510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K183602

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Progressively Motile Sperm Cells (PMSC)

D. Type of Test:

Qualitative

E. Applicant:

MotilityCount ApS

F. Proprietary and Established Names:

SwimCount Sperm Quality Test

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.5220, Automated differential cell counter

2. Classification:

   Class II

3. Product code:

   POV – Semen Analysis Device

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):
   The SwimCount Sperm Quality Test is a qualitative test that detects sperm concentration above or below 5,000,000 Progressive Motile Sperm Cells per mL (PMSCs/mL). The test is intended for use as an aid in the determination of a man's fertility status. For in vitro, over-the-counter use.

   The number of progressively motile sperm cells is only one factor that contributes to a male's fertility status. The SwimCount Sperm Quality Test does not provide a complete evaluation of a male's fertility status. For a comprehensive assessment of male fertility status the patient should consult a physician.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   Not applicable

4. Special instrument requirements:

   Not applicable

I. Device Description:

The SwimCount Sperm Quality Test is a qualitative test that detects sperm concentration above or below 5,000,000 Progressively Motile Sperm Cells per mL (PMSCs/mL). The SwimCount Sperm Quality Test Kit includes the following components:

- SwimCount Sperm Quality Test Device (consists of sample well, result window, action window, and slider)
- Semen Collection Cup (used to collect the sperm sample and the sample is to remain in the sample cup for 30 minutes)
- Semen Transfer Pipette (used to stir the semen sample 10 times before adding the sample to the SwimCount Sperm Quality Test Device and further used to collect 0.5 mL sample of semen from the sperm sample placed in the cup)
- SwimCount Sperm Quality Test Instructions for Use

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Fertell Male Fertility Test

2. Predicate 510(k) number(s):

   K041039

3. Comparison with predicate:

Similarities		
Item	Device **SwimCount Sperm Quality Test**	Predicate **Fertell Male Fertility Test**
Intended Use/ Indications for Use	The SwimCount Sperm Quality Test is a qualitative test that detects sperm concentration above or below 5,000,000 Progressive Motile Sperm Cells per mL (PMSCs/mL). The test is intended for use as an aid in the determination of a man's fertility status. For *in vitro*, over- the-counter use. The number of progressively motile sperm cells is only one factor that contributes to a male's fertility status. The SwimCount Sperm Quality Test does not provide a complete evaluation of a male's fertility status. For a comprehensive assessment of male fertility status the patient should consult a physician.	The Fertile Male Fertility Test is intended to measure motile sperm in semen as an adjunctive screen of male fertility for over-the-counter (OTC) home use.
Test Type	Qualitative	Same
Sample Type	Human Semen	Same
Test Setting	Over-the-Counter (OTC)	Same

Differences		
Item	Device	Predicate
Assay Principle	PMSCs are separated from the rest of the semen sample, stained and captured on a detection filter.	Sperm migration
Result Interpretation	The test result is read as color intensity and compared to two reference colors. The darker the color, the higher the number of PMSCs/mL.	Visual line; Colored label bound to sperm
Assay Cut-Off Level	5 M PMSCs/mL	10 M/mL motile sperm cells

K. Standard/Guidance Document Referenced (if applicable):

ISO 14971:2012 Medical Devices – Application of risk management to medical devices

ANSI/AAMI/IEC 62366:2007 Medical Devices – Application of usability to medical devices

CLSI EP07-A2 Interference Testing in Clinical Chemistry; Approved Guideline – Second edition

World Health Organization. (2010). *WHO Laboratory Manual for the Examination and Processing of Human Semen*, 5th Ed. Geneva: WHO Press

L. Test Principle:

A semen sample is collected in the supplied collection cup. The sample is left in the cup and allowed to liquefy. After liquefying for 30 minutes, 0.5 mL of semen sample is loaded into the sample well and the device is activated by moving the Slider forward, whereby the media is pushed into the swim-up chamber. A filter separates the semen from the swim-up compartment, allowing only the PMSCs to swim through the filter. The non-motile cells are retained in the semen compartment.

The swim-up compartment contains 700 µL Phosphate Buffered Saline (PBS) media with 0.05 % Thiazolyl Blue Tetrazolium Bromide (MTT), a dye staining living cells. The motile cells swimming into the chamber are stained purple by MTT stain. An enzyme in the mitochondria of the motile sperms cleaves the substrate and stains the progressive motile spermatozoa. The test device is incubated for 30 minutes at room temperature (18–30°C or 64–86°F). During this incubation time the progressive motile sperm swim through the filter and up into the swim-up compartment. After incubation, the Slider of the test device is pulled back and the buffer containing the stained motile sperm are aspirated out of the detection chamber by the syringe and the stained motile sperm are trapped on the detection filter letting the media pass through.

The test result is a color reaction which can be read by comparing the color intensity with the color scale at the result window of the device. The darker the color intensity is, the higher the concentration of PMSCs.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Repeatability was determined by analyzing the same sample (PMSCs/mL) repetitively over a short period of time under the same measurement conditions (same device lot/operator/location). Seven different progressively motile sperm concentrations (PMSCs/mL) covering the measuring range of the test were included. Semen samples were pooled from sperm donors and diluted in autologous semen

plasma to the following concentrations: 0 M, 1.9 M, 4.1 M, 6.2 M, 8.4 M, 10.1 M and 97.2 M PMSCs/mL, as determined by manual microscopy. The table below provides a summary of the overall repeatability study results:

Sample ID	M PMSCs/mL Manual sperm count	Expected result	# Of SwimCount Sperm Quality Test results < 5 M PMSCs/mL	# Of SwimCount Sperm Quality Test results ≥ 5 M PMSCs/mL	% correct
1	0	< 5	60	0	100%
2	1.9	< 5	60	0	100%
3	4.1	< 5	58	2	96.7%
4	6.2	≥ 5	26	34	56.7%
5	8.4	≥ 5	9	51	85.0%
6	10.1	≥ 5	0	60	100%
7	97.2	≥ 5	0	60	100%

Reproducibility was evaluated by analyzing the same sample with changes in the conditions (different operators/lots/locations and time points). Due to the instability of fresh semen samples, a modified precision study was conducted. Seven different samples at two timepoints (30 minutes and 60 minutes after collection) were analyzed. The following concentrations were tested based on manual microscopy: 0 M, 1.7 M, 3.9 M, 6.2 M, 9.1 M, 11.4 M and 116.5 M PMSCs/mL. The table below provides a summary of the overall reproducibility study results:

Semen Sample PMSC Concentration Levels		30 min. after collection	60 min. after collection
0 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	0	0
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%
1.7 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	1.7 M	1.7 M
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%
3.9 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	3.9 M	3.9 M
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%
6.2 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	6.2 M	6.2 M
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%

9.1 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	9.1 M	9.1 M
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%
11.4 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	11.4 M	11.4 M
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%
116.5 M PMSCs/mL	**Actual PMSC concentration (counted in a Microscope)**	116.5 M	116.5 M
	Reproducibility of SwimCount™ Sperm Quality Test	100%	100%

b. Linearity/assay reportable range:

Not applicable

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

Accelerated Stability

An accelerated stability study was conducted to demonstrate that the performance of the SwimCount Sperm Quality Test was not significantly impacted after 20 weeks with storage at 55°C (corresponding to 3 years of storage at room temperature). A semen sample containing 40 M PMSCs/mL as determined by manual microscopy, was measured on two freshly produced SwimCount devices and six SwimCount devices stored at 55°C for 20 weeks. The six SwimCount devices contained three different lots and each lot was tested in duplicate. Paired t-test was used to determine if the test results were significantly different for the devices stored at 55°C compared to freshly produced control devices. Results from the accelerated stability study demonstrate that there are no significant differences in the SwimCount results of the devices stored at 55°C for 20 weeks compared to freshly produced devices, supportive of a 3-year real time shelf-life claim.

Real Time Stability

In addition to the accelerated stability study, the shelf-life stability claim was further supported by performance studies using SwimCount device lots from the first production batch (July 2015). Three different lots were used in the precision study, detection limit study, and pre-condition study. The complete, fully assembled devices were stored at 20°C ± 5°C with humidity ranges of 20–65 RH (relative humidity). The temperature and humidity for each lot of SwimCount devices was recorded at the beginning of every month for 43 months. Results from the various performance studies and pre-condition study demonstrate that the device lots stored for 3 or more years at the time of testing showed no difference in performance compared to newly produced SwimCount devices. Stability testing results demonstrate that the SwimCount Sperm Quality Test is stable for 3 years at 15–30°C.

Transportation Test

A transportation study was conducted to evaluate the stability of the SwimCount Sperm Quality Test during transport. The devices were shipped in two different ways:

1) Simulating shipping from manufacturer directly to end-user in padded envelopes (one device per envelope).
2) Shipping in cardboard boxes to the distributors (may include several devices).

SwimCount Sperm Quality Test kits were packed in padded envelopes and cardboard boxes and transported by a shipping company from one domestic address to another. Upon arrival at the final shipping destination, the boxes were inspected visually for damage and the findings were documented, including photographs. In addition to the visual inspection, the function of the SwimCount device was tested. The test devices were examined for functionality by testing on sperm samples with known concentrations of PMSCs/mL and compared to devices, that have not been transported. Eight SwimCount Sperm Quality Test devices were tested, four devices with 2.5 M PMSCs/mL and four devices with 8.3 M PMSCs/mL.

Pre-Conditioning

To evaluate whether different climate conditions encountered during distribution have an effect on device performance, a simulation of different climate conditions was tested. The SwimCount device was "pre-conditioned" for 6 hours at laboratory ambient conditions, followed by the highest and lowest temperature and humidity extremes expected during normal transportation. These conditions were simulated by placing the SwimCount devices in an incubator and freezer. Three test devices were used for each condition and compared to controls stored at room temperature. Semen samples containing 3.5 M PMSCs/mL and 7.5 M PMSCs/mL were tested to examine potential additive/reductive impact.

The three environments and durations tested are illustrated in the table below:

Environment	**Time**	**Temperature**	**Relative Humidity (RH)**
Frozen	72 hours	-29°Celsius (-20°F)	25–35%
Tropical	72 hours	38° Celsius (100°F)	85% RH
Desert	72 hours	50° Celsius (120°F)	25–35%

Results for the pre-conditioning test met acceptance criteria. It was concluded that the the performance of the SwimCount Sperm Quality Test was not affected by frozen, tropical, and desert conditions that may be encountered during distribution, up to the limits tested.

Sample Stability

The stability of semen samples was evaluated on the SwimCount Sperm Quality Test by analyzing seven different samples at three timepoints (30 minutes, 60 minutes, and

90 minutes after collection). The following concentrations were tested based on manual microscopy: 0 M, 1.7 M, 3.9 M, 6.2 M, 9.1 M, 11.4 M and 116.5 M PMSCs/mL. No change in the PMSC concentration was observed at 30 minutes and 60 minutes after collection of the semen sample. Results from the sample stability study demonstrate that the SwimCount Sperm Quality Test provides accurate results for semen samples up to one hour after collection.

d. Detection limit:

To determine the detection limit of the SwimCount Sperm Quality Test, five semen samples were prepared from a pool of donor semen diluted in seminal plasma to the following concentrations: 3.9 M, 4.0 M, 5.0 M, 6.0 M, and 6.2 M PMSCs/mL, as determined by manual microscopy. The preparations and counting were performed by one operator. A second operator tested the blinded samples on the SwimCount Sperm Quality Test and read the results. Each concentration was tested in 40 replicates. The 4.0 M PMSCs/mL, 5.0 M PMSCs/mL and 6.0 M PMSC/mL concentrations were tested on two SwimCount lots for a total of 80 replicates per concentration/sample. The detection limit study results are shown in the table below.

Concentration (PMSCs/mL)	**Percent positive (Positive/Total)**	**Percent negative (Negative/Total)**
3.9 M	0 (0/40)	100 (40/40)
4.0 M	7.5 (6/80)	92.5 (74/80)
5.0 M	55.0 (44/80)	45.0 (36/80)
6.0 M	90.0 (72/80)	10.0 (8/80)
6.2 M	100 (40/40)	0 (0/40)

e. Analytical specificity:

The potential interference of various substances on SwimCount results was evaluated by testing elevated concentrations of the following:

Substance	**Test concentration/mL**
Gram positive bacteria: Staphylococcus epidermis	10^4
Gram negative bacteria: Escherichia coli	10^4
Neisseria gonorrhoeae	10^4
Chlamydia trachomatis	10^4
Urine	10 %

Saliva	10 %
Red Blood Cells (RBC)	10^7
White Blood Cells (WBC)	5×10^6
D-Norgestrel	10 ng/mL
β-Estradiol	600 pg/mL
Testosterone	120 ng/mL

Testing was performed in triplicate. Each potential interfering substance was spiked into semen samples from vasectomized men (containing semen plasma only) to investigate any additive effect of interfering substance. Each substance was also spiked into semen samples containing approximately 20 M PMSCs/mL to investigate any negative effect.

Results from the study identified urine, RBCs and WBCs as substances that may interfere with the test. All other tested substances caused no interference with the SwimCount Sperm Quality Test.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A multi-center clinical study was conducted to evaluate the performance of the SwimCount Sperm Quality Test as compared to manual sperm counting by manual microscopy (reference method). Semen samples were obtained from men seeking fertility treatment or from sperm donors. A total of 323 semen samples across four sites were included in the study. All semen samples were analyzed using Makler counting chambers and conventional microscopy and compared to the SwimCount Sperm Quality Test.

Out of the 323 semen samples included in the study, 15 samples were excluded resulting in a net total of 308 samples analyzed. The 15 samples were excluded for the following reasons: four men did not fulfill the criteria of a <2 days abstinence period, one man was diagnosed with globozospermia, one with hematospermia, five with leucospermia, two samples contained <0.5 mL semen and two samples were too viscous to be applied into the SwimCount Sperm Quality Test. A summary of the multi-site clinical study is provided below.

Multi-Center Clinical Test - Calculation based on Line Data		
	Manual Sperm Count Reference	
SwimCount™ Sperm Quality Test	***LOW (<5 M PMSCs/mL)***	***NORMAL (≥5 M PMSCs/mL)***
LOW (<5 M PMSCs/mL)	69	22
NORMAL (≥5 M PMSCs/mL)	3	214
	(4.17% false negative)	(9.32% false positive)
		95% Conf. Interval
Sensitivity	**95.83%**	88.30%-99.13%
Specificity	**90.68%**	86.23%-94.07%
Accuracy*	**91.88%**	89.90%-95.81%
Total No. of Semen Samples	**323**	
Otherwise exluded for analysis	15	
Included Net No. of Semen Samples	**308**	
*Accuracy calculation is based on the following formula: ((69+214)/(69+214+22+3))x100 = 91.88%		

Results from the multi-center clinical study revealed that results obtained by the SwimCount Sperm Quality Test were comparable with those obtained with conventional semen analysis. A sensitivity result of 95.83% and a specificity result of 90.68% and an accuracy of 91.88% was obtained based on 308 semen samples.

b. 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):

Lay-User Usability Study

A lay-user usability study was conducted to evaluate the simplicity and accuracy of the SwimCount Sperm Quality Test. The study was conducted to determine the lay-user's ability to perform and interpret the test as intended per the Instructions for Use.

Study participants (n=81) performed the SwimCount test at home following the instructions for use, including producing their own sample and evaluating the result as either LOW or NORMAL. After completing the test, the users were asked to complete a questionnaire including 18 questions regarding the ease of use of the device, understanding instructions for use, and test result interpretation. Users were also asked to take a picture of the SwimCount result and upload the picture along with the completed questionnaire. Lay-user results were then compared to a laboratory professional's reading of the uploaded SwimCount results.

There was 97.53% agreement (% of correct calls) between the SwimCount Sperm Quality Test result read by the lay-user at home and those obtained by laboratory professionals reading the same uploaded picture of the SwimCount test result. The overall summary of results of the SwimCount Sperm Quality Test Consumer Use Study are illustrated in the table below:

SwimCount Sperm Quality Test - % of Correct Calls - Consumer Use Study								
Study	**No. of Lay-Users**	**Total No. of Samples**	**Total No. of Responses per Lay-User/ID**	**Corrected for errors**	**Total No. of Net Responses from Lay-Users/ID**	**Correct Answers**	**Not Correct Answers**	**% of Correct Calls by Lay-Users**
Consumer Use Study Lay-User Study	**81**	**81**	**1**	**0**	**81**	**79**	**2**	**97.53%**

User Interpretation Study

In addition to the user study, a user interpretation study was carried out. The 81 study participants were asked to interpret 10 SwimCount test result pictures (N=810). This was accomplished via questionnaire including 10 pictures of a SwimCount Sperm Quality Test result, each including both LOW and NORMAL Sperm Quality Test results. Out of 810 pictures, 791 were read correctly and 19 pictures were read incorrectly for a total of 97.65% of correct calls by lay-users as shown in the below table:

Consumer Interpretation Study - Lay User Study

	Manual Sperm Count Reference	
SwimCount™ Sperm Quality Test	***LOW (<5 M PMSCs/mL)***	***NORMAL (≥5 M PMSCs/mL)***
LOW (<5 M PMSCs/mL)	322	17
NORMAL (≥5 M PMSCs/mL)	2	469
	(0.62% false negative)	(3.50% false positive)

		95% Conf. Interval
Correct Calls by Lay-Users	**97.65%**	96.70%-98.81%

Total Number of Participants	**81**
Pictures Read Per Participant	10
Total Number of Pictures Read	**810**

The data demonstrate that lay users are able to perform the test as intended.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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