510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K161493

B. Purpose for Submission:
New device

C. Measurand:
Motile Sperm Concentration (MSC)

D. Type of Test:
Qualitative measurement of motile sperm concentration (MSC) with the use of YO software application developed specifically for Apple iPhone 5 or Samsung Galaxy 3 smartphones.

E. Applicant:

Medical Electronics Systems, Ltd.

F. Proprietary and Established Names:

YO™ Home Sperm 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 YO™ Home Sperm Test is a smartphone based home test which provides a qualitative assessment of motile sperm concentration (MSC) in human semen. MSC is one aspect of a male semen examination. The YO™ Home Sperm Test does not provide a comprehensive evaluation of a male's fertility status and is intended for over-the-counter, in vitro use only.

2. Indication(s) for use:

   Same as the Intended Use

3. Special conditions for use statement(s):

   Smartphone Apps for Apple iPhone 5 or Samsung Galaxy 3

4. Special instrument requirements:

   Apple iPhone 5 or Samsung Galaxy 3

I. Device Description:

The YO Home Sperm Test is designed to work with home users smartphones (Apple iPhone 5 and Samsung Galaxy 3) with the downloadable YO software application and the YO Clip to measure motile sperm concentration of home users' seminal fluid. The seminal fluid collected in the semen sample cup is liquefied with the addition of chymotrypsin with eosin. Then using the disposable plastic pipette, the liquefied seminal fluid is loaded into the coverslipped slide. The coverslipped slide containing the seminal fluid is then inserted into the YO Clip already attached to the home users' smartphone.

The YO™ Home Sperm Test is packaged in a kit that is sufficient to run two complete tests. The kit consists of:

- Two semen collection cups
- Two vials of liquefying powder (chymotrypsin with eosin)
- Two disposable pipettes for sample aspiration
- Two fixed coverslip slides for sample testing
- One YO Clip that attaches to the smartphone and houses the fixed coverslip slide
- One plastic zip-lock Sperm Clip storage bag

J. Substantial Equivalence Information:

1. Predicate device name(s):
   SpeckCheck® Fertility (Princeton BioMeditech Corporation)
   SQA-V Sperm Analyzer (MES, Ltd.)

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

K100341
K021746

3. Comparison with predicate:

Similarities			
Item	Device YO™ home test	Predicate	
		SQA-V K021746	SpermCheck® Fertility K100341
Intended Use	YO™ is a smartphone based home tst which provides a qualitative assessment of motile sperm concentration (MSC) in human semen. MSC is a semen parameter commonly assessed in a male fertility examination. The YO™ home test does not provide a comprehensive evaluation of a male's fertility status and is intended for over-the-counter, in vitro use only.	The SQA-V is a point-of-care, electro-optical device with on-screen visualization and image freezing capabilities for semen analysis. The SQA-V provides direct and calculated measurements for: • total sperm concentration (TSC, millions/mL) • percent motility (%MOT) and % progressive motility (%PMOT) • % normal morphology (%MORPH) • motile sperm concentration (MSC, millions/mL) and progressive MSC (PMSC) • functional sperm concentration (FSC, millions/mL)	SpermCheck® Fertility is a qualitative test that detects sperm concentration at or above 20,000,000 sperm/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 home use.
Sample Type	Male seminal fluid	Male seminal fluid	Male seminal fluid

Differences			
Item	Device	Predicate	
Technology	A specimen filled slide is inserted into a "Clip" which slides over the top of the Smartphone. Software downloaded onto the phone is used to capture and analyze the video of the motile sperm.	Desk-top unit consists of a light source, optical sensors, built-in video microscopy and an internal computer containing algorithms of semen parameters.	A one-step, immuno-chromatographic assay.
Measurement	Qualitative	Quantitative	Qualitative
Test Setting	Over-the-counter, Home use	Professional Use	Over-the-counter, Home use

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

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

EP12-A2: User Protocol for Evaluation of Qualitative Test Performance; Approved Guidline – Second Edition.

L. Test Principle:

The YO™ Home Sperm Test utilizes Smartphone Apps developed for the iPhone 5 and Galaxy 3 for the qualitative measure of motile sperm concentration (MSC) in human semen samples. The test measures MSC to be in the LOW MSC RANGE or MODERATE/NORMAL MSC range based on the cut-off of 6 million per milliliter (6M/mL) motile sperm. If the MSC is < 6M/mL the result is considered to be in the LOW MSC RANGE and if the MSC is ≥ 6 M/mL the result is considered as MODERATE/NORMAL MSC RANGE. The YO test system software recommends seeking follow-up with medical professional when the YO Home Sperm Test reports results in the LOW MSC RANGE.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision study was conducted at two testing sites. Testing was performed using 67 fresh semen samples collected in-house at MES site and testing 76 fresh semen samples collected at a second site (Ruppin College). The collected semen samples were divided into three groups: positive (MSC < 4 M/mL); close to cut-off (borderline, MSC 4 M/mL to 8 M/mL), and negative (MSC > 8 M/mL). The three groupings were based on MSC values strictly from the YO Home Sperm Test system. The samples were tested in duplicate by four operators using two phones of each type (iPhone 5 and Galaxy 3), four lots of Clips and four lots of slides with total of 480 measurements per site. The study is presented in the table below:

Site 1: MES	Positive	Negative	Total	% Positive	% Negative
Positive (< 4M/mL)*	38	0	19x2 phone types = 38	100	0
Borderline (4-8 M/mL)*	20	16	18x2 phone types = 36	56	44
Negative (> 8 M/mL)*	0	60	30x2 phone types = 60	0	100

Site 2: Ruppin College	Positive	Negative	Total	% Positive	% Negative

Positive (< 4M/mL)*	62	0	31x2 phone types = 62	100	0
Borderline (4-8 M/mL)*	27	21	24x2 phone types = 48	56	44
Negative (> 8 M/mL)*	0	42	21x2 phone types = 42	0	100

Overall	Positive	Negative	Total	% Positive	% Negative
Positive (< 4M/mL)*	100	0	50x2 phone types = 62	100	0
Borderline (4-8 M/mL)*	47	37	42x2 phone types = 48	56	44
Negative (> 8 M/mL)*	0	102	51x2 phone types = 42	0	100

*The three groupings were based on MSC values strictly from the YO test system.

b. *Linearity/assay reportable range:*

Not applicable

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

Real time stability study was completed for 2 months and accelerated stability study for 5 months that corresponds to one year was conducted. Real time stability testing is ongoing.

d. *Detection limit:*

The detection limit was conducted by assaying four MSC levels in duplicate by four operators using four phones of two types (iPhone 5 and Galaxy 3) and four Clip lots. The iPhone 5 is represented by "Phone 1 and Phone2" and Galaxy 3 by "Phone 3 and Phone 4". The results are provided in the table below:

All units MSC M/mL

Sample	Target	Assigned by SQA-V	YO™ Results				% Pos/Neg
			YO™ Phone 1	YO™ Phone 2	YO™ Phone 3	YO™ Phone 4	
1	0	0	Low/Low	Low/Low	Low/Low	Low/Low	100% Pos
2	2-3	2.7	Low/Low	Low/Low	Low/Low	Low/Low	100% Pos
3	5-6	5.6	Low/MN	Low/Low	Low/Low	MN/MN	62.5% Pos 37.5% Neg
4	8-9	8.1	MN	MN	MN	MN	100% Neg

Note: Low - LOW MSC RANGE; MN - MODERATE/NORMAL MSC RANGE

The data demonstrated 3 M/mL MSC as the limit of detection (2 times lower than 6 M/mL cut-off) and 0 for the limit of blank. The results for the sample with the MSC level close to the cut-off (5.6 MSC M/mL) were reported to be 62.5% for results in the LOW MSC RANGE and 37.5% for results at the NORMAL/MODERATE MSC RANGE.

e. Analytical specificity:

Intereference testing was conducted with the potential contaminants listed in the below table. Each of the interfering substances were tested with three semen samples in the LOW MSC RANGE and three semen samples in the MODERATE/NORMAL MSC RANGE that were compared against neat semen samples at the LOW and MODERATE/NORMAL MSC RANGE. Results from the study show there was no interference from the listed interferents in table below except the hormone, D-norgestrel. Study results showed that D-norgestrel lowered the motile sperm concentration (MSC) and is indicated as an interefering hormone in the device labeling.

Contaminant	Origin	Original Concentration	Amount Added	Tested Concentration
Vitamin B	Sigma Aldrich (Cat # V2876)	>98%	5%	50 mg/mL
Testosterone	Sigma Aldrich (Cat # 86500)	>99%	5%	50 mg/mL
Yeast	Acumedia (Cat # 7184A)	>98%	5%	9.8×10^8 CFU/mL
E. coli	ATCC (Cat # 8739)	10^9	5%	5×10^7/mL
RBC	Blood bank of Israel	80% hematocrit	5%	6.1×10^6/mL
WBC	Blood bank of Israel	10^9	5%	5×10^7/mL
Urine	Male	NA	5%	50 mg/mL
Saliva	Male	NA	5%	50 mg/mL
Agglutination	Achieved by heating samples	NA	NA	NA
D-norgestrel	Sigma Aldrich (Cat # N2260)	>99%	5%	50 mg/mL
B-estradiol	Sigma Aldrich (Cat # E8875)	>99%	5%	50 mg/mL

f. Assay cut-off:

The MSC assay cut-off was assessed using 100 fresh clinical semen samples consisting of MSC values approximately 50/50 above and below the 6M/mL MSC cut-off. These samples included 10% of contrived samples to supplement samples close to the cut-off. The study was conducted with two smartphone types (one iPhone 5 and one Galaxy 3) compared to the predicate device, SQA-V using four Clip lots and four slide lots of YO Home Sperm Test kit. The testing was completed in parallel within two minutes of each other on the SQA-V and YO™ to reduce the impact on the sampling time. A summary of the MSC cut-off study results are

presented in the below tables:

iPhone

Candidate Method	Comparative Method		
	Positive	Negative	Total
Positive	51	1	52
Negative	3	45	48
Total	54	46	100

% PPA = 100 x a/(a+c) = 94.4% PASS
% NPA = 100 x d/(b+d) = 97.8% PASS

Galaxy

Candidate Method	Comparative Method		
	Positive	Negative	Total
Positive	50	2	52
Negative	4	44	48
Total	54	46	100

% PPA = 100 x a/(a+c) = 92.6% PASS
% NPA = 100 x d/(b+d) = 95.7% PASS

Combination of both Phones

Candidate Method	Comparative Method		
	Positive	Negative	Total
Positive	101	3	104
Negative	7	89	96
Total	108	92	200

% PPA = 100 x a/(a+c) = 93.5% PASS
% NPA = 100 x d/(b+d) = 96.7% PASS

2. Comparison studies:

   a. Method comparison with predicate device:

   See Consumer Use Study (3.c. below)

   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):

   Consumer Use Study:

   Medical Electronic Systems (MES) conducted a consumer use study to evaluate the YO™ Home Sperm Test system in the hands of the intended home users. The study

was performed at three clinical sites, one in Israel and two in the U.S. The study enrolled and tested a total of 316 semen samples collected from: male subjects with no known fertility issues, a partner in a couple having difficulty conceiving, diagnosed with male factor infertility, and post-vasectomy patients or post-vasectomy reversal patients. After the test subject collected the semen samples, either the subject and/or the tester analyzed the collected sample with the YO™ Home Sperm Test kit using only the instructions provided in the kit. A separate study of YO™ Home tests using the same ejaculate, phone type and lot of YO™ test materials were tested by a trained health care professional (HCP) and by two SQA-V systems. This study design was utilized to compare YO™ results obtained by:

- Home users versus a trained healthcare professional
- Home users versus a predicate/reference method, SQA-V
- Trained healthcare professional versus a predicate/reference method, SQA-V

The results from the study are presented in percent positive agreement (PPA) and negative percent agreement (NPA) for LOW MSC RANGE (MSC < 6M/mL) and MODERATE/NORMAL MSC RANGE (MSC ≥ 6M/mL). The overall results from all three sites combined are shown in the tables below:

YO™ clinical validation (Overall at 3 sites)

AGREEMENT: A vs. B

YO™ by Lay User (A)	YO™ by Trained User (B)		
	Positive	Negative	Total
Positive	87	3	90
Negative	3	223	226
Total	90	226	316
% PPA = 100 x a/(a+c)	96.7%	PASS	
% NPA = 100 x d/(b+d)	98.7%	PASS	

AGREEMENT: A vs. C

YO™ by Lay User (A)	SQA-V (C)		
	Positive	Negative	Total
Positive	81	9	90
Negative	4	222	226
Total	85	231	316
% PPA = 100 x a/(a+c)	95.3%	PASS	
% NPA = 100 x d/(b+d)	96.1%	PASS	

AGREEMENT: B vs. C

YO™ by Trained User (B)	SQA-V (C)		
	Positive	Negative	Total
Positive	83	7	90
Negative	2	224	226
Total	85	231	316
% PPA = 100 x a/(a+c)	97.6%	PASS	
% NPA = 100 x d/(b+d)	97.0%	PASS	

The table below is provided to show the PPA and NPA by phone type between home users and the reference method, SQA-V.

Phone Type – Galaxy

		SQA-V		
Galaxy 3		Low	M/N	Total
	Low	33	6	39
	M/N	1	96	97
	Total	34	102	136

PPA = 33/34 = 97.1% 95% CI: (84.7%; 99.9%)
NPA = 96/102 = 94.1% 95% CI: (87.6%; 97.8%)

Phone Type = iPhone

		SQA-V		
iPhone 5		Low	M/N	Total
	Low	48	3	51
	M/N	3	126	129
	Total	51	129	180

PPA = 48/51 = 94.1% 95% CI: (83.8%; 98.8%)
NPA = 126/129 = 97.7% 95% CI: (93.4%; 99.5%)

Lay users who participated in the consumer user clinical study were asked to provide their opinion of the test and its labeling. This was accomplished via a questionnaire. The questions posed to the 316 participants are provided in the table below along with the results.

All Site Data, n = 316

Question # 1: Were the directions and pictures in the YO™ TEST PROCEDURE		
#	QUESTION	RESPONSE %
1	Very clear and easy to follow	81.70
2	Somewhat clear and fairly easy to follow	14.71
3	Neutral	1.96
4	Some unclear, but could be followed	1.31
5	Unclear and difficult to follow	0.33

Question # 2: Were the instructions for SAMPLE PREPARATION		
#	QUESTION	RESPONSE %
1	Very clear and easy to follow	84.97
2	Somewhat clear and fairly easy to follow	11.76
3	Neutral	1.96
4	Some unclear, but could be followed	1.31
5	Unclear and difficult to follow	0.00

Question # 3: Were the instructions for ATTACHING THE YO SPERM CLIP TO THE PHONE		
#	QUESTION	RESPONSE %
1	Very clear and easy to follow	90.85
2	Somewhat clear and fairly easy to follow	5.88
3	Neutral	2.94
4	Some unclear, but could be followed	0.33
5	Unclear and difficult to follow	0.00

Question # 4: Were the instructions for FILLING THE YO SLIDE WITH SAMPLE		
#	ANSWER	RESPONSE %
1	Very clear and easy to follow	66.89
2	Somewhat clear and fairly easy to follow	22.95
3	Neutral	6.23
4	Some unclear, but could be followed	3.93
5	Unclear and difficult to follow	0.00

Question # 5: Were the YO ANIMATIONS AND VIDEOS		
#	ANSWER	RESPONSE %
1	Very clear and easy to follow	89.18
2	Somewhat clear and fairly easy to follow	8.52
3	Neutral	0.66
4	Some unclear, but could be followed	1.31
5	Unclear and difficult to follow	0.33

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   Not applicable

N. Instrument Name:

The YO Clip, YO slide, and the downloadable software application for smartphones, (iPhone 5 and Galaxy 3)

O. System Descriptions:

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes _X_____ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes __X_____ or No _____

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X_____ or No _____

3. Specimen Identification:

Not availabe

4. Specimen Sampling and Handling:

   The home users are to collect their semen samples in the collection cup provided in the YO™ Home Sperm Test kit. After collecting the sample, the liquefying powder that contains chymotrypsin with eosin is added into the cup. Then the sample containing the liquefying reagent is mixed with using gentle circular rotation for 10–15 seconds. After mixing, the sample is to rest for 12 minutes before running the test. It is recommended that users allow 2 to 7 days without ejaculating before collecting their semen sample. The sample can sit for up to one hour. Condoms and lubricants should not be used when collecting a semen sample. Proctective power free non-latex gloves are recommended for anyone other then the subject testing his own specimen. Hands should be washed with soap and water before and after handling the semen sample or any component of the test kit.

5. Calibration:

   The calibration curve was established by assaying 152 semen samples using four smartphones (two of each type, iPhone 5 and Galaxy 3) and two SQA-V reference systems.

6. Quality Control:

   The YO system is equipped with a built-in software electronic check to detect misalignment of the clip and slide. The built-in electronic check is also able to detect that an empty slide not filled with liquefied seminal fluid.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Disinfection study: MES Ltd., selected the EPA registered (Registration # 70627-60) Oxivir TB wipes with 0.5% hydrogen peroxide manufactured by Diversey, Inc as the disinfectant of choice for the YO Home Sperm Test system. The disinfection study was conducted at the Accuratus Lab Services in Eagan, MN. The reports from this disinfection study utilizing Duck Hepatitis B Virus as a Surrogate Virus for Human Hepatitis B Virus were provided in this 510(k) submission.

The study concluded Oxivir TB wipes (Lot 15107VX01), a ready to use pre-saturated towelette demonstrated complete inactivation of duck Hepatitis B virus following a one minute exposure time at room temperature (21.0°C) under the conditions of the investigation and in presence of a 5% fetal bovine serum organic soil for all replicates (three lots) of the coupon material surfaces of: iPhone 5 (front, back and button), Galaxy 3 (front, back, and button) and YO™ Clip.

Disinfection Robustness Study: To assess robustness from cleaning and disinfection with Oxivir TB wipes, a simulated a cleaning and disinfecting protocol as would be utilized by home users was conducted to observe signs of thin silver streaks, cracking, swelling, dissolving, softening or brittleness of the phone case, display and buttons on the smartphone and YO™ Clip. The study was conducted on each of the smartphone types (iPhone 5 and Galaxy 3) and YO Clip by disinfecting 20 times using the recommended disinfecting towelettes (Oxivir Wipes) during the process of testing 20 semen samples. The study tested 10 "LOW" and 10 "Moderate/Normal" MSC samples compared to the reference method, SQA-V. The study produced ≥ 90% PPA and ≥ 90% NPA between YO™ Home Test kit and SQA-V for the disinfection and cleaning protocol and 100% material compatibility for the robustness study with the Oxivir TB wipes.

Q. Proposed Labeling:

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

R. Conclusion:

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