510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k171103

B. Purpose for Submission:

New device

C. Measurand:

Thyroid-stimulating hormone (TSH)

D. Type of Test:

Chemiluminescent Enzyme Immunoassay

E. Applicant:

Fujirebio Diagnostics, Inc.

F. Proprietary and Established Names:

Lumipulse G TSH-III Immunoreaction Cartridges

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JLW	II	21 CFR 862.1690, Thyroid stimulating hormone test system	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use

2. Indication(s) for 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 stimulating 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.

3. Special conditions for use statement(s):

   For prescription use.

4. Special instrument requirements:

   LUMIPULSE G1200 System

I. Device Description:

The Lumipulse G TSH-III Immunoreaction Cartridges consist of the following:

1) Antibody-coated particle solution containing 200 µg/mL mouse anti-human monoclonal antibody-coated particles, protein stabilizers (bovine and mouse) and chemical stabilizers in 0.15 M sodium chloride/Tris buffer.

2) Enzyme-labeled antibody solution containing 0.3 µg/mL alkaline phosphatase-labeled mouse anti-TSH monoclonal antibody, protein stabilizers (bovine and mouse), and chemical stabilizers in 0.15 M sodium chloride/MES buffer.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Abbott ARCHITECT TSH

2. Predicate 510(k) number(s):

   k983442

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate Device: Lumipulse G TSH-III k171103	Predicate Device: Abbott ARCHITECT TSH k983442
Intended Use	Assay for the quantitative determination of TSH	Same
Assay Range	0.02 - 100 μIU/mL	0.00 - 100 μIU/mL
Assay Type	Two-step sandwich immunoassay based on chemiluminescent technology	Same
Principle of Operation	Automated Quantitative Chemiluminescent Enzyme Immunoassay	Chemiluminescent Microparticle Immunoassay
Specimen Type	Serum	Serum or plasma

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

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Methods, 3rd Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach, 2nd Edition

CLSI EP07-A2: Interference Testing in Clinical Chemistry, 2nd Edition

CLSI EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples, 3rd Edition

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, 2nd Edition

CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents, Approved Guideline

CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, 3rd Edition

L. Test Principle:

Lumipulse G TSH-III is an assay system for the quantitative measurement of TSH in serum specimens based on CLEIA technology by a two-step sandwich immunoassay method on the LUMIPULSE G1200 System. TSH in specimens specifically binds to mouse anti-human TSH monoclonal antibody on the particles, and antigen-antibody immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials.

Alkaline phosphatase-labeled mouse anti-human TSH monoclonal antibody 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 (3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane disodium salt) contained in the substrate solution is dephosphorylated by the catalysis of alkaline phosphatase indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal is proportional to the amount of TSH.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Five panels (4 native serum pools and one spiked serum pool) were each assayed over 20 days, in duplicate, two runs per day, for a total of 80 results per sample. A multi-site precision study was also conducted using four serum panels at three additional sites, where the panels were run in triplicate, twice per day, for five days. Lot-to-lot precision studies for three paired reagent and calibrators lots were also performed at one site using four serum panels tested in triplicate, two runs per day, for five days. All lots of reagents and the multi-site precision study yielded similar results.

The results of the 20-day precision study are shown in the table below (n = 80 for each panel):

Sample	Mean (μIU/mL)	Within Run		Between Run		Between Day		Within Laboratory (Total)	
		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%

b. Linearity/assay reportable range:

Linearity

A high TSH serum pool was created using native samples with known high TSH values. The high TSH serum pool was serially diluted with a low sample TSH pool that was created by ultrafiltration of charcoal adsorbed human serum to create 14 TSH serum pools. All 14 TSH serum pools were assayed four times.

The results are summarized in the table below:

Sample number	Expected concentration (µIU/mL)	Mean concentration (µIU/mL)
1	220.00	227.804
2	127.571	135.220
3	71.531	75.283
4	27.565	27.828
5	10.708	10.450
6	4.101	3.834
7	1.254	1.210
8	0.400	0.394
9	0.160	0.159
10	0.058	0.059
11	0.024	0.021
12	0.012	0.012
13	0.007	0.006
14	0.001	0.001

The linear regression equation obtained was:

$y = 1.03(x) + 0.001$; $R^2 = 0.9962$

The linearity study supports the claimed measuring range of 0.02 to 100 µIU/mL.

Dilution Recovery

Verification studies were performed to determine the sample recovery after a 1:10 dilution is performed either manually or automatically by the LUMIPULSE G1200 system. Several serum samples were spiked with TSH WHO International Standard to target values up to 900 µIU/mL. Each sample was diluted 1:10 manually and onboard the LUMIPULSE G1200 system with the Lumipulse G Specimen Diluent 1. All samples were run in triplicate. The average percent differences for the diluted sample versus the expected concentration was within 10%. The dilution study results support the sponsor's labeling claims that samples with TSH concentrations above the 100 µIU/mL may be diluted 1:10 either manually or on-onboard the analyzer to obtain results up to 1000 µIU/mL.

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

Traceability:

The Lumipulse G TSH-III calibrators 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) provided by the National Institute for Biological Standards and Control.

Reagent Stability:

The shelf life for the Lumipulse G TSH-III Immunoreaction Cartridges is 12 months at 2 -10 °C, and can be stored on-board the LUMIPULSE G1200 System for a maximum of 30 days. The shelf-life stability protocols and acceptance criteria were reviewed and found to be acceptable.

d. Detection limit:

Limit of Blank:

Two panels of zero analyte serum were created by ultrafiltration of charcoal adsorbed human serum. The panels were tested in duplicate using two LUMIPULSE G1200 Instruments and two reagent lots over 15 testing days (n = 60 for each panel and lot combination). The limit of blank was estimated by the 95th percentile of 60 values for each lot. The limit of blank was determined to be 0.001 µIU/mL.

Limit of Detection:

Lumipulse G TSH-III Calibrator 2 Solution Stock was diluted with ultrafiltration charcoal adsorbed human serum to create eight low-level TSH serum pools. Samples were tested using two reagent lots over 15 days of testing (n = 60 for each panel and lot combination). The limit of detection was determined to be 0.002 µIU/mL.

Limit of Quantitation:

The limit of quantitation was determined using eight low-level TSH serum pools. The limit of quantitation was defined as the value at which the between run CV is 20%, and determined to be 0.006 µIU/mL.

The claimed measuring range is 0.02 - 100 µIU/mL.

e. Analytical specificity:

An interference study was conducted to evaluate the effect of endogenous interference substances using the Lumipulse G TSH-III on the LUMIPULSE G1200 system. Three native serum pools containing low (0.5 µIU/mL), medium (2-3 µIU/mL), and high concentrations (66-72 µIU/mL) of TSH were tested by spiking with potential interferents or an equivalent volume of diluent. A significant difference was defined as greater than 10% different in the test and control serum pools.

No significant interferences were observed for the substances and concentrations listed below:

Interferent	Test Concentration
Conjugated Bilirubin	60 mg/dL
Unconjugated Bilirubin	60 mg/dL
Triglycerides (Intralipid)	3000 mg/dL
Hemoglobin	500 mg/dL
Albumin	12 g/dL
Immunoglobulin G	5 g/dL
Biotin	19.7 mg/dL
Cholesterol	500 mg/dL
Uric Acid	24 mg/dL
Rheumatoid factor	1000 IU/mL

Exogenous interference:

The effect on quantitation of analyte in the presence of exogenous interferents was determined by comparing values obtained from samples spiked with drugs into three native human serum pools and tested with the Lumipulse G TSH-III on the LUMIPULSE G1200 system. The TSH analyte concentrations of the three serum pools were approximately 0.5 µIU/mL, 2 - 3 µIU/mL, and 66 - 72 µIU/mL. The sponsor defined non-significant interference as recovery within ±10%.

No significant interferences were observed for the substances and concentrations listed below:

Interferent	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
Carbamazepine	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	0.23 mg/dL
Theophylline	4 mg/dL

Cross-reactivity:

A cross-reactivity study was conducted according to CLSI-EP7-A2 to evaluate the potential cross-reactivity of the assay. Potential cross-reactants were added into test pools, and an equivalent volume of diluent added to control pools. Cross-reactivity was calculated as follows:

% cross-reactivity = [(mean concentration of spiked sample - mean concentration of unspiked sample) / spiked concentration] x 100

The following potentially cross-reacting compounds at the indicated concentrations, tested with TSH concentrations of approximately 0.5 µIU/mL, 2 - 3 µIU/mL, and 66 - 72 µIU/mL, did not interfere with the performance of the device.

Potential Cross-Reactant	Concentration Tested
FSH	5000 mIU/mL
hCG	200000 mIU/mL
hGH	100 ng/mL
LH	1000 mIU/mL

Human Anti-Mouse Antibodies:

To determine the susceptibility of Lumipulse G TSH-III to potential human anti-mouse antibody (HAMA) interference, three native serum pools with low, medium, and high TSH values were spiked with HAMA to a target of 1268 ng/mL or an equivalent volume of diluent. Three replicates of each test and control serum pool were tested. No HAMA interference at a concentration up to 1268 ng/mL was observed.

High Dose Hook Effect:

To determine any hook effect, TSH was spiked into a low TSH serum pool to create target TSH concentrations of at least 5000 µIU/mL. The signal levels of individual replicates of all samples with mean concentrations greater than 100 µIU/mL, up to 5000 µIU/mL of TSH, were higher than signal responses at 100 µIU/mL. The sponsor concluded there was no high dose hook effect when samples up to 5000 µIU/mL were assayed.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      One-hundred and forty-one native serum specimens were tested using the candidate device on the LUMIPULSE G1200 System and the Abbott ARCHITECT TSH assay (predicate device). The results of weighted Deming regression are shown in the table below:

N	Sample Range (µIU/mL)	Slope (95% CI)	Intercept (95% CI)	r
141	0.030 to 89.930	0.9689 (0.9259, 1.0119)	-0.0037 (-0.0064, -0.0010)	0.9838

   b. *Matrix comparison:*

      Not applicable. Only serum samples are recommended for use with this assay.

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:

   Remnant human serum samples from males and females over age 21 were obtained from commercial vendors. Samples were obtained from subjects that were self-reportedly healthy individuals with known TSH values that ranged between 0.3 - 5.0 µIU/mL. Reference ranges were calculated using the central 95% interval (2.5th - 97.5th percentile) according to CLSI EP28-A3c. The reference interval is 0.389 - 3.764 µIU/mL.

N. Proposed Labeling:

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

O. Conclusion:

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