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

January 13, 2017

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

Re: K163534
Trade/Device Name: Lumipulse® **G** FSH-N Calibrators
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 Dickerson:

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,

Courtney H. Lias -S

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)*

k163534

Device Name
Lumipulse® *G* FSH-N Calibrators

Indications for Use *(Describe)*

Lumipulse *G* FSH-N Calibrators are for in vitro diagnostic use in the calibration of Lumipulse *G* FSH-N 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.

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Section 5 510(k) SUMMARY

Lumipulse® ***G*** FSH-N Calibrators

Date: January 9, 2017

510(k) Number: k163534

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*** FSH-N Calibrators
Classification: Class II
JIT
75, Clinical Chemistry
21 CFR § 862.1150

Predicate Device: k012399
Roche Diagnostics Corporation
Elecsys FSH-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:

Master calibration data are recorded in a two-dimensional bar code on the Lumipulse ***G*** FSH-N Immunoreaction Cartridge case. The calibration curve is created based on recorded master calibration data and the calibration data. The follicle-stimulating hormone (FSH) concentration of a specimen is automatically calculated from the calibration curve. The result of the calculation is reported in mIU/mL.

Lumipulse® ***G*** FSH-N Calibrators:

Lumipulse® ***G*** FSH-N Calibrators REF 230930
Each calibrator kit contains one bottle each of calibrators 1 – 2 and consists of the following:

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

Device Intended Use:

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

Device Indications for Use:
Same as Intended Use

Substantial Equivalence:

Comparison between the Lumipulse *G* FSH-N Calibrators and Roche Diagnostics Corporation, Elecsys FSH-II CalSet

Calibrator Set		
Similarities and Differences		
Parameter	**Lumipulse *G* FSH-N Calibrators (Proposed Device)**	**Elecsys FSH-II CalSet (Predicate Device) K012399**
Format	Liquid; Ready for use	Lyophilized
Matrix	Tris buffer with bovine stabilizer	Human serum with added human FSH
Levels	Two levels	Two levels
Intended Use	Lumipulse ***G*** FSH-N Calibrators are for *in vitro* diagnostic use in the calibration of Lumipulse ***G*** FSH-N on the LUMIPULSE ***G*** System.	Elecsys FSH II CalSet used for calibrating the quantitative Elecsys FSH assay on the Elecsys and cobas e immunoassay analyzers.
Stability	Stable at 2-10ºC until expired	Stable at 2-8ºC until expired

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*** FSH-N are prepared gravimetrically and are traceable to the 1st International Standard, 1997 (code 92/510) provided by the National Institute for Biological Standards and Control (NIBSC).

Value Assignment

FSH, Antigen Grade, is obtained from CLINIQA. The 1st stock solution (working stock solution) is prepared by dissolving FSH antigen in 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer and then assigned a provisional value based on the measurement in the Lumipulse ***G*** FSH-N assay by device of LUMIPULSE ***G*** with calibration of secondary calibrators. The calibrator levels 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 teritary 250 mIU/mL calibrator value and adding them together gravimetrically. The 0 mIU/mL Calibrator (Calibrator 1) is just the 2-amino-2-hydroxymethyl-1,3-propandiol-based buffer. The tertiary 250 mIU/mL calibrator is rate-matched to the respective secondary calibrator based on the measurement in the Lumipulse ***G*** FSH-N assay and adjusted if necessary. The measurement of tertiary calibrators (each 10 replicates) and secondary calibrators (each 10 replicates) are performed by device of LUMIPULSE ***G*** at 3 times. The mean ratio is the mean counts of the secondary calibrator (10 replicates) to the respective tertiary calibrator (10 replicates). The acceptable rate mean ratio is 0.97 – 1.03. This solution is stored at 2 to 10 °C.

2. Stability

Long-term stability conducted at Fujirebio, Inc. (Tokyo, Japan)

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. Real-time stability studies for shelf-life and open-vial claims have been conducted and acceptance criteria were met.

*Note: (The LUMIPULSE ***f*** System uses the same Lumipulse ***G*** FSH-N Calibrators as the LUMIPULSE ***G***1200 System)

Long-term stability

The long-term stability data were obtained on the LUMIPULSE ***f*** System by measuring the Lumipulse ***G*** FSH Calibrators (3 Lots) and samples in replicates of 2 using Lumipulse ***G*** FSH Immunoreaction Cartridges (3 Lots) that were stored at 10°C after 0, 3, 7, and 13 months. Sensitivity, accuracy and reproducibility were calculated.

Sensitivity

FSH solutions of 0 and 2 mIU/mL were measured in replicates of 3 at each test point and the luminescence ratio (2 mIU/mL / 0 mIU/mL FSH) were calculated. The results met the criterion of the ratio of ≥20.

Accuracy

3 serum samples ranged (10.5 – 185.0 mIU/mL) were tested in replicates of 3, measurements at each time point and the variation of ratios against the assigned values were calculated. The results met the criterion within ± 20% for each replicate.

Reproducibility

3 serum samples ranged (10.5 – 185.0 mIU/mL) were tested in replicates of 6 measurements and CVs of measured values at each time point were calculated. The results met the criterion of 10% CV or less for each sample.

The results of sensitivity, accuracy and reproducibility confirmed that all long-term stability performance up to 13 months met the criteria. Therefore, the shelf life of the Lumipulse ***G*** FSH-N Calibrators stored at 2-10°C for 12 months was confirmed.

Real Time (Intended Storage) Stability Studies conducted at Fujirebio Diagnostics, Inc. (Malvern, PA)

Real-time (Intended Storage) stability is being evaluated as follows:
In the on-going real-time stability study, the Lumipulse ***G*** FSH-N calibrators are stored at 2-10ºC. The FSH-N calibrators are tested in duplicate at Month 0 (study initiation), 6, 12 and 13 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. For all 3 lots, time Point 2 (month 6) was the second time point for testing and the acceptance criteria was met.

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

Open-Vial (in-use) Stability Studies conducted at Fujirebio Diagnostics, Inc. (Malvern, PA)

Open-Vial (in-use) stability is being evaluated as follows:
In the on-going real-time stability study, the Lumipulse ***G*** FSH-N calibrators are stored at 2-10ºC. The FSH-N calibrators are tested in duplicate at Month 0 (study initiation), 6, 12, and 13 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. For all 3 lots, time Point 2 (month 6) was the second time point for testing and the acceptance criteria was met.

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

Transport Simulation

a. Transport Simulation study conducted at Fujirebio, Inc. (Tokyo, Japan)

The transport simulation stability of the Lumipulse ***G*** FSH-N Calibrators that are packed for overseas transportation was examined in terms of temperature.

For the temperature test, the calibrators were stored in the following condition: 37 °C 48±2 hours → -20 °C 48±2 hours → 30 °C 96±4 hours → 4 °C 24±2 hours.

To determine the impact of temperature on the Lumipulse ***G*** FSH-N Calibrators, a performance analysis was conducted.

The performance analysis calculated sensitivity and accuracy. For sensitivity, the luminescence ratio (FSH-N calibrator 2 / FSH-N calibrator 1) was calculated. The criterion was a ratio greater than or equal to 21. For accuracy, the variation for each calibrator was calculated using the ratio of the measured values (n=1) against the assigned values. The criterion was ratios within 100±20%.

The luminescence ratio was 90 under control conditions and 87 under stress conditions and met the criteria of ≥ 10. The accuracy ranged from 99-108% under control conditions and 96-104% under stress conditions and met the criteria of 100±20%.

The results of the performance analysis confirmed that all stability criteria for transport simulation tests were met. Therefore, the temperature stress used in the test had no impact on the Lumipulse ***G*** FSH-N.

b. Transport Simulation Stability Study Studies conducted at Fujirebio Diagnostics, Inc. (Malvern, PA)

Transport simulation of the Lumipulse ***G*** FSH-N 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*** FSH-N Calibrators, a performance analysis was conducted.

After each stress condition, all Lumipulse ***G*** FSH-N ICs and Lumipulse ***G*** FSH-N Calibrators were moved to the next cycle temperature. After all cycles were complete, a visual inspection was performed and the Lumipulse ***G*** FSH-N calibrators were stored at the intended storage condition of 2-10ºC. Stressed Lumipulse ***G*** FSH-N 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. The stability study is still ongoing.

Shelf life

The shelf life for Lumipulse ***G*** FSH-N Calibrators is 12 months at 2–10°C.

Transport conditions

Lumipulse ***G*** FSH-N 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:
Not applicable.

e. Analytical specificity:
Not applicable.

f. Assay cut-off:
Not applicable.

1 Comparison studies:
Not applicable.

a. Method Comparison
Not applicable.

b. *Matrix Comparison*
Not applicable.

2 Clinical studies:
Not applicable.

a. Clinical sensitivity:
Not applicable

b. Clinical specificity:
Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):
Not applicable

3 Clinical cut-off**:**
Not applicable.

4 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.