CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW240024

II. Parent Document Number

K243114

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

Medical Electronic Systems Ltd.

V. Proprietary and Established Names

SQA-iOw Sperm Quality Analyzer

VI. Measurand (analyte)

Measured parameters:

- Sperm Concentration, M/mL
- Motile Sperm Concentration (MSC), M/mL
- Progressively Motile Sperm Concentration (PMSC), M/mL
- Normal Forms (Normal Morphology), %

Calculated parameters:

- Total Motility (PR + NP), %
- Progressive Motility (PR), %
- Non-Progressive Motility (NP), %
- Immotile (IM), %

VII. Sample Type(s)

Semen

VIII. Type of Test

Semen Parameters

IX. Test System Description

A Overview

The SQA-iOw Sperm Quality Analyzer is an automated device that tests human semen samples. It provides direct and calculated measurements for total sperm concentration, percent motility, percent immotile, percent non-progressive motility, percent normal forms, motile sperm concentration, progressively motile sperm concentration, and functional sperm concentration. After collection and preparation, 0.6 mL of semen sample is manually aspirated into a disposable SQA capillary sample delivery system and inserted into the SQA-iOw measurement chamber. The testing process takes approximately 75 seconds. The system performs an automatic self-test and auto-calibration upon start up, and checks device stability before each sample is run. Sample testing is performed by capturing electrical signals as sperm moves through a light source in the SQA-iOw optical block. These light disturbances are converted into electrical signals which are then analyzed by the SQA-iOw software.

B Test System Components

- SQA-iOw Sperm Quality Analyzer
- USB cable
- SQA disposable capillaries
- Cleaning kit:
  - Long cleaning brush
  - Fibrous material cleaning paddles (single use)
  - Sponge-tipped drying paddles (single use)
  - Cleaning fluid (50% ethanol, 49.5% distilled water, 0.5% Tween 20) (single drop dispenser)

C Results Interpretation

After approximately 75 seconds, test results will be displayed. An indicator arrow will appear if the results are high or low based on the reference values or the WHO defaults. If there is no arrow, the test results are either in the normal range or there is no reference value for the parameter. Results are displayed automatically and, if out of range, a corrective action alert will be shown.

X. Specific Contents for CLIA Waiver

A Demonstrating “Simple”:

The information below demonstrates how the SQA-iOw Sperm Quality Analyzer is simple per the FDA guidance “*Recommendations for Clinical Laboratory Improvement Amendments of*

1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices" (FDA, 2020).

Guidance Criteria	**How Addressed on the SQA-iOw system**
Is a fully automated instrument, or a unitized, or self-contained test.	The SQA-iOw is an automated self-contained instrument that uses unitized, disposable components.
Uses direct unprocessed specimens such as capillary blood (fingerstick), venous whole blood, nasal swabs, throat swabs, or urine.	The system uses ejaculated semen.
Needs only basic, non-technique-dependent specimen manipulation, including any for decontamination.	All reagents (liquefication agent) and QC materials are pre-packaged and require no manipulation. The materials only require simple mixing. The device provides simple instructions on the on-screen interface.
Needs only basic, non-technique-dependent reagent manipulation, such as "mix reagent A and reagent B".	
Needs no operator intervention during the analysis steps.	Once the capillary unit is inserted, sample analysis is completed automatically without operator intervention.
Needs no technical or specialized training with respect to troubleshooting or interpretation of multiple, or complex error codes.	Technical or specialized training is not required for troubleshooting or error code interpretation. Error messages and pop-up instructions are embedded as part of the interface.
Needs no electronic or mechanical maintenance beyond simple tasks, e.g., changing a battery or power cord.	There is no maintenance required other than periodic cleaning of the capillary chamber. Cleaning instructions are included in the IFU. No electronic or mechanical maintenance is required.
Produces results that require no operator calibration, interpretation, or calculations.	System automatically reports results. The operator never performs calibration or calculation. The system runs an automatic self-test and auto-calibration upon start-up.
Produces results that are easy to determine, such as "positive or negative", a direct readout of numerical values, the clear presence or absence of a line, or obvious color gradations.	Results are printed as numeric values or percentages. An indicator arrow will appear if the results are high or low based on the reference values.
Includes quick reference instructions (Quick Reference Guide, Operator's Instrument Manual (if applicable), etc.) that are written at no higher than a 7th grade reading level (see Section VI).	The reading grade level, as determined by the Flesch-Kincaid program, assigns a reading grade level of 7.4. The document includes several technical terms that cannot be modified if wishing to retain accuracy, and the text is appropriate for the 7th grade level.

	The instrument software includes an instructional video that the operator can follow.

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

   Potential sources of error that could adversely affect system performance were identified and mitigated first through system design and then through additional cautions in the labeling. The identified risks which could result in erroneous test results were evaluated in flex studies which stressed the functional limits of the test.

2. Fail-Safe and Failure Alert Mechanisms:

   Based on the risk analysis, a series of fail-safe and failure alert mechanisms have been implemented as risk control measure:
   - Automatic self-test and auto-calibration upon start-up.
   - If the self-test fails, the device will not operate.
   - The device assures an accurate self-test which requires a capillary free chamber. If a capillary is located in the device chamber during self-test, the device will not initiate the automatic self-test or allow the device to proceed with testing.
   - A capillary needs to be in the measurement chamber to run a test. The device does not allow testing without a testing capillary in the measurement chamber (capillary sensor).
   - The device design does not enable improper insertion of the testing capillary into device or use of an unauthorized, manufacturer supplied capillary.

3. Flex Studies: Two SQA-iOw calibrated devices were used (one for flexed conditions and the other as a control condition) with one (1) operator. Below studies were conducted within 10 minutes between test and reference instruments. Acceptance criteria is either no result or invalid or %Bias is acceptable. Sperm concentration, Motility, Progressive motility, Non-progressive motility, Immotile, Morphology, MSC, and PMSC were evaluated.

   a) **Under-filling**: Study was conducted using three semen samples (low, middle, high) based on concentration in duplicates. Conditions tested included: Control (0.6mL), Capillary underfilled by 10%, Capillary underfilled by 25% (meniscus evident), and Capillary underfilled by 50%.

      Results
      The control and 10% underfilling of the testing capillary with sample met the acceptance criteria. Samples with 25% and 50% underfilling of the required volume failed to pass acceptance criteria.

b) **Non-level surface**: Study was conducted using three semen samples (low, middle, high) based on concentration in duplicates. Control (level surface), 10-degree angle, 20-degree angle, and 30-degree angles were tested.

Results
Samples passed acceptance criteria for non-level surfaces at 10 degrees and 20 degrees. The device cannot operate at 30-degree angles because the capillary cannot be inserted into the measurement chamber.

c) Amount of liquefaction powder: Study was conducted using three semen samples (low, middle, high) based on concentration in duplicates. Control (5 mg), 2.5 mg, 1.25 mg, 0.5 mg were tested.

Results
Low level samples cannot be aspirated into the testing capillary without proper liquefaction. Incorrect amount of liquefaction powder, 0.5–2.5 mg added to low level samples resulted in no results been reported. Middle and high levels samples with 0.5–2.5 mg liquefaction powder added passed acceptance criteria.

d) **Waiting time for liquefaction:** Study was conducted using three semen samples (low, middle, high) based on concentration in duplicates. Control (10 mins), 25, 20, 15, 5 and 0 minutes were tested.

Results
Samples liquefied for 0 and 5 minutes cannot be aspirated and therefore no erroneous results can be reported. Samples for 15–25 minutes passed acceptance criteria. Device includes clear on-screen instructions with 10-minute timing for sample liquefaction.

e) **Amount of swirling**: Study was conducted using three semen samples (low, middle, high) based on concentration in duplicates. Control (30 seconds), no swirling, 10 seconds, 20 seconds, 40 seconds, and 50 seconds were tested. Concentration, Motility, Progressive, Non-progressive, Immotile, Morphology, MSC, and PMSC were evaluated.

Results
Swirling the samples for 0–50 seconds passed acceptance criteria. The device includes clear on-screen instructions to swirl samples for 30 seconds.

f) **Vibrations**: Study was conducted using three semen samples (low, mid, high) based on concentration in duplicates. Control (no centrifuge) and a centrifuge spinning on the same bench as the flexed SQA-iOw device, at different speeds (500, 1000, and 2000 rpm) were tested. Concentration, Motility, Progressive, Non-progressive, Immotile, Morphology, MSC, and PMSC were evaluated.

Results

Low level samples failed the acceptance criteria at 500 rpm. Samples passed acceptance criteria for 1000-2000 rpm. The need to perform SQA-iOw testing away from centrifuges or other equipment with vibrations has been made clear as a mitigation in the labeling.

g) **Temperature/Humidity**: Study was conducted using three semen samples (low, mid, high) based on concentration in duplicates. Devices were stored in temperature-controlled chambers and evaluated at room temperature (recommended condition) and conditions outside the recommended storage conditions: high temperature and humidity (80% humidity and 40°C), high temperature and low humidity (10–20% humidity and 40°C), and low temperature (4–8°C). Concentration, Motility, Progressive, Non-progressive, Immotile, Morphology, MSC, and PMSC were evaluated.

Results
All samples failed acceptance criteria for low temperature (4–8°C) and high temperature at both low and high humidity conditions. As mitigation, semen sample testing should be conducted at ambient room temperature 20–25°C (68–78°F) and ambient relative humidity about 40% which is stated in the labeling and Quick Reference Guide (QRG).

h) **Plugging and unplugging the device**: The device was repeatedly plugged and unplugged five times. One batch of control beads with three levels (High, Low, Negative) were tested in duplicate. Concentration was evaluated.

Results
Repeat plugging and unplugging (five times) did not affect sample results and all samples met the acceptance criteria.

C Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

1. Clinical Study Design:

A clinical study was conducted to evaluate the performance of the SQA-iOw Sperm Quality Analyzer in the hands of the intended users when performed in a CLIA waived setting.

Study Sites
Testing was performed at three fertility centers representative of CLIA waived sites.

Operators
Nine untrained operators participated in the clinical study. Operators had no laboratory training or prior knowledge of the system operation and included nurses and office staff.

Subjects (patients)
A total of 398 samples were collected from male subjects. Professional users split the samples and liquefication was conducted separately by untrained users for the candidate device and trained users for the comparator device.

2. Comparative Method

Testing with the comparative method (CM), the SQA-V Sperm Analyzer, was performed by trained operators.

3. Allowable Total Error (ATE) and Limit of Erroneous Results (LER)

The allowable total error for each semen parameter was set to values presented in the table below.

Measured Parameter	**ATE**
Sperm Concentration, M/mL	ATE is ±4 M/ml for values ≤16 M/mL; and ATE ±25% for values >16 M/mL
Morphology, %	ATE is ±1.2% for values ≤4%; and ATE ±30% for values >4%
MSC, M/mL	ATE is ±2.45 M/ml for values ≤7 M/mL; and ATE ±35% for values >7 M/mL
PMSC, M/mL	ATE is ±1.8 M/ml for values ≤5 M/mL; and ATE ±35% for values >5 M/mL

Calculated Parameter	**ATE**
Motility, %	ATE is ±12.6% for values ≤42%; and ATE ±30% for values >42%
Progressive Motility, %	ATE is ±7.5% for values ≤30%; and ATE ±25% for values >30%
Immotile, %	ATE is ±6% for values ≤20%; and ATE ±30% for values >20%

Limit of erroneous results (LER) for each semen parameter was set by two regions

Parameters	**LER Zone**
	X≤5th percentile, Y≥50th percentile); or X≥50th percentile, Y≤5th percentile

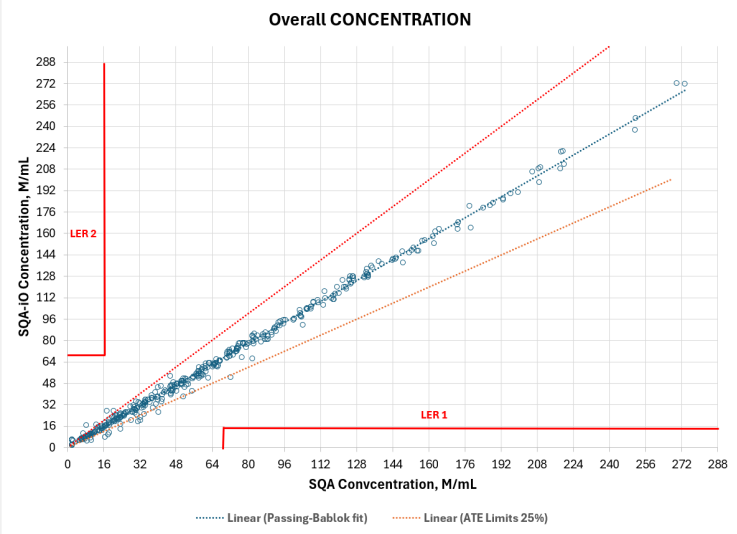
At least 95% of the tested samples fall within the ATE limits and no tested samples should fall into the LER zone.

4. Data Analysis

For each semen parameter, the following data analyses were performed:

- Scatter plot of the data with ATE and LER.
- Percent of SQA-iOw System results within ATE and LER.
- Passing-Bablok regression analysis was performed and biases at medical decision levels (levels from 5th percentile from WHO laboratory manual for the examination and processing of human semen, 6th edition) calculated along with 95% confidence intervals.
- Qualitative analysis based on medical decision levels

Sperm Concentration (M/mL)



ATE analysis

Range of CM	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	133	127	6	95.5%
Intermediate	133	130	3	97.7%
High	132	132	0	100.0%
Combined	398	389	9	97.7% 95%CI (95.8%, 98.9%)

LER Percent of samples inside of LER
0.0% (0/398) 95% CI: (0.0%, 0.0%)

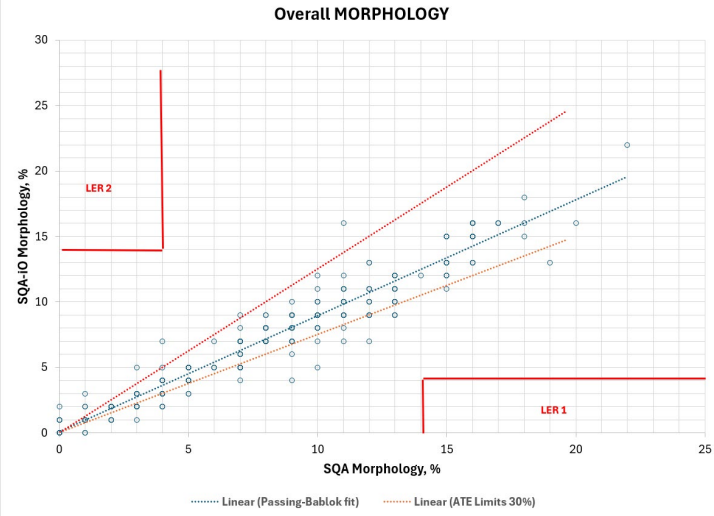
Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
Sperm Concentration, M/mL	380	6 – 272.5	0.05 (-0.18, 0.27)	0.98 (0.97, 0.98)	16	-0.37	-2.3 (-0.8, -3.8)

Agreement analysis (positive percent agreement (PPA) and negative percent agreement (NPA))

SQA-iOw	SQA-V	
	<16	>16
<16	61	5
>16	2	330
Total	63	335
PPA: 96.8% (61/63), 95% CI: (89.1%, 99.1%) NPA: 98.5% (330/335), 95% CI: (96.6%, 99.4%)		

Normal Forms (Morphology, %)



ATE analysis

Range of CM	Range	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	0-6	112	103	9	92.0%
Intermediate	7-9	139	136	3	97.8%
High	10-22	122	114	8	93.4%
Combined	0-22	373	353	20	95%; 95CI: (91.9%, 96.5%)

LER Percent of samples inside of LER
0.0% (0/373) 95% CI: (0.0%; 0.0%)

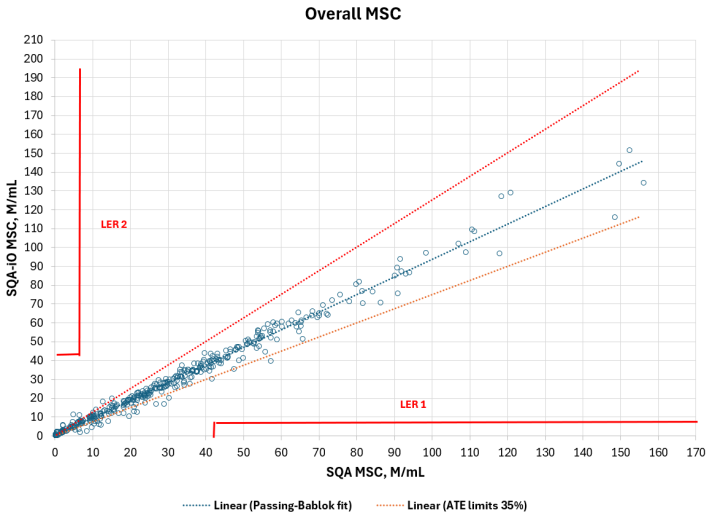
Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
Morphology, %	373	0–22	-1.00 (-1.00, 0.00)	1.00 (0.90, 1.00)	4	-1	-25.0 (-20.6, -29.4)

Agreement analysis (PPA and NPA)

SQA-iOw	SQA-V	
	<4	>4
<4	84	14
>4	3	272
Total	87	286
PPA: 96.6% (84/87), 95% CI: (90.3%, 98.8%) NPA: 95.1% (272/286), 95% CI: (92%, 97.1%)		

MSC (M/ml)



ATE analysis

Range of CM	Range	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	0.2-15.2	133	119	14	89.5%
Intermediate	15.5-37.6	133	128	5	96.2%
High	37.7-156.1	132	132	0	100.0%
Combined	0.2-156.1	398	379	19	95.2% 95CI: (91.8%, 96.3%)

LER Percent of samples inside of LER
0.0% (0/398) 95% CI: (0.0%; 0.0%)

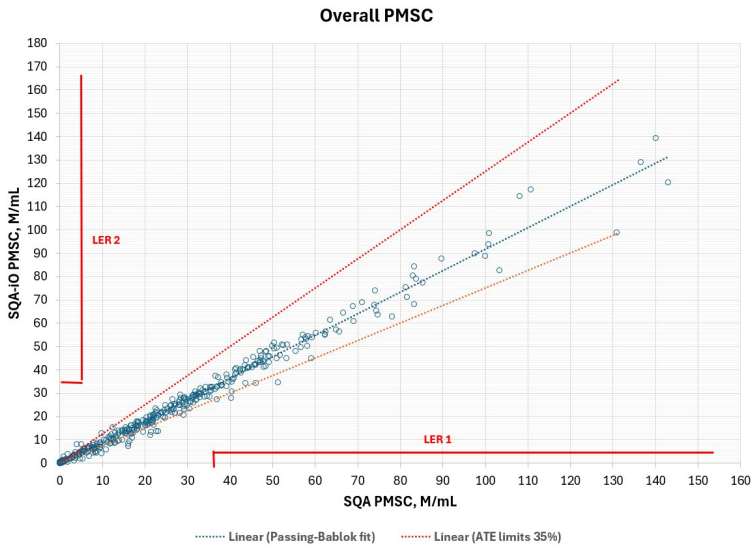
Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
MSC, M/mL	380	0.2–151.7	0.27 (0.05, 0.46)	0.95 (0.93, 0.95)	7	-0.4	-5.7 (-3.4, -8.0)

Agreement analysis (PPA and NPA)

SQA-iOw	SQA-V	
	<7	>7
<7	72	6
>7	8	312
Total	80	318
PPA: 90% (72/80), 95% CI: (81.5%, 94.8%) NPA: 98.1% (312/318), 95% CI: (95.9%, 99.1%)		

PMSC (M/mL)



ATE analysis

Range of CM	Range	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	0-14.6	128	115	13	89.8%
Intermediate	14.7-32.7	128	120	8	93.8%
High	32.8-142.9	125	125	0	100.0%
Combined	0-142.9	381	360	21	95% 95CI: (92.0%, 96.6%)

LER Percent of samples inside of LER
0.0% (0/381) 95% CI: (0.0%; 0.0%)

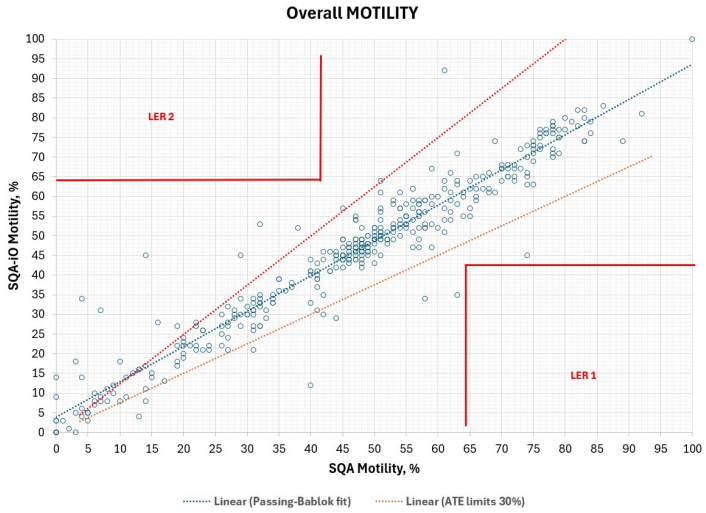
Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
PMSC, M/mL	380	0–139.5	-0.17 (-0.31, 0.00)	0.92 (0.91, 0.93)	5	-0.8	-16 (-12.3, -19.7)

Agreement analysis (PPA and NPA)

SQA-iOw	SQA-V	
	<5	>5
<5	58	10
>5	2	311
Total	60	321
PPA: 96.7% (58/60), 95% CI: (88.6%, 99.1%) NPA: 96.9% (311/321), 95% CI: (94.4%, 98.3%)		

Motility (%)



ATE analysis

Range of CM	range	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	0-42	133	123	10	92.5%
Intermediate	43-55	136	132	1	97.1%
High	55-100	129	126	6	97.7%
Combined	0-100	398	381	17	95.7%; 95%CI (93.3%, 97.3%)

LER Percent of samples inside of LER
0.0% (0/398) 95%CI: (0.0%; 0.0%)

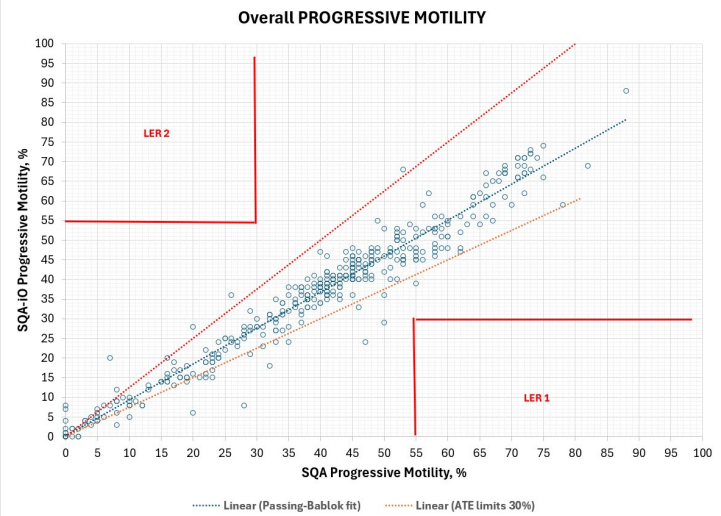
Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
Motility, %	380	0–100	1.94 (1.13, 2.77)	0.94 (0.92, 0.96)	42	-2.1	-5.0 (-2.8, -7.2)

Agreement analysis (PPA and NPA)

SQA-iOw	SQA-V	
	<42	>42
<42	127	7
>42	6	258
Total	133	265
PPA: 95.5% (127/133), 95% CI: (90.5%, 97.9%) NPA: 97.4% (258/265), 95% CI: (94.6%, 98.7%)		

Progressive Motility (%)



ATE analysis

Range of CM	Range	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	0-35	127	116	11	91.3%
Intermediate	36-47	128	127	1	99.2%
High	48-88	124	120	4	96.8%
Combined	0-88	379	363	16	95.8% 95%CI (93.3%, 97.4%)

LER Percent of samples inside of LER
0.0% (0/379) 95%CI: (0.0%; 0.0%)

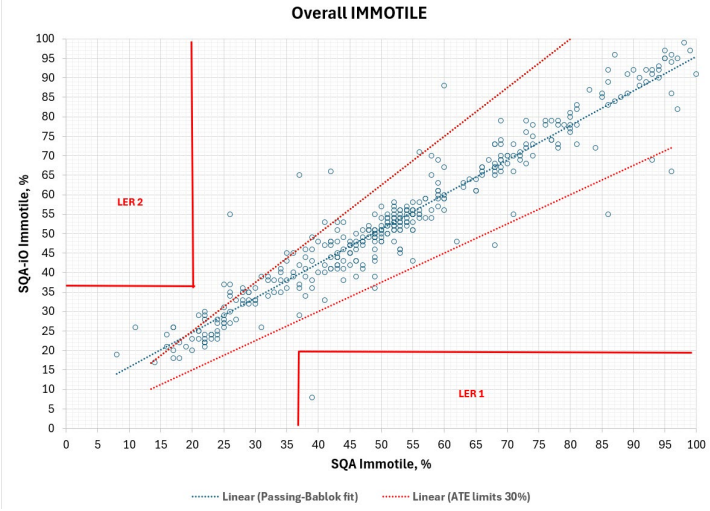
Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
Progressive Motility, %	379	0–88	-0.26 (-0.79, 0.00)	0.94 (0.93, 0.96)	30	-0.7	-2.3 (-0.8, -3.8)

Agreement analysis (PPA and NPA)

SQA-iOw	SQA-V	
	<30	>30
<30	100	14
>30	2	263
Total	102	277
PPA: 98.0% (100/102), 95% CI: (93.1%, 99.5%) NPA: 94.9% (263/277), 95% CI: (91.7%, 97.0%)		

Immotile (%)



ATE analysis

Range of CM	Range	N	Inside ATE (n)	Outside ATE (n)	Percentage of observations inside ATE
Low	0-45	134	119	15	88.8%
Intermediate	46-56	125	125	0	100.0%
High	57-99	120	116	4	96.7%
Combined	0-99	379	360	19	95.0% 95% CI: (92.3%, 96.8%)

LER Percent of samples inside of LER
0% (1/379) 95%CI: (0.0%; 1.5%)

Bias estimation by regression analysis

Parameter	N	Range	Intercept (95% CI)	Slope (95% CI)	MDL	Bias	%Bias (95%CI)
Immotile, %	379	0–99	3.37 (2.47, 4.35)	0.95 (0.93, 0.97)	20	2	10.0 (7.0, 13.0)

Agreement analysis (PPA and NPA)

SQA-iOw	SQA-V	
	>58	<58
>58	258	5
<58	4	108
Total	262	113
PPA: 98.5% (258/262), 95%CI: (96.1, 99.4%) NPA: 95.6% (108/113), 95%CI: (90.1%98.1%)		

Non-Progressive Motility (%)

Agreement analysis (PPA and NPA)

NPA at the 95th percentile (MDL=32) is 99.7% (98.5%, 100%). The dataset is not statistically powered for the calculation of PPA.

Conclusion
The study results demonstrate that risk of erroneous results is insignificant.

5. Questionnaire: Nine operators across the three sites were asked to complete a questionnaire that polled their opinions of the procedural steps (critical tasks) to address ease of use. The multiple-choice responses were presented as a 5-point Likert scale, where rankings ranged from "strongly agree" (5) to "strongly disagree" (1). Results from the questionnaire demonstrate that the SQA-iOw is simple to use for the operators.

D Labeling for Waived Devices

The labeling consists of:

- The User Manual and QRG contain a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test. 42 CFR 493.15(e)(1).
- SQA-iOw Quick Reference Guide (QRG) are written at no higher than a 7th grade reading level and pictures and diagrams have been provided, as appropriate.

XI. Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver grant decision.