DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

FUJIREBIO DIAGNOSTICS, INC
DIANA DICKSON
DIRECTOR, CLINICAL AND REGULATORY SCIENCE
201 GREAT VALLEY PARKWAY
MALVERN PA 19355

January 12, 2017

Re: K163521
Trade/Device Name: Lumipulse® G LH Calibrators
Regulation Number: 21 CFR 862.1150
Regulation Name: Calibrator
Regulatory Class: II
Product Code: JIT
Dated: December 14, 2016
Received: December 15, 2016

Dear Diana Dickson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

k163521

Device Name

Lumipulse® *G* LH Calibrators

Indications for Use *(Describe)*

Lumipulse *G* LH Calibrators are for in vitro diagnostic use in the calibration of Lumipulse *G* LH on the LUMIPULSE *G* System.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Section 5 510(k) SUMMARY

Lumipulse® ***G*** LH Calibrators

Date: January 6, 2016

510(k) Number: k163521

Submitter: Fujirebio Diagnostics, Inc.
201 Great Valley Parkway
Malvern, PA 19355

Contact Person: Stacey Dolan
Manager, Regulatory Affairs
Phone: (610) 240-3843
Fax: (610) 240-3803
Email: dolans@fdi.com

Device Name: Lumipulse® ***G*** LH Calibrators
Common Name: Human Luteinizing Hormone
Classification: Class II
JIT
75, Clinical Chemistry
21 CFR § 862.1150

Predicate Device: k111023
Abbott Laboratories
Abbott ARCHITECT® LH Calibrators

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:

The Lumipulse® ***G*** LH Calibrator kit contains 2 bottles (1.5mL each) of Lumipulse® ***G*** LH Calibrators 1 and 2. Calibrators 1 and 2 contain luteinizing hormone (LH) in 0.15M sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: sodium azide.

Lumipulse® ***G*** LH Calibrators CAL 230916, Liquid 1x2 concentrations
Each calibrator kit contains one bottle each of Calibrators 1 – 2. The calibrator kit is packaged separately.

CAL 1 0 mIU/mL LH calibrator (1 × 1.5 mL)
CAL 2 250 mIU/mL LH calibrator (1 × 1.5 mL)
*Contains luteinizing hormone (LH) in 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: sodium azide

The Lumipulse® ***G*** LH calibrator set is designed specifically for use on the LUMIPULSE® ***G*** System which has been previously cleared under k142895.

Device Name:
Lumipulse ***G*** LH Calibrators

Device Intended Use:
Lumipulse ***G*** LH Calibrators are for *in vitro* diagnostic use in the calibration of Lumipulse ***G*** LH on the LUMIPULSE ***G*** System.

Device Indications for Use:
Same as Intended Use

Substantial Equivalence:

Comparison between the Lumipulse *G* LH Calibrators and Abbott ARCHITECT LH Calibrators

Similarities and Differences		
Parameter	**Lumipulse *G* LH Calibrators (Proposed Device)**	**Abbott ARCHITECT LH Calibrators (Predicate Device) K111023**
Intended Use	Lumipulse ***G*** LH Calibrators are for *in vitro* diagnostic use in the calibration of Lumipulse ***G*** LH on the LUMIPULSE ***G*** System.	For the calibration of the ARCHITECT *i* System when used for the quantitative determination of human luteinizing hormone (LH) in human serum and plasma.
Analyte	Luteinizing hormone	same
Composition	• Calibrators 1-2: Luteinizing hormone (from human pituitary) • Calibrators 1-2: Diluent: Tris buffer with protein (bovine) and chemical stabilizers • Calibrators 1-2: Preservative: Sodium azide	• Calibrators B-F: Luteinizing hormone (from human pituitary) • Calibrator A-F: Diluent: Phosphate buffer with protein stabilizers (bovine) • Calibrators A-F: Preservatives: ProClin 300, ProClin 950
LH Calibrators	• 2 levels • 0 and 250 mIU/mL human luteinizing hormone	• 6 levels • 0.00, 1.00, 3.50, 15.00, 50.00, 250.00 mIU/mL human luteinizing hormone
Standardization/Traceability	Calibration of the LUMIPULSE ***G*** LH is traceable to in-house reference calibrators, whose	The calibrators are referenced to the World Health Organization

Similarities and Differences		
Parameter	**Lumipulse *G* LH Calibrators (Proposed Device)**	**Abbott ARCHITECT LH Calibrators (Predicate Device) K111023**
	values have been assigned to the 2nd International Standard, 1988 (code: 80/552) provided by the National Institute for Biological Standards and Control (NIBSC).	(WHO) Luteinizing Hormone (LH) Human, Pituitary 2nd International Standard 80/552.

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

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Not applicable.

   b. Linearity/assay reportable range:
   Not applicable.

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

   Traceability

   The calibrators for use with Lumipulse ***G*** LH are prepared gravimetrically and are traceable to the 2nd International Standard, 1988 (code: 80/552) provided by the National Institute for Biological Standards and Control (NIBSC).

   Value Assignment

   LH Antigen Grade is obtained from CLINIQA. A working stock solution is prepared by dissolving LH antigen in 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer. The working stock solution is assigned a provisional value based on the measurement (6 replicates) using Lumipulse ***G*** LH on the LUMIPULSE ***G*** system with secondary calibrators. Lumipulse ***G*** LH Calibrators are made by calculating the amount of working stock solution and 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer required to achieve the desired 250 mIU/mL calibrator value (Lumipulse ***G*** LH Calibrator 2) and adding them together gravimetrically. The 0 mIU/mL calibrator (Lumipulse ***G*** LH Calibrator 1) only contains the 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer. Lumipulse ***G*** LH Calibrator 2 is rate-matched to the respective secondary calibrator based on the measurement in Lumipulse ***G*** LH and adjusted if necessary. The measurement of Lumipulse ***G*** LH calibrators (10 replicates) and secondary calibrators (10 replicates) are performed on three runs on the LUMIPULSE ***G*** system. The mean ratio is the mean counts of the secondary calibrator to the respective Lumipulse ***G*** LH calibrator. The acceptable rate mean ratio for the 3 runs is 0.95 – 1.05. This solution is stored at 2 to 10 °C.

Calibrator	Target Values (mIU/mL)	Target Ranges (mIU/mL)
Level 1	0	N/A
Level 2	250	238 - 262

Stability

Stability of the calibrators is determined by long-term stability study (Tokyo, Japan) using the LUMIPULSE Forte (***f)*** instrument (only sold in Japan). Intended storage and transport stability study is still on-going (Malvern, PA). Based on real-time stability study the sponsor determined that the calibrators have a shelf-life stability of 12 months when stored at 2-10ºC. The sponsor's protocol and acceptance criteria was reviewed and found to be acceptable.

*Note: (The LUMIPULSE ***f*** System uses the same Lumipulse ***G*** LH Immunoreaction Cartridges and Calibrators as the LUMIPULSE ***G***1200 System).

See Section 14 – Sterilization and Shelf Life for more stability study related data and information.

1. Studies conducted at Fujirebio, Inc. (Tokyo, Japan)

Shelf-Life Stability

Three lots of Lumipulse ***G*** LH Calibrators were tested on real-time stability with Lumipulse forte (***f***), a predecessor instrument of LUMIPULSE ***G***1200. LUMIPULSE ***f*** and LUMIPULSE ***G***1200 have a confirmed agreement rate.

Three lots of Lumipulse ***G*** LH Calibrators were stored at 10°C for Month 0, 3, 7 and 13 and tested for sensitivity, accuracy and within-run reproducibility.

The results met the criteria for up to 13 months in the 3 lots of Lumipulse ***G*** LH Calibrators. Thus it was demonstrated that the LUMIPULSE ***G*** LH Calibrators were stable up to 13 months at 10°C on the LUMIPULSE ***f*** System.

- Regarding the sensitivity, 0 and 20 mIU/mL LH solutions were tested at each test point in replicates of 3 and the ratio of the amount of the luminescence ("20 mIU/mL" /"0 mIU/mL" LH) were calculated. The criterion was 20 or higher in the ratio.
- Regarding the accuracy, 3 samples that ranged 5.850-162.217 mIU/mL were tested in replicates of 3 at each time point and the ratios of the measured values to the pre-assigned values were confirmed. The criterion was that the ratios should be within 100 +/- 20% for each replicate.
- Regarding within-run reproducibility, 4 samples that ranged 5.850-162.217 mIU/mL were tested in replicates of 6 at each time point. The criterion for the precision was 10% or lower in the CV for each sample.

Shelf-Life
The shelf life of Lumipulse ***G*** LH Calibrators is 12 months at 2 – 10ºC.

Transport Conditions

The transport simulation stability of Lumipulse ***G*** LH packed for overseas transport was examined in terms of temperature change.

Temperature change: The Lumipulse ***G*** LH Immunoreaction Cartridges, Lumipulse ***G*** LH Calibrators, LUMIPULSE ***G*** Substrate, LUMIPULSE ***G*** Wash Solution and LUMIPULSE ***G*** Specimen Diluent 1 were subjected to the following temperature stress: 37 °C 48 +/- 2 hours → -20 °C 48 +/- 2 hours → 30 °C 96 +/- 4 hours → 4 °C 24 +/- 2 hours, according to the stress condition in the internal protocol. Then a visual inspection was carried out for the Lumipulse ***G*** LH Cartridges and it was confirmed that they cleared the criteria. Also a sensitivity test and accuracy test were conducted and compared with the intended condition (control). The sensitivity testing was conducted with 0 and 2 mIU/mL LH solutions and the criterion was the ratio of the amount of luminescence ("2 mIU/mL" / "0 mIU/mL" LH) to be 21 or higher. The accuracy testing was conducted with 3 control samples (concentration: 4.1-55.6 mIU/mL with LUMIPULSE ***G***1200) and 4 serum samples (concentration: 11.1-294.0 mIU/mL with LUMIPULSE ***G***1200) in replicates of 1 for control samples and 2 for the serum samples with LUMIPULSE ***G***1200, and the criteria of each value after the stress were 100 +/- 20% of the reference value of each serum sample.

The results of the sensitivity test and accuracy met the criteria. Therefore, the temperature change described above did not affect the performance of Lumipulse ***G*** LH using the LUMIPULSE ***G***1200 System.

Lumipulse ***G*** LH Calibrators are shipped at 2-10°C.

2. Studies conducted at Fujirebio Diagnostics, Inc. (Malvern, PA)

Real Time (Intended Storage and Open Use)

Real-time (Intended Storage and open use) stability is being evaluated as follows:
In the on-going real-time stability study, the Lumipulse ***G*** LH calibrators are stored at 2-10ºC. The LH calibrators are tested on one Lumipulse ***G***1200 instrument in duplicate at specified intervals over the shelf life of the device up to the planned shelf life plus one month (13 months).

Real-time intended storage stability is calculated based on the percent difference for the panels at each time point when compared to the value received at Time Point 0 (study initiation). The mean concentration of each panel from each time point must be within ±10% mean concentration at Study Initiation. The % CV value of each panel at each time point must be ≤ 10%. For all 3 lots, Time Point 2 (6 months) was the second time point for testing. The Lumipulse ***G*** LH Calibrators were determined to be stable at the intended storage conditions for up to 6 months for all 3 lots.

The testing will continue with this stability protocol until data to support a claim of 12 months is achieved.

Transport Simulation Stability Study
Transport simulation of the Lumipulse ***G*** LH calibrators was examined in terms of temperature. For the temperature test, the calibrators were stored in the following condition: 37 °C 24±2 hours → 25 °C 24±2 hours → -20 °C 24±2 hours → 6 °C 24±2 hours. To determine the impact of temperature on the Lumipulse ***G*** LH Calibrators, a performance analysis was conducted.

After each stress condition, all Lumipulse ***G*** LH ICs and Lumipulse ***G*** LH Calibrators were moved to the next cycle temperature. After all cycles were complete, a visual inspection was performed and the Lumipulse ***G*** LH calibrators were stored at the intended storage condition of 2-10ºC. Stressed Lumipulse ***G*** LH IC's and Calibrators were tested within 3 calendar days after the completion of all cycles. Calibrators were tested in duplicate, controls in replicates of 1 and panels in replicates of 3.

At study initiation, the assay met the acceptance criteria of %CV ≤10% for all transport conditions tested. This stability study is still ongoing.

Transport Conditions
Lumipulse ***G*** LH Calibrators are shipped at 2-10°C.

d. Detection limit:
Not applicable.

e. Analytical specificity:
Not applicable

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method Comparison with predicate device:
Not applicable.

b. Method Comparison
Not applicable.

c. *Matrix Comparison*
Not applicable.

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**:**
Not applicable.

Proposed Labeling

The labeling satisfies the requirements of 21 CFR Part 809.10.

Standard/Guidance Document Referenced:

- ISO 17511:2003 Measurement of Quantities in Biological Samples - Metrological Traceability of Values Assigned to Calibrator and Control Materials
- CLSI EP25-A – Evaluation of Stability of *In Vitro* Diagnostic Reagents: Approved Guideline
- 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)
- Guidance Document - Guidance for Industry - Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators; Final

Conclusion

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