce risk for any misuse, the package insert states "*The Lumipulse **G** TSH-III Immunoreaction Cartridges can be stored on-board the LUMIPULSE **G** System for a maximum of 30 days*".

The package insert recommends calibrator curve storage on the LUMIPULSE ***G***1200 for a maximum of 30 days.

Transport Conditions

Lumipulse ***G*** TSH-III Immunoreaction Cartridges and the Lumipulse ***G*** TSH-III Calibrators are shipped at 2-10°C.

Materials will be shipped to the end user using an insulated container and a predetermined configuration of gel (cold and/or frozen) packs to maintain the product for up to 72 hours when stored at ambient temperature.

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ)/ Functional Sensitivity (FS) of the Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 is ≤ 0.006 µIU/mL.

1) LoB and LoD
   The LoB for Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System was 0.0010

µIU/mL. The LoD for Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System was 0.002 µIU/mL, determined consistent with the CLSI guideline EP17-A2. Eight low level specimens were tested over 6 weeks using two LUMIPULSE ***G***1200 Systems and two Lumipulse ***G*** TSH-III lots giving 480 determinations for each panel.

2) LoQ/FS

FS is defined as the concentration of TSH that can be measured with an interassay CV of 20%. The LoQ/FS for the Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System was 0.006 µIU/mL, determined consistent with the NACB Guideline: Laboratory Support for the Diagnosis and Monitoring of Thyroid Disease. Based on this study, the Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System meets the definition of a third generation TSH assay.

e. Analytical specificity:

Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System demonstrated an average interference of ≤10% (for each compound) in a study consistent with the guidelines in the CLSI Protocol EP7-A2. Human serum specimens with TSH concentrations of approximately 0.566, 2.530, and 67.515 µIU/mL were supplemented with potentially interfering compounds. The following compounds were tested using Lumipulse ***G*** TSH-III and found not to interfere with the assay.

Endogenous Interferences	**Test Concentration**
Free Bilirubin (unconjugated)	60 mg/dL
Conjugated Bilirubin	60 mg/dL
Triglycerides (Intralipid 20% Emulsion)	3,000 mg/dL
Hemoglobin	500 mg/dL
Total Protein (Human Serum Albumin)	12 g/dL
Immunoglobulin G (IgG)	5 g/dL
Cholesterol	500 mg/dL
Uric Acid	24 mg/dL
Human Anti-Mouse Antibodies (HAMA)	1,268 ng/mL
Rheumatoid Factor (RF)	1,000 IU/mL

Therapeutic Drug Interferences	**Test Concentration**
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	65 mg/dL
Amiodarone	0.6 mg/dL
Atropine	20 mg/dL
Ascorbic Acid	6.5 mg/dL
Caffeine	6 mg/dL
Carbamezapine	1.2 mg/dL
Dexamethasone	0.06 mg/dL
EDTA	0.1 mg/dL

Ethanol	1%
Furosemide	6 mg/dL
Gentisic Acid	2 mg/dL
Heparin	3000 U/L
Ibuprofen	50 mg/dL
Prednisone	0.03 mg/dL
Propranolol HCL	0.23 mg/dL
Theophylline	4 mg/dL

Lumipulse ***G*** TSH-III on the LUMIPULSE ***G***1200 System was evaluated for cross-reactivity of the assay with other substances that are similar in structure to TSH in a study consistent with the guidelines in the CLSI Protocol EP7-A2. Human serum specimens with TSH concentrations of approximately 0.566, 2.530, and 67.515 µIU/mL were supplemented with potentially cross-reacting compounds. The following compounds were tested at the concentrations listed below and the level of TSH in the samples was then determined.

Interferent #	Interferent	Sample ID	Mean Concentration with Cross-reactant (µIU/mL) (n=3)	Mean Concentration without Cross-reactant (µIU/mL) (n=3)
1	FSH (5000 mIU/mL)	Serum Pool1	0.564	0.555
		Serum Pool2	2.419	2.355
		Serum Pool3	68.301	69.236
2	hCG (200,000 mIU/mL)	Serum Pool1	1.218	0.538
		Serum Pool2	2.564	2.282
		Serum Pool3	67.427	67.387
3	hGH (100 ng/mL)	Serum Pool1	0.693	0.666
		Serum Pool2	2.466	2.572
		Serum Pool3	66.279	67.052
4	LH (1000 mIU/mL)	Serum Pool1	0.581	0.569
		Serum Pool2	2.337	2.491
		Serum Pool3	67.548	70.063

2. <u>Comparison studies:</u>

a. Method Comparison

The Lumipulse ***G*** TSH-III method comparison as performed on the LUMIPULSE ***G***1200 system in a study consistent with the guidelines in CLSI EP9-A3.

The weighted Deming regression method was used to compare Lumipulse ***G*** TSH-III to

Abbott ARCHITECT TSH. The serum samples tested ranged from 0.026 to 84.299 µIU/mL for Lumipulse ***G*** TSH-III and 0.030 to 89.930 µIU/mL for ARCHITECT TSH. The data are summarized in the following table.

Lumipulse *G* TSH-III vs. Abbott ARCHITECT TSH				
n	**Correlation Coefficient (r)**	**Intercept (95% CI)**	**Slope (95% CI)**	**Average Bias (µIU/mL)**
141	0.9838	-0.0037 -0.0064 to -0.0010	0.97 0.93 to 1.01	-1.051

3. Expected values/Reference range**:**

0.389-3.764 µIU/mL

These values correspond to the 2.5th and 97.5th percentiles of results obtained from a total of 116 healthy test subjects examined. It is recommended that each laboratory establish its own range, which may be unique to the population it serves depending upon geographical, patient, and environmental factors.

Standard/Guidance Document Referenced:

- CLSI EP5-A3 - Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP28-A3c - Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline-Third Edition
- CLSI EP17-A2 - Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline Second Edition
- CLSI EP6-A - Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP9-A3 – Measurement Procedure Comparison and Bias Estimation Using Patient Samples; approved Guideline – Third Edition
- CLSI EP7-A2 – Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition
- CLSI EP25-A – Evaluation of Stability of *In Vitro* Diagnostic Reagents: Approved Guideline
- Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable - Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff
- Guidance for Industry and Food and Drug Administration Staff - eCopy Program for Medical Device Submissions (December 3, 2015)
- Guidance for Industry and Food and Drug Administration Staff - Refuse to Accept Policy for 510(k)s (August 4, 2015)

Conclusion

The results of these analytical (nonclinical) and clinical studies demonstrate that the Lumipulse ***G*** TSH-III assay is substantially equivalent to the performance of the Abbott ARCHITECT TSH assay.