510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

K150817

B. Purpose for Submission:

New Device

C. Measurand:

Glucose in fresh capillary whole blood obtained from the fingertip

D. Type of Test:

Quantitative, Amperometric Assay (Glucose Oxidase)

E. Applicant:

Labstyle Innovations Ltd.

F. Proprietary and Established Names:

Dario Blood Glucose Monitoring System

G. Regulatory Information:

1. Regulation section:

   21 CFR§ 862.1345, Glucose Test System
   21 CFR § 862.1660; Quality Control Material (assayed and unassayed)

2. Classification:

   Class II, Class I (exempt)

3. Product code:

   NBW, CGA, JJX

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for Use below.

2. Indication(s) for use:

   The Dario Blood Glucose Monitoring System consists of the Dario Blood Glucose Meter, Dario Glucose Test Strips, Dario Glucose Control Solutions and the Dario App as the display component of the Dario Blood Glucose Monitoring System. The Dario Blood Glucose Monitoring System is intended for the quantitative measurement of glucose (sugar) in fresh capillary whole blood samples drawn from the fingertips. The Dario Blood Glucose Monitoring System is intended to be used by a single person and should not be shared.

   The Dari Blood Glucose Monitoring System is intended for self-testing outside the body (in vitro diagnostic use) by people with diabetes at home to monitor the effectiveness of diabetes control. The Dari Blood Glucose Monitoring System should not be used for the diagnosis of or screening of diabetes or for neonatal use.

   The Dario Blood Glucose Test Strips are for use with the Dario Blood Glucose Meter to quantitatively measure glucose (sugar) in fresh capillary whole blood samples drawn from the fingertip.

   The Dario™ Glucose Control Solutions are for use with the Dario™ Blood Glucose Meter and the Dario™ Blood Glucose Test Strips to check that the meter and test strips are working together properly and that the test is performing correctly.

3. Special conditions for use statement(s):

- For Over-the-Counter use
- Single-patient use only
- Not for testing glucose levels of neonates
- Not for the diagnosis of, or screening for diabetes
- Not for testing glucose levels of arterial or venous blood
- Not for testing glucose from sites other than the fingertip
- Not for testing patients critically ill, in shock, dehydrated or hyperosmolar

4. Special instrument requirements:
   Dario Blood Glucose Meter
   Apple platform Smart Mobile Device, with iOS 6.1 or above

I. Device Description:

The Dario Blood Glucose Monitoring System consists of the Dario Blood Glucose meter (dongle), 25 Dario Test Strips housed in a disposable cartridge (sold separately), lancets (sold separately), Dario Control Solution Levels 1 and 2 (sold separately), Disposable Covers (for the mobile devices), User Manual and Quick User Guide, the Dario Application Software (needs to be downloaded from App Store or Google Play). The Dario BGMS can be used with Apple platform smart mobile devices, with operating system versions iOS 6.2 or above. The Dario Control solutions were previously cleared in k082683 as SD Check Gold and are renamed in this submission.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Gmate SMART Blood Glucose Monitoring System; Philosys, Inc.

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

   K131230

3. Comparison with predicate:

Similarities		
Item	Device Dario Blood Glucose Monitoring System	Predicate Gmate SMART Blood Glucose Monitoring System (K131230)
Indication For Use	Intended for the quantitative measurement of glucose in fresh capillary blood samples by people with diabetes at home to monitor the effectiveness of diabetes control	Same
Assay Detection Method	Amperometry	
Enzyme	Glucose Oxidase	
Measuring Range	20-600 mg/dL	
Hematocrit Range	20-60%	Same
Altitude	10,000 feet	Same
Coding	Not required	Same
Display	Connected to smart-device or mobile device to display measurement results	Same
Power Source	Powered by audio phone	Same

Similarities		
Item	Device Dario Blood Glucose Monitoring System	Predicate Gmate SMART Blood Glucose Monitoring System (K131230)
	jack connected to smartphone or mobile device	
Operating System	iOS	Same

Differences		
Item	Device	Predicate
Sample volume	0.3 µL	0.5 µL
Test time	6 sec	5 sec
Sample type	Fingertip	Fingertips, forearm, upper arm, palm, thigh or calf
Temperature Range	50-113^{0}F (10-45^{0}C)	50-104^{0}F (10-40^{0}C)
Dimensions LxWxH (mm)	40.2 x 16.1 x 9.8	43 x 21 x 9
Weight (g)	4.0	4.2
Software Application	Dario App	Gmate SMART App

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

ISO 10993-1:2003, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.

EN 13640, Stability Testing of In Vitro Diagnostic Reagent

IEC 61010-1:2001, Safety requirements for electrical equipment for measurement, control and laboratory use – Part 1: General Requirements.

EN 61326-1:2006, Electrical equipment for measurement, control and laboratory use – EMC requirements part 1: General requirements.

EN 61326-2-6, Electrical equipment for measurement, control and laboratory use - EMC requirements Part 2-6: Particular requirements – In vitro diagnostic (IVD) medical equipment

IEC 61010-2-101:2002, Safety requirements for electrical equipment for measurement, control and laboratory use – Particular requirements for In Vitro Diagnostic (IVD) Medical Equipment.

IEC 60068-2-64:1993, Environmental testing Part 2: Test methods – Test Fh: vibration, broad-band random (digital control) and guidance.

CLSI EP6-A:2005, Interference Testing in Clinical Chemistry, Approved Guideline

CLSI EP7-A2:2003, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

L. Test Principle:

The Dario Blood Glucose Monitoring System measures glucose electrochemically. The glucose biosensor is capable of recognizing the glucose present in whole blood or control solutions by virtue of the glucose specificity of the enzyme glucose oxidase present on the glucose test strip. A voltage is applied and the glucose concentration is calculated by the meter from the electrical current. The final results are communicated to the smart mobile device through the audio jack.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The sponsor performed within-run precision studies using venous whole blood spiked to five (5) different glucose concentration ranges (30 to 50, 51 to 110, 111 to 150, 151 to 250, and 251 to 400 mg/dL). Fifty (50) samples were prepared at each glucose level, and each sample was analyzed in duplicate for a total of 100 results per glucose level. Results were collected using three (3) test strip lots and 10 meters. Results are summarized below:

Within-run precision for glucose:
Test Strip Lot 1

Glucose Level (mg/dL)	Number of tests	Mean (mg/dL)	SD (mg/dL)	CV (%)
30 to 50	100	48.3	1.1	2.4
51 to 110	100	74.7	1.3	1.7
111 to 150	100	172.2	1.8	1.4
151 to 250	100	216.0	6.7	3.1
251 to 400	100	344.2	5.6	1.6

Test Strip Lot 2

Glucose Level (mg/dL)	Number of tests	Mean (mg/dL)	SD (mg/dL)	CV (%)
30 to 50	100	47.6	1.2	2.6
51 to 110	100	73.7	2.1	3.0
111 to 150	100	125.4	2.6	2.1
151 to 250	100	213.1	3.4	1.6
251 to 400	100	339.2	6.7	2.0

Test Strip Lot 3

Glucose Level (mg/dL)	Number of tests	Mean (mg/dL)	SD (mg/dL)	CV (%)
30 to 50	100	47.8	1.3	2.7
51 to 110	100	73.7	1.6	2.2
111 to 150	100	126.3	1.8	1.4
151 to 250	100	214.4	5.1	2.4
251 to 400	100	346.0	7.6	2.2

Between-day precision was evaluated using three levels of glucose control solutions with concentrations 30 to 50, 96 to 144, and 280 to 420 mg/dL. Per day, each sample was measured with three (3) test strip lots and 10 meters. These tests were performed over 10 days, for a total of 300 results per glucose level. Results are summarized below:

Between-day precision for glucose:
Test Strip Lot 1

Glucose Level (mg/dL)	Number of tests	Mean (mg/dL)	SD (mg/dL)	% CV
30 to 50	100	48.9	2.5	5.2
96 to 144	100	103.0	3.2	3.1
280 to 420	100	294.5	7.0	2.4

Test Strip Lot 2

Glucose Level (mg/dL)	Number of tests	Mean (mg/dL)	SD (mg/dL)	% CV
30 to 50	100	48.7	2.3	4.7
96 to 144	100	104.8	3.2	3.0
280 to 420	100	296.7	8.6	2.9

Between-day precision for glucose:
Test Strip Lot

Glucose Level (mg/dL)	Number of tests	Mean (mg/dL)	SD (mg/dL)	% CV
30 to 50	100	48.0	2.0	4.2
96 to 144	100	103.9	2.5	2.4
280 to 420	100	295.5	5.4	1.8

b. Linearity/assay reportable range:

Linearity was evaluated in 2 studies:

Linearity in Study #1 was evaluated using three (3) test strip lots and 11 mixed pools of venous blood with glucose concentrations at 16, 86, 157, 230, 301,367,438, 510, 578, 649 and 728 mg/dL, as measured by the YSI reference method.

Linearity in Study #2 was evaluated at low concentrations, using three (3) test strip lots and six (6) mixed pools of venous blood with glucose concentrations at 16, 37, 57.5, 78.4, 99.2 and 118.8 mg/dL as measured by the YSI reference method. In both studies, each level was measured in replicates of five (5) with each of three (3) test strip lots and the values from the Dario™ Blood Glucose Monitoring System were compared with those obtained from the YSI-2300. Results from the combined regression analysis are as follows:

$y = 1.008x – 1.459$, $r^2 = 0.998$

The results of the study support the sponsor's claimed glucose measurement range of 20-600 mg/dL.

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

Traceability:
The Dario Blood Glucose Monitoring System is traceable to NIST SRM 917b. The method comparison study was performed using the candidate device and YSI as the reference method (see Section 2.a. above)

Test Strip Stability:
Test strip stability was assessed in accelerated and real-time studies. The testing protocols and acceptance criteria were reviewed and found to be acceptable. The manufacturer claims shelf life stability of 24 months and an open-vial stability of 6 months at the recommended storage conditions of 36°F-90°F (2°C-32°C) and 10-90% relative humidity. The instructions state not to refrigerate open test strip cartridges or put test strips in a freezer.

Control Solution Value Assignment and Stability:
The Dario Glucose Control Solutions Level 1 and Level 2 were previously cleared (k082683). The control solutions offered are Level 1 (range 90-140mg/dL) and Level 2 (range 170-240 mg/dL). The value assignment protocol and the stability protocols and acceptance criteria were reviewed under k082683. The control solutions are stable for 24 months and for 3 months after opening when stored at the recommended storage conditions of 46°F-86°F (8°C-30°C) and 10-90% humidity.

d. Detection limit:

See linearity study in Section M1b above.

e. Analytical specificity:

Interference studies were performed by spiking venous blood with two levels of glucose concentrations (65 and 250 mg/dL). Each of these samples was divided into a test pool and a control pool and each potential endogenous and exogenous interfering substance was added to the test pool. Each substance was tested at three concentrations. Each sample was analyzed 10 times with the Dario meter and the % difference between the individual measurements and the reference (YSI) calculated. The sponsor defines no significant interference as ≤10% difference relative to YSI. Results are presented in the table below:

Potential Interfering Substances Tested	**Concentration with no Significant Interference (mg/dL)**
Acetaminophen	6 mg/dL
Acetyl-salicylic acid	120 mg/dL
Ascorbic Acid (Vit. C)	4 mg/dL
Bilirubin	35 mg/dL
Cholesterol	506 mg/dL
Creatinine	30 mg/dL
Dopamine	2.5 mg/dL
Ethanol	400 mg/dL
Fructose	15 mg/dL
Galactose	60 mg/dL
Gentisic Acid	1.8 mg/dL
Glutathione	4.6 mg/d
Hemoglobin	200 mg/dL
Heparin	0.003 mg/dL (3000 U/L)
Ibuprofen	50 mg/dL
Lactose	25 mg/dL
Levodopa	4 mg/dL
Maltose	132mg/dL
Maltotetraose	120 mg/dL
Maltotriose	240 mg/dL
Mannitol	800 mg/dL
Mannose	5 mg/dL
Methyl-Dopa	2 mg/dL
Sodium Fluoride	200 mg/dL
Sodium Salicylate	63 mg/dL
Sorbitol	10 mg/dL
Tetracycline	5 mg/dL
Tolazamide	5 mg/dL
Tolbutamide	100 mg/dL

Triglyceride	900 mg/dL
Urea	500 mg/dL
Uric Acid	11 mg/dL
Warfarin	1 mg/dL
Xylitol	25 mg/dL
Xylose	50 mg/dL

The following limitations have been added to the labeling:

If you are taking acetaminophen containing drugs (e.g. Tylenol) or Vitamin C (ascorbic acid) you may get inaccurate results with this system.

If you have a disease or condition in which uric acid levels in your blood may be elevated (>11 mg/dL), such as gout, you may get inaccurate results with this system.

If you have very high levels of triglyceride (>810mg/dL), you may get inaccurate results with this system.

This system should not be used when undergoing xylose absorption tests.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

See lay user study in section M.3.c

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):

To assess the performance of the Dario Blood Glucose Monitoring System in the

hands of the intended users the sponsor performed a study with 100 diabetic lay user participants. Participants obtained and tested their own fingerstick samples with the Dario BGMS. Blood glucose results from the Dario meter obtained by the lay user were compared to the YSI 2300 reference value. The samples ranged from 24 to 479 mg/dL as measured by YSI. The results are summarized in the tables below:

Lay-user vs. YSI:

For glucose concentrations <75 mg/dL

within ± 5 mg/dL	within ± 10 mg/dL	within ± 15 mg/dL
4/11 (36.4%)	9/11 (81.8%)	11/11 (100%)

For glucose concentrations ≥ 75 mg/dL

Within ± 5 %	within ± 10 %	within ± 15 %	within ± 20 %
39/89 (43.8%)	68/89 (76.4%)	85/89 (95.5%)	88/89 (98.9%)

Results of linear regression analysis:

$y = 0.992x + 2.782$, $r^2 = 0.9967$.

Subject usability was assessed using a questionnaire. 94% of subjects reported the operation of the meter to be average, easy, or very easy. 90% of subjects reported being satisfied or very satisfied with the meter.

Flesch-Kincaid readability assessment was conducted and the results demonstrated that the User Manual, quick start guide, test strip package insert and control solution package insert were written at an 8th grade level or less.

4. Clinical cut-off

Not applicable

5. Expected values/Reference range:

Expected glucose values without diabetes:

Status	Range
Before eating (FPG)	<100 mg/dL
Two hours after meals	<140 mg/dL

American Diabetes Association: Standard of Medical Care in Diabetes 2015, Diabetes Care, vol.38, supplement 1, S14-S87, 2015.

N. Instrument Name:

Dario Blood Glucose Meter

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:
   There is no sample identification function with this device. Samples are applied directly to the test strip as they are collected.

4. Specimen Sampling and Handling:
   The glucose test is intended to be used with capillary whole blood from the finger, palm, and forearm only. The whole blood sample is applied directly to the test strip by capillary action.

5. Calibration:
   There is no calibration required by the user for the DA12-B1 and DA12-B2 blood glucose meters. The meters are automatically coded.

6. Quality Control:
   Two levels of glucose control solutions are available with this system, but are sold separately. Recommendations on when to test the control materials are provided in the labeling. The user is cautioned not to use the meter if the control result falls outside these ranges.

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

1) Hematocrit Study: The effect of different hematocrit levels on the performance of the Dario Blood Glucose Monitoring System was evaluated using venous whole blood samples with hematocrit levels of 15, 20, 25, 30, 35, 40, 45, 50, 55, 60 and 65% spiked with glucose to achieve three (3) concentrations at 50-70, 100-200, and 250-300 mg/dL. Each sample was then tested using 10 Dario Meters and three (3) lots of test strips. The values were compared with those obtained from YSI 2300 analyzer. The % biases relative to YSI were acceptable within the claimed hematocrit range of 20 to 60%.

2) Altitude study: Capillary fingerstick samples with glucose concentrations ranging from 48 to 423.5 mg/dL were collected from 52 participants at 10,152 feet above sea level. Results were obtained from each participant sample in on the Dario for each of 3 test strip lots compared to additional fingerstick samples measured on the YSI. The results demonstrate acceptable bias to YSI to support the claims in the labeling that altitudes up to 10,000 feet (3048 meters) have no significant effect on blood glucose measurements from the Dario meter.

3) Sample volume study: The sponsor performed a study to support the claimed minimum sample volume for the Dario system. Blood samples with three levels of glucose (50-65, 100-120, and 200-250 mg/dL) were tested at six sample volumes (0.1, 0.2, 0.3, 0.4, 0.5, 0.75, 0.8, and 1.0 µL) and values obtained were compared to YSI values. Results support the claimed minimum sample volume of 0.3 µL.

4) Temperature and humidity studies: The sponsor performed temperature and humidity studies using venous blood samples at five glucose concentrations (approximately 60, 110, 200, 300, and 475 mg/dL) to evaluate temperatures ranging from 12±2°C to 43±2°C and relative humidity from 10% to 90%. Meter results were compared to YSI values. Six temperature and humidity combinations were tested including low temperature/low humidity, low temperature/high humidity, average temperature/low humidity, average temperature/high humidity, high temperature/low humidity, and high temperature/high humidity. The results support the claims in the labeling that the system can be used in conditions of 50 to 113°F (10 to 45°C) with relative humidity of 10 to 90%.

5) Infection Control Studies: The device is intended for single-patient use only. Super Sani-Cloth wipes with EPA registration #9480-4 were validated demonstrating complete inactivation of live hepatitis B virus for use with the test strips cartridge cap, Dario meter and Dario BGMS housing device . The sponsor also demonstrated that there was no change in performance or in the external materials of the test strips cartridge cap, Dario meter and Dario BGMS housing device after 156 cleaning and disinfection cycles (one cycle includes one cleaning wipe plus one disinfecting wipe) to simulate 3 years of single-patient use. Labeling was reviewed for adequate instructions for the validated cleaning and disinfection procedures.

6) EMC testing was certified and appropriate compliance certificates were provided.

7) Customer service is available Monday through Friday 9:00 am to 5:00 pm PST by calling 1-800-895-5921.

Q. Proposed Labeling:

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

R. Conclusion:

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