February 27, 2020

MFB Fertility, Inc.
℅ Mary Vater
Quality & Regulatory Consultant
Medical Device Academy, Inc.
345 Lincoln Hill Rd.
Shrewsbury, VT 05738

Re: K191462
Trade/Device Name: Proov Test
Regulation Number: 21 CFR 862.1620
Regulation Name: Progesterone Test System
Regulatory Class: Class I, meets the limitation to the exemption 21 CFR 862.9(a) and 862.9(b)
Product Code: QKE
Dated: January 22, 2020
Received: January 23, 2020

Dear Mary Vater:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Acting Deputy Director
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K191462

Device Name
Proov Test

Indications for Use *(Describe)*
Proov test is intended for the detection of pregnanediol glucuronide (PdG, the major urine metabolite of progesterone) in urine and can be used as an aid for confirmation of ovulation.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR §807.92:

I. Submitter

MFB Fertility Inc.
1630A 30th Street PMB 143
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Tel: +1-720-507-6699
Sponsor Person: Amy Beckely
Email: Amy@mfbfertility.com
Date Prepared: February 24, 2020

II. Contact

Mary Vater, Medical Device Academy, Inc.
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Shrewsbury, Vermont, 05738, USA
Tel: +1.523.6988
Email: mary@fdaecopy.com

III. Device

510(k) Number:	K191462
Name of Device:	Proov Test
Classification Name:	Progesterone Test System
Regulation:	21 CFR §862.1620
Regulatory Class:	Class I
Classification Code:	QKE

IV. Predicate Device

510(k) Number:	K040923
Device Name:	IBL Progesterone LIA Test
Manufacturer:	IBL GMBH

V. Device Description

The Proov Test is intended for measuring pregnanediol glucuronide (PdG) in first morning urine during the luteal phase of the monthly female reproductive cycle. The Proov Test is a disposable lateral flow test strip, consisting of a test area and control area. The urine sample is applied to the strip by dipping. The sample moves by lateral flow into the test area, and then the control area. The test area has PdG-specific reagents impregnated on it to detect the present of PdG in the urine. The control area has antibodies impregnated to be used as internal control for proper assay function. The test strip is intended for use outside the body (in vitro diagnostic use) and provides qualitative results with a single red line indicating a positive result for PdG and two red lines indicating a negative result for PdG in urine. Women can use Proov Test at multiple times during their menstrual cycle to confirm ovulation.

VI. Indications for Use

Proov test is intended for the detection of pregnanediol glucuronide (PdG, the major urine metabolite of progesterone) in urine and can be used as an aid for confirmation of ovulation.

VII. Comparison of Technological Characteristics with the Predicate Device

The following characteristics were compared between the subject device and the predicate device in order to demonstrate substantial equivalence:

- Indications for Use – The predicate and subject devices intended for the purposes of ovulation confirmation.
- Materials – The Proov Test is an IVD made of materials commonly found in lateral flow IVD devices. Biocompatibility is not of concern for IVD devices.
- Design – The subject device has the same technological characteristics as the use of the competition principle and use of antigen to compete for the binding site of the targeted antibody.
- Energy Source – The subject device is an analog IVD device and therefore no energy source is needed.
- Performance Testing – Analytical testing was performed on the subject device to demonstrate that the Proov Test accurately and reproducibly measures PdG.
- Clinical Testing - Clinical testing was performed on the subject device to demonstrate that the Proov Test accurately confirms ovulation and that users are able to reach accurate conclusions when compared to expert analysis of the test results.

	Proov Test (Subject Device)	**IBL Progesterone LIA Test**	**Comments on Substantial Equivalence**
Indications for Use	Proov test is intended for the detection of pregnanediol glucuronide (PDG, the major urine metabolite of progesterone) in urine and can be used as an aid for confirmation of ovulation.	Luminescence immunoassay for the in vitro diagnostic quantitative measurement of active free progesterone (a female hormone) in saliva. Measurements obtained by this device may be used in the diagnosis and treatment of disorders of the ovaries and can be used as an aid for confirmation of ovulation.	The devices are both used for the confirmation of ovulation.
Materials	Antibody and Antigen Nitrocellulose Membrane Colloidal Gold Conjugate Pad Sample Pad	– Microtiter Plate coated with rabbit anti-mouse antibody – Progesterone Antiserum (mouse anti-progesterone antibody) – Standards A-G (0, 20, 25, 50, 100, 300, and 1000 pg/mL); progesterone in buffer with BSA and stabilizers – Controls Level I and II	The Proov Test is an IVD made of materials commonly found in lateral flow IVD devices. Biocompatibility is not of concern for IVD devices.

		– Assay Buffer (Tris buffer with BSA and stabilizers) – Enzyme Conjugate (alkaline phosphate [calf] conjugate with stabilizers) – Chemiluminescence Reagent AP (acridan based substrate) – Wash Buffer (Tris buffer with Tween and stabilizer) – Adhesive Foil	
Design	In vitro diagnostic device consisting of disposable lateral flow test strip, consisting of a test area and control area. The urine sample is applied to the strip by dipping. The sample moves by lateral flow into the test area, and then the control area. The test area has PdG-specific reagents impregnated on it to detect the presence of hormone metabolites in urine. The test strip is intended for use outside of the body, and provides qualitative results with a single red line indicating a positive result for PdG and two red lines indicating a negative result for PdG in urine. Presence of PdG confirms that ovulation has occurred.	Device is an ELISA based on the competition assay principle. An unknown amount of antigen present in the sample and a fixed amount of enzyme labeled antigen compete for the binding sites of the antibodies/antigens coated onto the wells. Results of samples can be determined directly using the standard curve.	The subject device is similar to the predicate device with use of the competition principle and use of antigen to compete for the binding site of the targeted antibody.
Analyte	Pregnanediol Glucuronide (PdG)	Progesterone	The predicate measures progesterone and the subject device measures a progesterone metabolite, PdG.
Method	Lateral flow Immunoassay/competition principle	ELISA Immunoassay/competition principle	Immunoassay/competition principle, therefore equivalent.
Specimen	Urine	Saliva	Both are clinically valid specimens for targeted analyte.
Intended Population	For over-the-counter and prescription uses	Prescription use	Proov has been successfully validated with lay-users.
Reading	Visual, colloidal gold	Luminescence	Subject device is

Indicator			qualitative and the predicate is quantitative. Comparison of Proov vs. ELISA method to support equivalence.
Performance Testing	Precision/Reproducibility Study Traceability Control Detection Limit Analytical Specificity/Interference/Cross-Reactivity Specific Gravity and pH Hook Effect Comparison Study Lay User Study	Precision/Reproducibility Linearity Traceability Control Detection Limit Analytial Specificity Comparison Studies	The testing conducted was similar for both the predicate and subject devices with the exception that the predicate device required liniarity testing, which is not applicable to a lateral flow assay.

VIII. Performance Characteristics

Analytical Performance

a. Precision

Precision studies were conducted with male urine samples spiked with six (6) concentrations of PdG: -100%, -50%, -25%, cutoff, +25%, and +50% of the threshold were run in replicates of ten (10) each within one assay run to determine within-lot precision. Between lot reproducibility was determined by replicate measurements of ten (10) different urine samples in three (3) different lots. Between technician reproducibility was determined in ten (10) different test runs of three (3) different technicians. The results obtained are summarized in the following table

PDG Concentration	-100% (0 ug/mL)	-50% (2.5 ug/mL)	-25% (3.75 ug/mL)	Cut-Off (5 ug/mL)	50% (6.25 ug/mL)	75% (7.5 ug/mL)
Positive Results/ Negative Results	0 + / 90 -	0 + / 90 -	0 + / 90 -	41 + / 49 -	90 + / 0 -	90 + / 0 -

The cut-off value of 5 ug/mL is verified for the device.

b. Linearity

Not applicable, these are visually read devices.

c. Traceability

The tests calibrated against PdG standards.

d. Shelf Life

The devices are stable at 4-30℃ (39-86F) for 24 months based on the accelerated stability study at 42℃.

e. Detection Limit (sensitivity)

5 ug/ml PdG

f. Interference/Cross Reactivity

Potential interfering substances found in human urine of physiological or pathological conditions were added to negative male urine and male urine spiked with PdG 25% above the cut-off level.

These urine samples were tested using three batches of the device. The following compounds showed no interference at the concentrations shown as summarized in the following table.

Substances	***Concentration***
LH	*600 mIU/ml*
HCG	*1000 mIU/ml*
Progesterone	*100 ng/ml*
Pregnanediol	*60 ug/ml*
Estone-3-Glucuronide	*600 ng/ml*
Acetaminophen	*20 mg/dl*
Ascorbic Acid	*20 mg/dl*
Caffeine	*20 mg/dl*
Glucose	*2000 mg/dl*
Ampicillin	*20 mg/dl*
Ketone	*1%*
Acetylsalicylic Acid	*20 mg/dl*
Atropine	*20 mg/dl*
Gentisic Acid	*20 mg/dl*
Hemoglobin	*500 mg/dl*
Tetracycline	*20 mg/dl*
Nitrite Positive	*1%*
Phenothiazine	*20 mg/dl*
Ethanol	*1%*
Albumin	*100 mg/dl*

g. Effect of Urine Specific Gravity and Urine pH

To investigate the effect of urine specific gravity and urine pH, negative urine samples and urine spiked with PdG 25% above cut-off levels with a 1.000 to 1.025 specific gravity or urine samples with pH 4.25 to 9 were used. These samples were tested using three batches of device. Results were all positive for samples above the +25% cut-off and all negative for negative samples.

h. Hook Effect.

Negative urine samples were spiked with PdG at concentrations of ranging from 50 ug/ml to 1 mg/ml. Three lots of the devices were tested. The results demonstrated that no hook effect was observed at PdG concentrations up to 1 mg/ml

i. Comparison studies:

The method comparison studies for the Proov Test were compared to a validated PDG EIA procedure. The PDG content from 94 urine samples collected from apparently healthy females individuals were assessed by both methods. All samples were blind- labeled and Proov Tests results were read by three different technicians. Proov results were compared to PDG ELISA results. Results are presented below.

Proov Test		Low negative by ELISA (less than -50%)	Near Cutoff Negative by ELISA (Between -50% and cut-off)	Near Cutoff Negative by ELISA (Between cut-off and + 50%)	High Positive by ELISA (greater than +50%)
Viewer A	Positive	0	4	13	18
	Negative	48	11	0	0
Viewer B	Positive	0	1	13	18
	Negative	48	14	1	0
Viewer C	Positive	0	0	12	18
	Negative	48	15	1	0

Discordant Results

Viewer	Sample #	ELISA Result	Viewer Results
Viewer A	12	4.4	positive
Viewer A	41	4.6	positive
Viewer A	66	4.7	positive
Viewer A	16	4.8	positive
Viewer B	16	4.8	positive
Viewer B	46	5.2	negative
Viewer C	46	5.2	negative

j. Lay User Study:

A lay user study was performed at three intended user sites with 101 lay persons testing the devices. They had diverse educational and professional backgrounds and were all women ranged in age from 18 to 65 years. Urine samples were prepared at the following concentrations; +/- 75%, +/-50%, +/-25% of the cutoff by spiking PdG into simulated urine. Each sample was aliquoted into individual containers and blind-labeled. Each participant was provided with the package insert, 1 or 2 blind labeled sample and 1 or 2 devices. The results demonstrate that lay women can correctly read Proov results over 99% of the time (121 of the 121 samples).

PDG conc	# neg	# pos	% correctly interpreted
1.25	20	0	100
2.5	20	0	100
3.75	21	0	100
6.25	0	20	100
7.5	0	20	100
8.75	0	20	100

Lay-users were also given surveys on the ease of understanding the package insert instructions. 92% of lay users indicated that the device instructions and testing were easy or very easy. A Flesch-Kincaid reading analysis was performed on each package insert and the scores revealed a reading Grade Level of 8.

IX. Conclusions

The overall performance data in this submission supports that the MFB Fertility, Inc. Proov Test is substantially equivalent to the predicate device.