DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

January 13, 2017

FUJIREBIO DIAGNOSTICS, INC.
STACEY DOLAN
MANAGER, REGULATORY AFFAIRS
201 GREAT VALLEY PARKWAY
MALVERN PA 19355

Re: K163546
Trade/Device Name: Lumipulse® **G** Progesterone-N
Regulation Number: 21 CFR 862.1150
Regulation Name: Calibrator
Regulatory Class: II
Product Code: JIT
Dated: December 15, 2016
Received: December 16, 2016

Dear Stacey Dolan:

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)*
k163546

Device Name
Lumipulse® G Progesterone-N

Indications for Use *(Describe)*
Lumipulse G Progesterone-N Calibrators

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

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

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Section 5 510(k) SUMMARY

Lumipulse® ***G*** Progesterone-N

Date: January 9, 2017

510(k) Number: k163546

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

Predicate Device: k152526
ROCHE DIAGNOSTICS
Elecsys Progesterone III 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*** Progesterone-N Calibrator kit contains 3 bottles (1.5 mL each) of Lumipulse ***G*** Progesterone-N Calibrators 1, 2, and 3. Calibrators 1, 2, and 3 contain progesterone in 0.15 M sodium chloride in MES buffer with protein (bovine) and chemical stabilizers. Preservative: sodium azide.

Lumipulse ***G*** Progesterone-N Calibrators CAL 230893, Liquid 1x3 concentrations
Each calibrator kit contains one bottle each of Calibrators 1 – 3. The calibrator kit is packaged separately.

CAL 1	0 ng/mL Progesterone calibrator (1 × 1.5 mL)
CAL 2	0.5 ng/mL Progesterone calibrator (1 × 1.5 mL)
CAL 3	40 ng/mL Progesterone calibrator (1 × 1.5 mL)

*Contains progesterone in 0.15 M sodium chloride in MES buffer with protein (bovine) and chemical stabilizers. Preservative: sodium azide.

Device Intended Use:

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

Device Indications for Use:
Same as Intended Use

Substantial Equivalence:

Comparison between the Lumipulse *G* Progesterone-N Calibrators and Roche Diagnostics Elecsys Progesterone II CalSet

Calibrator Set		
Similarities and Differences		
Parameter	**Lumipulse *G* Progesterone-N (Proposed Device)**	**Elecsys Progesterone II CalSet (Predicate Device) K152526**
Intended Use	Lumipulse ***G*** Progesterone-N Calibrators are for *in vitro* diagnostic use in the calibration of Lumipulse ***G*** Progesterone-N on the LUMIPULSE ***G*** System.	Progesterone III CalSet is used for calibrating the quantitative Elecsys Progesterone III assay on the Elecsys and **cobas e** immunoassay analyzers.
Instrument System	LUMIPULSE ***G*** System	Elecsys and **cobas e** immunoassay analyzers
Analyte	Progesterone	Same
Number of Calibrators	3 calibrators	2 calibrators
Standardization/Traceability	Calibration of the LUMIPULSE ***G*** Progesterone-N are prepared gravimetrically and are traceable to ERM-DA347 and BCR-348R by IRMM (Institute for Reference Materials and Meausrements)	The assay is traceable via ID-GC/MS (isotope dilution gas chromatography/mass spectrometry) to highly purified progesterone by weight analogous to BCR-348R and ERM-DA347.
Level	• 3 levels of 0 ng/mL, 0.5 ng/mL-40 ng/mL	• 2 levels 0.080 ng/mL-53 ng/mL • Concentrations are lot specific
Form	Liquid – ready to use	Same
Matrix	Sodium chloride in MES buffer with protein (bovine) and chemical stabilizers. Preservative: sodium azide.	Human 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*** Progesterone-N are prepared gravimetrically and are traceable to ERM-DA347 and BCR-348R by IRMM (Institute for Reference Materials and Measurements).

   Value Assignment
   Progesterone, ≥ 99 % is obtained from SIGMA-ALDRICH. The Progesterone solution was prepared by dissolving Progesterone, ≥ 99 % in ethanol. The Progesterone solution is spiked into 2-Morpholinoethanesulfonic acid-based buffer and then assigned a provisional value based on the measurement in the Lumipulse ***G*** Progesterone-N assay. The mean value (6 replicates) by LUMIPULSE ***G*** was assigned a provisional value. This solution is used as 1st stock solution (working stock solution). The calibrator levels are made by calculating the amount of working stock solution and 2-Morpholinoethanesulfonic acid-based buffer required to achieve the desired tertiary 40 ng/mL calibrator value and adding them together gravimetrically. Dilutions are made gravimetrically using one part of the tertiary 40 ng/mL calibrator and 2-Morpholinoethanesulfonic acid-based buffer to obtain secondary 0.5 ng/mL calibrator. The 0 ng/mL Calibrator (Calibrator 1) is just the 2-Morpholinoethanesulfonic acid-based buffer. These tertiary calibrators are rate-matched to the respective secondary calibrator based on the measurement in the Lumipulse ***G*** Progesterone-N assay and adjusted if necessary. The measurement of tertiary calibrators (10 replicates) and secondary calibrators (10 replicates) are performed 3 runs each using LUMIPULSE ***G***. The mean ratio is the mean counts of each primary calibrator (10 replicates) to the respective original calibrators (10 replicates). The acceptable rate mean ratio is 0.95 – 1.05. This is the assigned value. This solution is stored at 2 to 10 °C.

2. Stability

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

   The long-term stability data were obtained on the LUMIPULSE G1200 System by measuring the Progesterone-N calibrators and samples for 3 lots of reagents that were

stored at 10°C for 0, 1, 2, 3, 6, 9 months. Sensitivity, accuracy and reproducibility were calculated.

Sensitivity
Lumipulse ***G*** Progesterone-N Calibrator 1 and Lumipulse ***G*** Progesterone-N Calibrator 2 in duplicate at each test point and the luminescence ratio (Progesterone-N calibrator 1/ Progesterone-N calibrator 2) were calculated. The results met the criterion of the ratio of 1.2 or greater.

Accuracy
3 samples of serum (3.15 - 24.42 ng/mL) were tested in replicates of 6, measurements at each time point and the variation of the measured values to the assigned values were calculated. The results met the criterion within 100 ± 20% for each replicate.

Reproducibility
3 samples (3.15 - 24.42 ng/mL) were tested in replicates of 6 and CVs of measured values at each time point were calculated. The results met the criterion of 15% or less for each sample.

The results of sensitivity, accuracy and reproducibility confirmed that all long-term stability performance up to 9 months met the criteria. Therefore, the shelf life of the Lumipulse ***G*** Progesterone-N Calibrators stored at 2-10°C for 9 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*** Progesterone-N calibrators are stored at 2-10°C. The Progesterone-N calibrators are tested in duplicate at specified intervals of 4 months and 9 months over the shelf life of the device up to the planned shelf life plus one month (10 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 4) was the second time point for testing. The Lumipulse ***G*** Progesterone-N calibrators were determined to be stable at the intended storage conditions for up to 4 months for all 3 lots; therefore acceptance criteria were met.

The testing will continue with this stability protocol until data to support a claim of 9 months is achieved.

The shelf life for Lumipulse ***G*** Progesterone-N Calibrators is 9 months at 2–10°C.

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 open-vial stability study(included in the real-time stability study), the Lumipulse ***G*** Progesterone-N calibrators are stored at 2-10°C and all 3 calibrators were opened and closed at the start of the study. (Time Point). The Progesterone-N calibrators are tested in duplicate at specified intervals of 4 months and 9 months over the shelf life of the device up to the planned shelf life plus one month (10 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).

Time Point 2 (Month 4) was the second time point for testing. Acceptance criteria were met for this time point. The testing will continue with this stability protocol until data to support a claim of 9 months is achieved.

Transport Simulation

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

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

For the temperature test, the calibrators were stressed at the following conditions: 37 °C 48±2 hours (Cumulative Interval 2 days) → -20 °C 48±2 hours (Cumulative Interval 4 days) → 30 °C 96±2 hours (Cumulative Interval 8 days) → 4 °C 24±2 hours (Cumulative Interval 9 days).

To determine the impact of temperature on the Lumipulse ***G*** Progesterone-N Calibrators, a performance analysis was conducted. The concentration of the panel replicates were determined by using the calibration curve generated for each condition.

The performance analysis calculated sensitivity and accuracy. For sensitivity, the luminescence ratio (Progesterone-N calibrator 1 / Progesterone-N calibrator 2) was calculated. The criterion was a ratio greater than or equal to 1.2. The accuracy of each panel was the acceptance criteria of variation within 100±20%.

The luminescence ratio was 1.6 and met the criteria of ≥ 1.2. The accuracy ranged from 86-120% 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*** Progesterone-N.

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

Transport simulation of the Lumipulse ***G*** Progesterone-N 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 ± 2°C 24±2 hours → 6°C ± 2°C 24±2 hours. To determine the impact of temperature on the Lumipulse ***G*** Progesterone-N Calibrators, a performance analysis was conducted.

After each stress condition, all Lumipulse ***G*** Progesterone-N ICs and Lumipulse ***G*** Progesterone-N Calibrators were moved to the next cycle temperature. After all cycles were complete, a visual inspection was performed and the Lumipulse ***G*** Progesterone-N calibrators were stored at the intended storage condition of 2-10ºC. Stressed Lumipulse ***G*** Progesterone-N 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 and the appearance of the IC met the visual inspection criteria. At 4 months, the mean concentration of each panel was within ± 10% of the mean concentration at Study Initiation for all transport conditions tested. The assay met the acceptance criteria of %CV ≤ 10% for all transport conditions tested and the appearance of the IC met the visual inspection criteria. The stability study is ongoing.

Lumipulse ***G*** Progesterone-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.

3. Comparison studies:

a. Method Comparison:
Not applicable.

b. Method Comparison:

Not applicable.

c. *Matrix Comparison:*
Not applicable.

4. 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.

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

6. 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.