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: K163544
Trade/Device Name: Lumipulse® G Prolactin
Regulation Number: 21 CFR 862.1150
Regulation Name: Calibrator
Regulatory Class: II
Product Code: JIT
Dated: December 15, 2016
Received: December 16, 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)*

k163544

Device Name
Lumipulse® *G* Prolactin

Indications for Use *(Describe)*
Lumipulse *G* Prolactin Calibrators

Lumipulse *G* Prolactin Calibrators are for in vitro diagnostic use in the calibration of Lumipulse *G* Prolactin 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*** Prolactin

Date: January 6, 2017

510(k) Number: k163544

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*** Prolactin Calibrators
Classification: Class II
JIT
75, Clinical Chemistry
21 CFR § 862.1150

Predicate Device: k052982
ROCHE DIAGNOSTICS
Cobas Elecsys Prolactin II Calset

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

Lumipulse® ***G*** Prolactin Calibrators CAL 230954, Liquid 1x2 concentrations
Each calibrator kit contains one bottle each of Calibrators 1 – 2. The calibrator kit is packaged separately.

CAL 1 0 ng/mL Prolactin calibrator (1 × 1.5 mL)
CAL 2 400 ng/mL Prolactin calibrator (1 × 1.5 mL)
* Contains prolactin in 0.15 M sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: sodium azide.

Device Name:
Lumipulse ***G*** Prolactin Calibrators

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

Device Indications for Use:
Same as Intended Use

Substantial Equivalence:

Comparison between the Lumipulse *G* Prolactin Calibrators and Roche Diagnostics Cobas Elecsys Prolactin II Calset

Calibrator Set		
Similarities and Differences		
Parameter	**Lumipulse *G* Prolactin (Proposed Device)**	**Cobas Elecsys Prolactin II Calset (Predicate Device) K052982**
Intended Use	Lumipulse ***G*** Prolactin Calibrators are for *in vitro* diagnostic use in the calibration of Lumipulse ***G*** Prolactin on the LUMIPULSE ***G*** System.	Elecsys Prolactin II CalSet is used for calibrating the quantitative Elecsys Prolactin II assay on the Elecsys immunoassay systems.
Instrument System	LUMIPULSE ***G*** System	Elecsys and **cobas e** immunoassay analyzers
Analyte	Prolactin	Same
Number of Calibrators	2 calibrators	Same
Standardization/Traceability	The calibrators for use with Lumipulse ***G*** Prolactin are prepared gravimetrically and are traceable to the 3rd International Standard, 1988 (code: 84/500) provided by the National Institute for Biological Standards and Control (NIBSC).	The assay is standardized using the 3rd IRP WHO Reference Standard 84/500
Level	• 2 levels 0 ng/mL and 400 ng/mL	• 2 levels • Low: approx. 2 µIU/mL • High: approx. 2,000 µIU/mL
Form	Liquid – ready to use	Same
Matrix	Sodium chloride in Tris buffer with protein stabilizer (bovine). Preservative: sodium azide.	Buffered equine serum

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*** Prolactin are prepared gravimetrically and are traceable to the 3rd International Standard, 1988 (code: 84/500) provided by the National Institute for Biological Standards and Control (NIBSC).

   Value Assignment

   Prolactin Antigen Grade is obtained from CLINIQA. The working stock solution is prepared by dissolving Prolactin antigen in 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer. The working stock solution is assigned a provision value based on the measurement using LUMIPULSE ***G*** Prolactin on the LUMIPULSE ***G*** System with secondary calibrators. Lumipulse ***G*** Prolactin 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 400 ng/mL calibrator value (Lumipulse ***G*** Prolactin Calibrator 2) and adding them together gravimetrically. The 0 ng/mL Calibrator (Lumipulse ***G*** Prolactin Calibrator 1) only contains the 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer. Lumipulse ***G*** Prolactin Calibrator 2 is rate-matched to the respective secondary calibrator based on the measurement in Lumipulse ***G*** Prolactin and adjusted if necessary. The measurement of Lumipulse ***G*** Prolactin Calibrators (10 replicates) and secondary calibrators (10 replicates) are performed on 3 runs using the LUMIPULSE ***G*** System. The mean ratio is the mean counts of the secondary calibrator to the respective Lumipulse ***G*** Prolactin Calibrator. The acceptable rate mean ratio is 0.95 – 1.05. This solution is stored at 2 to 10 °C.

Calibrator	Target Values (ng/mL)	Target Range (ng/mL)
Cal 1	0 ng/mL	N/A
Cal 2	400 ng/mL	380 – 420 ng/mL

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 accelerated 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*** Prolactin Immunoreaction Cartridges and Calibrators as the LUMIPULSE ***G***1200 System)

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

1.1 Long-term stability

The long-term stability data were obtained on the LUMIPULSE G System by measuring the Prolactin calibrators and samples for 3 lots of reagents that were stored at 10°C for 0, 3, 7, and 13 months. Sensitivity, specificity and reproducibility were calculated.

The results of sensitivity, accuracy and reproducibility confirmed that in a 13-month test, standards were met and the product passed. Therefore, the shelf life of the Lumipulse ***G*** Prolactin Calibrators stored at 2-10°C for 12 months was confirmed.

1.2 Transport Simulation

Transportation Testing (Temperature Stress Testing) data were obtained by stressing reagents, calibrator (standard solution), substrate solution, wash solution, and diluent under the following conditions: 37°C, 48 hours ± 2 hours → -20°C, 48 hours ± 2 hours → 30°C, 96 hours ± 4 hours→ storage conditions (4°C), 24 hours ± 2 hours. Sensitivity, accuracy, and visual inspection were performed.

Visual assessment of 5 items was 0/28 under control conditions and 0/28 under stress conditions, thus meeting the specification. Sensitivity was 162 under control conditions and 171 under stress conditions, in each case meeting the S/N≥51 specification. Accuracy (versus test values) was 95-101% under control conditions and 99-109% under stress conditions, in each case meeting the specification for "within 100 ± 20%."Therefore, the results of sensitivity, accuracy, and visual inspection all met specification.

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

2.1 Real Time (Intended Storage) Stability

Real-time (Intended Storage) stability is being evaluated as follows:
In the on-going real-time stability study, the Lumipulse ***G*** Prolactin calibrators are stored at 2-10°C. The Prolactin calibrators are tested 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).

Time Point 2 (Month 6) was the second time point for testing. The Lumipulse ***G*** Prolactin 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.

2.2 Transport Simulation Stability Study

Transport simulation of the Lumipulse ***G*** Prolactin calibrators was examined in terms of temperature. For the temperature test, the calibrators were stored in the following condition: 37°C ± 2°C 24±2 hours → 25°C ± 2°C 24±2 hours → -20°C ± 10°C 24±2 hours → 6°C ± 4°C 24±2 hours. To determine the impact of temperature on the Lumipulse ***G*** prolactin Calibrators, a performance analysis was conducted.

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

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

Shelf life

The shelf life for Lumipulse ***G*** Prolactin Calibrators is 12 months at 2–10°C, based on the long-term stability study conducted at Fujirebio Inc. and the Real Time Stability study conducted at Fujirebio Diagnostics, Inc..

Transport Conditions

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

2.3 Open-vial (In-Use) Stability

Open-vial (In-use) stability is being evaluated as follows:
In the on-going open-vial stability study (included in the real-time stability study), the Lumipulse ***G*** Prolactin calibrators are stored at 2-10°C and both calibrators were opened and then closed at the start of the study (Time Point). The Prolactin calibrators are tested in duplicate at specified intervals (6 months and 12 months) over the shelf life of the device up to the planned shelf life plus one month (13 months).

Open-vial (in-use) 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%.

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

d. Detection limit:
Not applicable.

e. Analytical specificity:
Not applicable.

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method Comparison:
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 Labelling

The labelling 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 (February 22, 1999)

Conclusion

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