Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
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510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K190702

B Applicant

Fujirebio Diagnostics, Inc.

C Proprietary and Established Names

Lumipulse G whole PTH

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CEW	Class II	21 CFR 862.1545 - Parathyroid Hormone Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Parathyroid hormone (PTH 1-84)

C Type of Test:

Quantitative, chemiluminescent immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

For in vitro diagnostic use

Lumipulse G whole PTH is a Chemiluminescent Enzyme Immunoassay (CLEIA) for the quantitative measurement of PTH (1-84) in human serum and plasma on the LUMIPULSE G System. Measurements of parathyroid hormone levels are used in the differential diagnosis of hypercalcemia and hypocalcemia resulting from disorders of calcium metabolism.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Lumipulse G1200 System

IV Device/System Characteristics:

A Device Description:

Lumipulse G whole PTH is an assay system, including a set of immunoassay reagents and calibrators.

Lumipulse G whole PTH Immunoreaction Cartridges REF 230190
The Lumipulse G whole PTH Immunoreaction Cartridges consists of 3 × 14 tests. Each kit contains the following:

1. Antibody-Coated Particle Solution
   (Liquid when used, 200 µL/Immunoreaction Cartridge).
   Contains 200 µg/mL anti-PTH polyclonal antibodies (goat)-coated ferrite particles, protein stabilizers (bovine and goat) and chemical stabilizers in MES buffer.
   This solution contains gelatin and turns into gel at 15 °C or lower.
   Preservative: ProClin 300

2. Enzyme-Labeled Antibody Solution
   (Liquid, 120 µL/Immunoreaction Cartridge).
   Contains 0.2 µg/mL alkaline phosphatase (ALP: calf)-labeled anti-PTH polyclonal antibody (goat), protein stabilizers (bovine) and chemical stabilizers in MES buffer.
   Preservative: ProClin 300

Lumipulse G whole PTH Calibrators CAL 230206, Liquid 1 x 2 concentrations
Each calibrator kit contains one bottle each of Calibrators 1 and 2. The calibrator kit is packaged separately.

CAL 1: 0 pg/mL whole PTH calibrator (1 × 3.0 mL)
CAL 2: 5000 pg/mL whole PTH calibrator (1 × 1.5 mL)
*Contains ProClin 300 as a preservative in processed human serum.

B Principle of Operation:

Lumipulse G whole PTH is an assay system, including a set of immunoassay reagents and calibrators, for the quantitative measurement of whole parathyroid hormone (whole PTH) in specimens based on Chemiluminescent Enzyme Immunoassay (CLEIA) technology by a one-step sandwich immunoassay method on the LUMIPULSE G System. In the first reaction, alkaline phosphatase (ALP: calf)-labeled anti-PTH polyclonal antibody (goat), PTH in specimens, and anti-PTH polyclonal antibody (goat) - coated ferrite particles specifically bind to form antigen-antibody immunocomplexes. The particles are washed and rinsed to remove unbound materials. The Substrate Solution is then added and mixed with the particles in the enzyme reaction. AMPPD (3-(2'-spiroadmantane)-4-methoxy-4-(3"-phosphoryloxy)phenyl-1,2-dioxetane disodium salt) contained in the Substrate Solution is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Finally, the luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of the dephosphorylated AMPPD. The Luminescent signal is proportional to the amount of whole PTH.

V Substantial Equivalence Information:

A Predicate Device Name(s):

LIASON 1-84 PTH Assay

B Predicate 510(k) Number(s):

K150879

C Comparison with Predicate(s):

Device & Predicate Device(s):	K190702	K150879
Device Trade Name	Lumipulse G whole PTH	LIASON 1-84 PTH Assay
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the quantitative measurement of PTH (1-84) in human serum and plasma. Measurements of parathyroid hormone levels are used in the differential diagnosis of hypercalcemia and hypocalcemia resulting from disorders of calcium. metabolism.	Same
Measured Analyte	Parathyroid Hormone (1-84)	Same

Device & Predicate Device(s):	K190702	K150879
Device Trade Name	Lumipulse G whole PTH	LIASON 1-84 PTH Assay
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the quantitative measurement of PTH (1-84) in human serum and plasma. Measurements of parathyroid hormone levels are used in the differential diagnosis of hypercalcemia and hypocalcemia resulting from disorders of calcium. metabolism.	Same
Classification	Class II	Same
Measuring Range	4.0 - 1800 pg/mL	Same
Product Code	CEW	Same
Regulation	21 CFR § 862.1545	Same
Sample Type	Human serum and plasma (K_2EDTA, Lithium Heparin, and Sodium Heparin)	Same
Antibody	Goat Polyclonal	Same
General Device Characteristic Differences		
Reagent Storage	Store at 2-10°C	Store at 2-8°C
Sample Size	150 µL (for Sample Cups) 300 µL (for Sample Tubes)	150 µL
Instrument	LUMIPULSE G System	LIAISON Analyzer
Methodology	Chemiluminescent Enzyme Immunoassay	Chemiluminescent immunoassay
Calibrators	2 level set (1 vial/level): • Level 1: 0 pg/mL • Level 2: 5000 pg/mL	4 level set (1 vial/level): • Level 1: 10 pg/mL • Level 2: 80 pg/mL • Level 3: 400 pg/mL • Level 4: 1450 pg/mL

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition
- CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A; Statistical Approach; Approved Guideline
- CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition
- CLSI EP14-A2, Evaluation of Matrix Effects; Approved Guideline-Second Edition

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A 20-day, lot-to-lot, and site-to-site precision study were performed in accordance with the CLSI EP05-A3 guideline.

20-Day Precision:
The single-site precision study was conducted by testing a panel of 2 controls and seven samples (panels 1-7) prepared from pooled human serum containing native analyte. The samples were assayed in duplicate per run with 2 runs per day across 20 nonconsecutive days (n=80 for each sample) using one LUMIPULSE G1200 System and one lot of Lumipulse G whole PTH. The results of the precision studies are summarized below:

Sample	Mean (pg/mL) n = 80	Within-Run		Between Run Within Day		Between-Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Control Level 1	38.7	1.10	3%	0.28	1%	0.25	1%	1.16	3%
Control Level 2	291.7	4.62	2%	3.43	1%	2.30	1%	6.19	2%
Serum 1	8.4	0.34	4%	0.00	0%	0.00	0%	0.34	4%
Serum 2	37.2	0.85	2%	0.78	2%	0.00	0%	1.15	3%
Serum 3	84.8	1.72	2%	0.57	1%	0.25	0%	1.83	2%
Serum 4	258.8	5.37	2%	1.90	1%	2.60	1%	6.26	2%
Serum 5	404.7	7.91	2%	5.28	1%	5.41	1%	10.94	3%
Serum 6	813.6	15.35	2%	14.31	2%	9.65	1%	23.10	3%
Serum 7	1385.3	30.80	2%	28.47	2%	12.87	1%	43.88	3%

Lot-to-Lot Precision:
The lot-to-lot study was conducted using 3 lots of Lumipulse G whole PTH (lots A, B, and C). Each lot was tested on a different LUMIPULSE G1200 System (n=3). A panel of 2 controls and 4 samples (panels 1-4) were assayed. Panels 1-4 were prepared from pooled human serum containing native analyte. The samples were tested in duplicate per run with 2 runs per day across 8 nonconsecutive days for a total of 16 precision runs per lot (n=32 replicates per lot). There were 96 replicates per panel across all 3 lots. The results are summarized below:

Sample	Replicates	Mean (pg/mL)	Inter-lot %CV
Control Level 1	96	39.1	4%
Control Level 2	96	293.0	2%
Serum 1	96	8.6	3%
Serum 2	96	38.0	3%
Serum 3	96	86.3	3%
Serum 4	96	261.2	3%

Site-to-Site Precision:
The site-to-site precision study was conducted across 1 internal site and 2 external sites. A panel of 5 pooled human serum samples with native analyte (panels 1-5) were assayed. Each sample was assayed in triplicate at 2 separate times of the day for 5 days using 3 LUMIPULSE G1200 instruments (one per site). Two lots of reagents were utilized for testing, and the data from both 5-day precision studies for Panels 1-5 were combined for the site-to-site analysis. The results of the reproducibility study are presented below:

Sample	Mean (pg/mL)	Between Sites		Between Days		Between Runs		Within Runs		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum 1	8.8	0.4	4.7%	0.1	1.1%	0.2	2.3%	0.3	3.4%	0.6	6.3%
Serum 2	36.8	1.2	3.4%	0.6	1.7%	1.8	4.9%	0.9	2.5%	2.5	6.7%
Serum 3	83.9	2.1	2.5%	0.9	1.0%	3.3	3.9%	2.2	2.6%	4.5	5.4%
Serum 4	254.6	5.3	2.1%	2.7	1.1%	12.3	4.8%	5.0	2.0%	14.5	5.7%
Serum 5	1270.1	39.0	3.1%	0.0	0.0%	44.8	3.5%	21.5	1.7%	63.2	5.0%

2. Linearity:

A linearity study was performed in accordance with the CLSI EP06 guideline. High and low serum sample pools were intermixed to create samples that contained native whole PTH with concentrations that ranged from 1.4 to 2190.3 pg/mL. Each sample was tested in quadruplicate. Data was analyzed by linear regression and the results are summarized below:

$$y = -0.36519 + 1.091572\ x;\ R^2 = 0.9984$$

The results of the linearity study support the claimed measuring range of 4.0 – 1800 pg/mL.

3. Analytical Specificity/Interference:

Cross Reactivity:
A cross-reactivity study was performed in accordance with the CLSI EP07-A2 guideline. Lumipulse G whole PTH on the LUMIPULSE G1200 System was evaluated for cross-reactivity of the assay with other substances that are similar in structure to whole PTH and truncated versions of whole PTH. Three test panels were prepared from pooled human serum containing native analyte. Each panel was split into 2 equal aliquots (test and control samples). Aliquot 1 (test) was spiked with the potential cross-reactant, Aliquot 2 (control) was spiked with an equal volume of solvent used to prepare stock solutions of cross-reactant. Test and control samples were run in triplicate. The acceptance criteria for cross-reactivity

was <0.1%. The % cross-reactivity was calculated for all samples using the following equation:

$$\% \text{ Cross-reactivity} = \frac{(\text{Mean Conc.}_{\text{Test}} (\text{pg/mL}) - \text{Mean Conc.}_{\text{Control}} (\text{pg/mL})) \times 100}{\text{Concentration Cross-reactant (pg/mL)}}$$

No cross reactivity was observed for the tested concentrations of each cross reactant

Cross Reactant	Concentration Tested (pg/mL)	% Cross Reactivity
Calcitonin	500000	< 0.001%
Osteocalcin	500000	< 0.001%
C-Telopeptide (β-crosslaps)	500000	< 0.001%
PTH (7-84)	200000	< 0.002%
PTH (1-34)	200000	< 0.002%
PTH (39-84)	200000	< 0.002%
PTH (39-68)	200000	< 0.002%
PTH (44-68)	200000	< 0.002%
PTH (53-84)	200000	< 0.002%
PTH (13-34)	200000	< 0.002%

Interfering Substances:

An endogenous and exogenous interference study was performed in accordance with the CLSI EP07-A2 guideline. Human serum specimen pools with native analyte were supplemented with potentially interfering compounds at levels listed in the table below. The sponsor defined non-interference as a difference of ≤ 10% from then control sample. The results of the interference study are summarized below:

Endogenous Substances	Highest Conc. Tested that did not interfere
Conjugated Bilirubin	44 mg/dL
Free Bilirubin (unconjugated)	20 mg/dL
Hemoglobin	510 mg/mL
Triglycerides (Intralipid 20% Emulsion)	3440 mg/mL
Cholesterol	503 mg/mL
Human Serum Albumin (Low)	4 g/dL
Human Serum Albumin (High)	12 g/dL
Human Anti-Mouse antibodies (HAMA)	4200 ng/mL
Rheumatoid Factor (RF)	5500 IU/mL
Alkaline Phosphatase	1.5 U/mL

Exogenous Substances	Highest Conc. Tested that did not interfere
Acetaminophen	22 mg/dL
Acetylsalicylic Acid	70 mg/dL
Salicylic Acid	71 mg/dL
Ibuprofen	53 mg/dL
Biotin	0.1 µg/dL
Alendronate	80.65 µg/mL
Etidronate	105 mg/dL
Pamidronate	19 mg/dL
Risedronate	6 mg/dL
Vitamin D2	253 ng/mL
Vitamin D3	289 ng/mL
Calcitrol	1.8 ng/mL
Alfacalcidol	3 µg/mL
Calcium Acetate	41 mg/mL
Magnesium Chloride	40 mg/dL
Aluminium Sulfate	40 mg/dL
Lanthanum Chloride	41 mg/dL
Doxycycline	49.1 µg/mL
Lisinopril	33.9 µg/mL

High Dose Hook Effect:

For Lumipulse G whole PTH on the LUMIPULSE G1200 System, no high dose effect was observed for samples containing approximately 80,000 pg/mL of whole PTH.

4. Assay Reportable Range:

The sponsor claims a measuring range of 4 – 1800 pg/mL. This range was supported by the results from the linearity, precision, limit of detection, and accuracy studies.

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

The Lumipulse G whole PTH (1-84) assay is traceable to the 1st International Standard (NIBSC code: 95/646) (NIBSC).

6. Detection Limit:

The sponsor provided detection limits following CLSI Guideline EP17-A2 guideline.
Limit of Blank (LoB): Four blank samples were tested in replicates of 5 in each run on 2 lot combinations per day for 3 days. Each lot combination was run on one LUMIPULSE G1200 instrument (n=2 total). All panels were tested in one run per day. For each lot combination, there was a total of 60 replicates. To calculate the LoB all blank sample measurement results were sorted from lowest to highest and the 95th percentile value was calculated. The maximum LoB across all lots and instruments was taken as the LoB estimate value. The LoB for Lumipulse G whole PTH on the LUMIPULSE G1200 System was determined to be 0.0 pg/mL.

Limit of Detection (LoD): Four low serum samples were tested in replicates of 5 on 2 lot combinations per day for 3 days. Each lot combination was run on one LUMIPULSE G1200 instrument (n=2 total). All panels were tested in one run per day. For each lot combination, there was a total of 60 replicates. LoD for both lots was determined following the parametric analysis, calculated according to the formula: $LoD = LoB + C_pSD_L$. The LoD for Lumipulse G whole PTH on the LUMIPULSE G1200 System was determined to be 0.295 pg/mL.

Limit of Quantitation (LoQ) Five low level serum samples were tested in replicates of 8 on 2 lot combinations per day for 5 days. Each lot combination was run on one LUMIPULSE G1200 instrument (n=2 total). All panels were tested in one run per day. For each lot combination, there was a total of 200 replicates. LoQ was calculated based on precision profile and defined as the lowest concentration with an imprecision of 10% CV. The LoQ for Lumipulse G whole PTH on the LUMIPULSE G1200 System was determined to be 2.128 pg/mL.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The Lumipulse G whole PTH method comparison study was performed to compare the results obtained from the Lumipulse G whole PTH to the LIAISON® 1-84 PTH assay on a total of 275 human serum samples. The samples tested ranged from 7.2 to 1644.6 pg/mL for Lumipulse G whole PTH for Lumipulse G whole PTH and 6.48 to 1750 pg/mL for LIAISON 1-84 PTH. The data analysis was conducted using the weighted Deming regression method and results are summarized in the following table:

Lumipulse G whole PTH vs. LIASON 1-84 PTH			
n	**Correlation Coefficient (r)**	**Intercept (95% CI)**	**Slope (95% CI)**
275	0.9808	-0.5351 (-1.2821 to 0.2119)	0.9909 (0.9726 to 1.0093)

2. Matrix Comparison:

The matrix comparison study was executed by testing seventy-one (71) matched sets of serum (red top and serum separator tubes (SST)) and plasma (K_2EDTA, sodium heparin and lithium heparin) samples. The results are presented in the following table:

Tube Type	n	Conc. Range (pg/mL)		Slope			Intercept			r
		Min	Max	Est.	Lower 95% CI	Upper 95% CI	Est.	Lower 95% CI	Upper 95% CI	
SST	71	7.2	1531.2	1.0128	0.9884	1.0372	-0.4836	-1.1220	0.1548	0.9995
K_2EDTA	71	5.1	1552.6	1.0117	0.9751	1.0482	-2.7210	-3.7703	-1.6717	0.9993
Lithium Heparin	71	6.5	1446.1	1.0062	0.9807	1.0317	-0.1995	-0.9244	0.5255	0.9984
Sodium Heparin	71	6.5	1487.4	1.0182	0.9783	1.0580	-0.3707	-1.4014	0.6601	0.9980

The study results support the sponsor's claim that human serum and plasma (K2 EDTA, lithium heparin and sodium heparin) are acceptable sample types to be used with this assay.

C Clinical Studies:

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The reference range study testing was conducted in compliance with Good Clinical Practice and 21 CFR parts 50, 56, and 812. A total of 147 serum specimens obtained from an apparently healthy adult population (22-72 years old) were tested using the Lumipulse G whole PTH per CLSI EP28. The observed ranges are listed below:

Group	n	Median (pg/mL)	Range (pg/mL) 5th and 95th Percentile
All	147	15.7	6.9 – 27.4
Apparently Healthy Females	68	16.2	8.7 – 29.7
Apparently Healthy Males	79	15.2	6.6 -23.2

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.