510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K153683

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Sperm concentration

D. Type of Test:

Centrifuged packed cell height via density gradient separation

E. Applicant:

Sandstone Diagnostics, Inc.

F. Proprietary and Established Names:

Trak® Male Fertility Testing System

G. Regulatory Information:

1. Regulation section:

   21 CFR § 864.5220, Automated differential cell counter

2. Classification:

   Class II

3. Product code:

   GKZ – Counter, Differential Cell

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   The Trak® Male Fertility Testing System is intended for semi-quantitative assessment of sperm concentration at 15 million sperm per milliliter (M/mL) or below, between 15 and 55 M/mL, and above 55 M/mL. Sperm concentration is only one factor that could impact a man's fertility status and time to pregnancy. For complete assessment of male reproductive health, the user should consult a physician. For *in vitro*, over the counter home use.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   Not applicable

4. Special instrument requirements:

   The Trak® Male Fertility Testing System (Trak) includes a small instrument, the Engine. It spins a test Prop to compact sperm cells within an introduced semen sample into a visible column.

I. Device Description:

The Trak® Male Fertility Testing System (Trak) includes a small instrument (the Engine), disposable units in which liquefied semen sample is introduced and the result is interpreted (the Prop), and consumables, including collection cups, control solution, and sample droppers.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   SpermCheck™ Fertility

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

   K100341

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The Trak® Male Fertility Testing System is intended for semi-quantitative assessment of sperm concentration at 15 million sperm per milliliter (M/mL) or below, between 15 and 55 M/mL, and above 55 M/mL. Sperm concentration is only one factor that could impact a man's fertility status and time to pregnancy. For complete assessment of male reproductive health, the user should consult a physician. For *in vitro,* over the counter home use.	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.
Test Locale	Home Use	Same
Sample Type	Human Semen	Same
Measurand	Sperm Concentration	Same

Differences		
Item	Device	Predicate
Test Type	Semi-Quantitative	Qualitative
Test Reporting	Visual readout of cell column height	Visual line
Test Principle	Centrifuged packed cell height	Chromatographic immunoassay
Primary Cut-off Result	15 M/mL (lower reference limit, WHO 5th edition guidelines)	20 M/mL (lower reference limit, WHO 4th edition guidelines)
Additional Reference Point	55 M/mL (indication of faster time to pregnancy based on Slama et. al. 2002 study)	None
Test Control Method	External quality control	Internal control line

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

EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*

EP12-A2: *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline - Second Edition*

L. Test Principle:

Trak uses the principle of density gradient separation to isolate sperm cells from human semen to provide an estimation of sperm concentration. The Trak Engine spins a test Prop to compact sperm cells within an introduced semen sample into a visible column (or "pellet"). The Prop gives a defined shape to the column, the height of which corresponds to the concentration of sperm cells in the sample. Since semen may also contain cell debris, immature sperm cells, and other contaminant particulates that could contribute to the apparent size of a pellet, it is necessary to filter out the contaminants. Trak achieves this filtering by removing contaminants from view based on density across a predefined liquid density medium.

During operation, approximately 0.17 mL of semen is metered by centrifugal action from the sample inlet into the metering chamber of the Prop. During rotation, the semen floats on "top" of the pre-loaded density medium. Sperm cells pass through the medium due to their high density while contaminants remain floating on the medium. When the spin sequence is complete, the sperm cells form a visible column that is displayed to the user for interpretation. Contaminants that are less dense than the liquid density medium are suspended "above" the medium, substantially separated from the sperm cells and are generally too diffuse to visualize.

M. Performance Characteristics (if/when applicable):

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

   a. Precision/Reproducibility:

   A one day precision study was carried out by three operators using three Engine/Prop lot combinations, two replicates per run, and two runs at each time point, for a total of 60 replicates per sperm concentration. Measurements were separated into five separate 4-hour time periods. Seven sperm concentrations were selected that challenged the 15 M/mL and 55 M/mL cut-offs. Sperm concentrations of approximately 13 M/mL, 15 M/mL, 17 M/mL, 18 M/mL, 46 M/mL, 57 M/mL, and 62 M/mL as evaluated by a Computer Aided Semen Analysis (CASA) system were tested by Trak. No significant difference in the performance was found within-run, between-runs, and between-operators/lots. A decrease in results over time period was noted for all of the lower level concentrations reflected by an elevated between-period component of variance. Trak results for a given sample decrease over time due to degradation of the semen sample, especially for lower concentration samples. The instructions for use (Owners Guide) indicate that the test is to be run within 2 hours following sample collection to ensure valid results. The following includes grand averages for each condition, sum for each category, and percent correct calls:

ID	CASA Result Average ± SD (M/mL)	# Trak Results ≤ 15 M/mL	# Trak Results > 15 M/mL		% Correct
			15 – 55 M/mL	>55 M/mL	
1	13.3 ± 0.9	60	0	0	100
2	15.4 ± 0.9	60	0	0	n/a
3	16.7 ± 0.1	30	30	0	50
4	18.2 ± 0.8	18	42	0	70
5	45.8 ± 2.6	0	60	0	100
6	56.7 ± 3.2	0	26	34	n/a
7	61.9 ± 3.8	0	0	60	100

Quality Control Precision

A precision study was conducted to establish the precision of the Trak QC material. Two lots each of two formulations of QC material intended to give Trak results of approximately 17.5 M/mL (Control Solution A) and 7.5 M/mL (Control Solution B) were each tested in duplicate in two separate runs per day over 20 non-consecutive days. Both formulations of the Trak QC material meet acceptance criteria, with 100% of results falling within the expected category.

b. Linearity/assay reportable range:

Not applicable

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

Track Prop Shelf Life

Real time stability testing was performed on three lots of Trak Props. At each time point, 20 Props from each lot were tested with concentrations of approximately 10 M/mL and 20 M/mL and visually evaluated against the 15 M/mL threshold. At each time point, one Prop from each lot was tested on cell-free seminal plasma as a control. All samples were freshly prepared from pooled and diluted semen samples at each time point. In order to validate the freshly composed samples, five replicates from each of the 10 M/mL and 20 M/mL samples were tested on Props assembled within 30 days of the tested time point. Results from Trak Props meet acceptance criteria out to a 6 month time point, and a 3 month expiry date is supported by current stability data. Real time stability testing is ongoing. Stability data is being maintained to extend the expiry date of the Trak Props.

Quality Control Shelf Life

Real time stability testing was performed on three lots of the “Level A” QC material. At the end of each predetermined time point, 10 replicates of the control were tested

on Trak Props and visually evaluated against the 15 M/mL threshold. After initial stability testing at specific time points, previously opened vials of the QC material will be re-capped and re-tested 3 months later to establish 3 month open vial stability. Results from the Trak QC material meet acceptance criteria out to a 2 month time point. Real time stability testing is ongoing. Stability data is being maintained to extend the expiry date of the QC material and establish stability of opened bottles.

d. Detection limit:

Two lots of Props, each containing a unique lot of the density medium were tested in three "days". Because sperm cells are not stable over time, separate time periods during a 24 hour day were used to represent the three days. Four low level sperm concentrations were obtained by dilution of pooled semen samples, and were confirmed by CASA. Each combination of "day" and sperm concentration was tested in five replicates to obtain 60 total replicates per Prop/reagent lot. The data demonstrated that low concentration samples were consistently assigned correctly into the ≤15 M/mL category, thereby meeting the specified acceptance criteria.

e. Analytical specificity:

The potential interference of various substances on Trak results was evaluated by testing elevated concentrations of saliva, urine, blood, leukocytes, E. coli, C. albicans, C. trachomatis, N. perflava, testosterone, D-norgestrel, and β-estradiol as interfering substances in the Trak test. Each concentration of interfering substance was spiked into semen containing approximately 10 M/mL sperm or 20 M/mL sperm, and tested alongside control semen where there were no added interfering substances. Each of these conditions was tested in 20 replicates on the Trak device and evaluated against the 15 M/mL threshold.

Each interfering substance was also spiked into semen samples of approximately 45 M/mL sperm or 65 M/mL sperm and tested alongside control semen in the absence of the interfering substances. Each of these conditions was tested in 10 replicates on the Trak device and evaluated against the 55 M/mL reference feature.

Of the tested interfering substances, only 3 M/mL leukocytes and 1% whole blood failed acceptance criteria for any tested concentration.

f. Assay cut-off:

<u>Near Cut-off Validation</u>

A study was conducted to demonstrate that Trak generates accurate results when samples near the cut-off values, 15 M/mL and 55 M/mL, are tested. Fresh semen samples were pooled and diluted to seven concentrations that challenged the 15 M/mL cut-off. The approximate concentrations formulated were 10 M/mL sperm, 11.5 M/mL sperm, 13 M/mL sperm, 15 M/mL sperm (at or near threshold), 17 M/mL

sperm, 18.5 M/mL sperm, and 20 M/mL sperm. Similarly, semen samples were pooled and diluted to seven concentrations that challenge the 55 M/mL cut-off. The approximate concentrations formulated were 45 M/mL sperm, 47 M/mL sperm, 50 M/mL sperm, 55 M/mL sperm (at or near threshold), 60 M/mL sperm, 63 M/mL sperm, and 65 M/mL sperm. The concentration of each pooled sample was verified to within 5% of target values by CASA and tested in 20 replicates on the Trak System. The table below shows a summary of the validation study, including sum for each category and percent correct calls.

ID#	CASA Result Average ± SD (M/mL)	# Trak ≤15 M/mL	# Trak >15 M/mL		% Correct
			15 – 55 M/mL	>55 M/mL	
1	10.2 ± 0.4	20	0	0	100
2	11.6 ± 0.3	20	0	0	100
3	13.2 ± 0.2	20	0	0	100
4	15.1 ± 0.5	19	1	0	n/a
5	17.1 ± 0.5	3	17	0	85
6	18.3 ± 0.4	0	20	0	100
7	20.8 ± 0.5	0	20	0	100
8	44.0 ± 3.1	0	20	0	100
9	47.0 ± 1.0	0	20	0	100
10	50.6 ± 2.3	0	20	0	100
11	54.1 ± 2.5	0	16	4	n/a
12	59.1 ± 2.2	0	9	11	55
13	62.9 ± 5.2	0	1	19	95
14	66.3 ± 1.1	0	0	20	100

The data support that Trak results are adequately close to reference values in the vicinity of both cut-offs.

Consumer Interpretation Study

A study was performed to demonstrate that Trak results are interpreted correctly by lay users. Lay users at two sites were presented with instructions for use, a Trak Male Fertility System, and a document packet containing an instructional comprehension quiz and images of Trak results for evaluation. Images of seven Trak Props representing results at 8 M/mL, 13 M/mL, 20 M/mL, 47 M/mL, 63 M/mL, 70 M/mL, and 85 M/mL were presented in a different randomized order to each subject. Users categorized each result according to their interpretation: ≤15 M/mL, 15–55 M/mL, or > 55 M/mL. Sixty-one subjects (28 male, 33 female) performing a total of 425 Prop interpretations were included in this study. Two interpretation forms were not correctly filled out and were excluded from the study. The subjects assigned the correct category in 414 instances.

		CASA Reference		
		≤ 15 M/mL	15–55 M/mL	> 55 M/mL
Subject Interpretation	≤ 15 M/mL	119	0	3
	15 – 55 M/mL	1	120	4
	> 55 M/mL	1	2	175

All acceptance criteria were met. The data support that lay users are able to interpret the Trak results.

2. Comparison studies:

   a. Method comparison with reference method:

   See Consumer Use Study

   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:

   A consumer use study was conducted to determine test performance when used by unassisted lay users following the instructions in the package insert. The study was conducted at three clinical sites in the United States. The study was conducted in two ways: 1) Performance of male subjects providing and testing their own semen specimen; 2) Performance of "tester" lay-persons recruited to test semen specimens provided by a subset of test subjects. Male subjects (n=239) providing and testing semen specimens were either presumptively healthy (by self-report), a partner in a couple having difficulty conceiving, diagnosed with male factor infertility, post-vasectomy patients, or post-vasectomy reversal patients.

Following collection of the specimen sample by the study subject, either the study subject or the tester analyzed the sample by Trak. After recording the results, a health-care professional (HCP) employed at the study site observed the Prop and recorded his/her own interpretation of the subject/tester results, and then performed his/her own Trak test using a saved aliquot of the original semen specimen provided by the subject. The HCP then recorded the result of the test. Trak results generated by subjects and testers agreed with results from the same specimens tested by HCPs on the Trak, indicating the quality of the instructions for use.

In parallel to Trak testing, an HCP technician employed at the site analyzed an additional aliquot of the original semen specimen on a Computer Aided Semen Analysis (CASA) system (Hamilton-Thorne CEROS™ Computer Aided Semen Analysis system) and recorded the results in M/mL. Study subjects, testers, and reference method operators were blinded to the test results from the other testers during the clinic visit.

Following the clinical study, lay readers were presented with each of the Props run by lay users at the clinical sites, and asked to interpret each result into one of three categories: ≤ 15 M/mL, 15–55 M/mL, or > 55 M/mL according to the product instructions. The lay interpretations were compared to the categorized reference CASA results from each clinical site. A summary of this analysis is provided below:

		Reference Value		
		≤ 15 M/mL	15–55 M/mL	> 55 M/mL
Subject Interpretation	≤ 15 M/mL	56	8	1
	15 – 55 M/mL	4	75	3
	> 55 M/mL	0	8	84

Trak showed the following agreements for each test result range compared to the CASA reference method:

15 M/mL or below: 93.3%
Between 15 M/mL and 55 M/mL: 82.4%
Above 55 M/mL: 95.5%

4. Clinical cut-off**:**

Not applicable

5. Expected values/Reference range:

Not applicable

N. Instrument Name:

Trak® Male Fertility Testing System

O. System Descriptions:

1. Modes of Operation:

   Not applicable

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

   Yes _____ or No ____X____

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

   Yes _____ or No ___X_____

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:

   No specimen identification is available.

4. Specimen Sampling and Handling:

   The semen sample should be collected in the sample collection cup provided with the kit. After sample collection, the lid is placed on the cup and the sample swirled in the cup for at least 15 seconds. The sample should be allowed to liquefy at room temperature for at least 30 minutes before testing. The test can be performed up to 2 hours after sample collection. It is recommended that users allow 2 to 7 days without ejaculating before collecting a semen sample. Condoms and lubricants should not be used when collecting a semen sample. Protective gloves are recommended when performing the test for someone else. Hands should be washed with soap and water before and after handling the semen sample or any component of the test kit.

5. Calibration:

   Not applicable

6. Quality Control:

The QC material is based on a suspension of polymer beads with a density range that overlaps with sperm cells. When tested on Trak, the QC material produces results that resemble the result produced with a semen sample. There are two control levels. Control A produces a Trak result in the MODERATE range close to the 15 M/mL cut-off (at approximately 17.5 M/mL). Control B produces a Trak result in the LOW range (at approximately 7.5 M/mL). Control A will be provided as part of the Trak system, while Control B will be available through customer service.

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

Cleaning Robustness

A study was conducted to assess whether the Trak Engine performs adequately after repeated cycles of cleaning and disinfection as would occur during end-use. Trak Props were tested in 10 replicates at each of the four different sperm concentrations intended to challenge the 15 M/mL threshold and 55 M/mL feature: approximately 10 M/mL, 20 M/mL, 45 M/mL and 65 M/mL. One set of Props was tested before cleaning and disinfection, and one set of Props was tested after 50 cycles of cleaning with soap and water and disinfection with Super Sani-Wipes, according to the proposed user instruction. Engine spin rates were checked against specifications before and after cleaning and disinfection. The data support the robustness of the Trak Engine to the intended cleaning and disinfection protocol.

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.