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WHITE PAPER:
PERFORMANCE EVALUATION FOR DARIO BLOOD GLUCOSE MONITORING
SYSTEM ACCURACY EVALUATION



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1. Purpose

To evaluate accurate testing in actual conditions of use of the Dario™ Diabetes Management Solution. With reference to the more stringent performance requirements to come into effect in May 2016 under the ISO 15197:2013, In vitro diagnostic test systems- Requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus.

2. Scope

2.1 The device used in this study was the Dario™ Blood Glucose Monitoring Solution (BGMS).

The device comprises of the following components:

- Dario™ Test Strip
- Dario™ Lancing Device
- Dario™ Blood Glucose Meter (Dongle)
- Smart Mobile Device Software

2.2 Intended Use

Dario™ Blood Glucose Monitoring System (BGMS) is indicated for the quantitative measurement of glucose in fresh capillary whole blood samples drawn from the fingertips. The system is intended to be used by a single patient and should not be shared.

The Dario™ BGMS is intended for self-testing outside the body (in vitro diagnostic use) by people with diabetes at home as an aid in monitoring the effectiveness of diabetes control.

The Dario™ BGMS is not to be used for the diagnosis of or screening of diabetes or for neonatal use.

2.3 The Dario Glucose Test Principle

The test is based on electrochemical biosensor technology and the principle of capillary action. The electrical current generated by the reaction of glucose with the reagent of the strip is measured by the meter and is displayed on an iOS-based smart mobile device (e.g., iPhone, iPod, iPad) as the corresponding blood glucose level. The strength of the current produced by the reaction depends on the amount of glucose in the blood sample.

2.4 Dario Evaluation History and Technical Background

Requirements of ISO 15197:2013; states that "95% of the measured glucose values shall fall within either + 0.83 mmol/L (+15 mg/dL) of the average

measured values of the reference measurement procedure at glucose concentrations <5.55 ml/L (<100 mg/dL) or within +15% at glucose concentrations >5.55 mmol/L (>100 mg/dL); and: "99% of individual glucose measured values shall fall within zones A and B of the Consensus Error Grid (CEG) for type 1 diabetes."

Table 1

Agency/Standard	Glucose Concentration	Limits for Deviation from the Reference Standard for Individual Results	Criteria for Accuracy Across All Results
ISO 15197:2003	< 75 mg/dL	± 15 mg/dL	95% within limits
	≥ 75 mg/dL	± 20%	
ISO 15197:2013	< 100 mg/dL	± 15 mg/dL	95% within limits
	≥ 100 mg/dL	± 15%	

Dario™ technology is based on OEM GOD strip technology which was recently evaluated by an independent laboratory. The OEM GOD strip technology BGMS accuracy study was performed by Institut für Diabetes-Technologie Forschungs- und Entwicklungsgesellschaft mbH an der Universität Ulm in January 2014. Three test strip lots were tested demonstrating accuracy of 95.5%, 98%, and 97%. The study results confirmed that the OEM system meets the accuracy requirements of the ISO 15197:2013. Thus indicating that the Dario™ strip technology complies with the same ISO 15197:2013 requirements.

A comparative observational user performance study was concluded on the Dario Diabetes Management Solution in March 2015. The objectives of the study were to evaluate the accuracy of blood glucose level results obtained from using Dario BGMS compared to YSI. The study conducted on 368 subjects showed that Dario complies with the requirements of ISO 15197:2013.

3. Overview

3.1 The study was conducted in an internal laboratory. The following individuals were involved in the performance of this study:

Operators

- Mr. SH Ha (Medical Technologist, SD Biosensor, Inc.)
- Ms. HS Park (QC, SD Biosensor, Inc.)
- Ms. YS Ahn (Nurse, YONSEI Medical Clinic)

3.2 Study condition: Overall studies by SMBG meter were followed in accordance with the Dario BGM system User Instruction Guide, i.e. same intended use condition.

4. Test Procedure

The Study was conducted over a day period, Dec 1 2014. A total of 78 subjects were recruited. Fresh capillary blood was obtained from each subject. The samples were adjusted to have a total of 100 samples, to cover a wide range of blood glucose concentrations, as described at the ISO 15197:2013 guideline. The range of glucose concentration that was tested 24-468 mg/dL. The samples were tested by using 6 Dario™ Blood Glucose Meters and Dario™ Test Strip (three different test strip lots: Lot No.: DBGS-20140109001, DBGS-20140109002, DBGS-20140109003) and by YSI, for a total of 600 results.

5. Result Analysis

The results and accuracy tables are represented in accordance with ISO 15197:2013 Standard for system accuracy comparing the results obtained with Dario™ BGMS to YSI.

Investigator presented regression equations with confidence intervals and plots showing all data points according to ISO 15197:2013.

Sample Distribution

Table 2: The category of glucose concentration tested
(These glucose concentrations were determined by YSI, reference equipment.)

Bin #	Glucose concentration (mg/dL)	n / total	Percentage of samples	Comment
1	< 50	5/100	5%	<u>modified capillary blood sample</u>
2	50 ~ 80	7/100	7%	<u>modified capillary blood sample</u>
		8/100	8%	capillary blood sample
3	81 ~ 120	20/100	20%	capillary blood sample
4	121 ~ 200	30/100	30%	capillary blood sample
5	201 ~ 300	15/100	15%	capillary blood sample
6	301 ~ 400	5/100	5%	capillary blood sample
		5/100	5%	<u>modified capillary blood sample</u>
7	> 400	5/100	5%	<u>modified capillary blood sample</u>

Evaluation Results

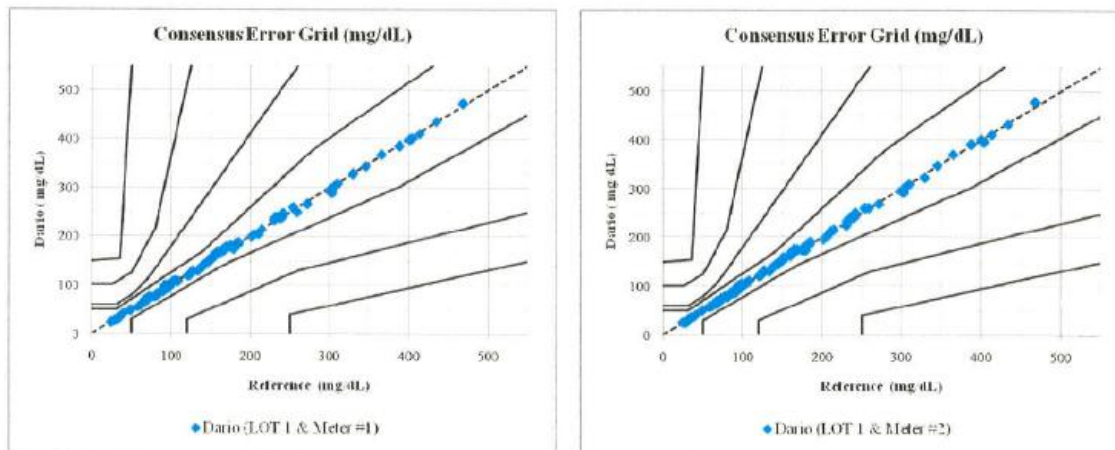
Individual results of the blood glucose monitoring system were plotted as the dependent variable and the average of the duplicate REF value as the independent variable:

Identical scales and intervals were used for the x- and y-axes. Slope and y-intercept were calculated by regression analysis procedure (EXCEL/TOOL/DATA ANALYSIS/Regression Analysis).

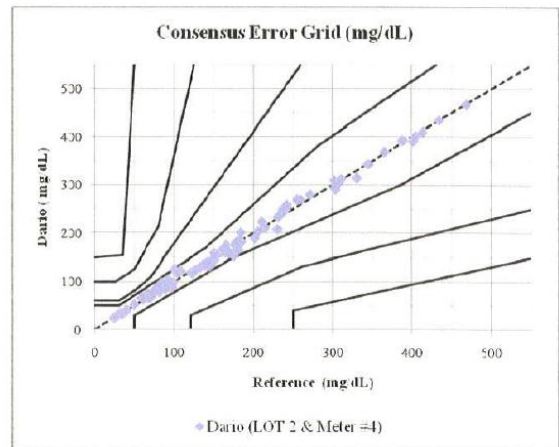
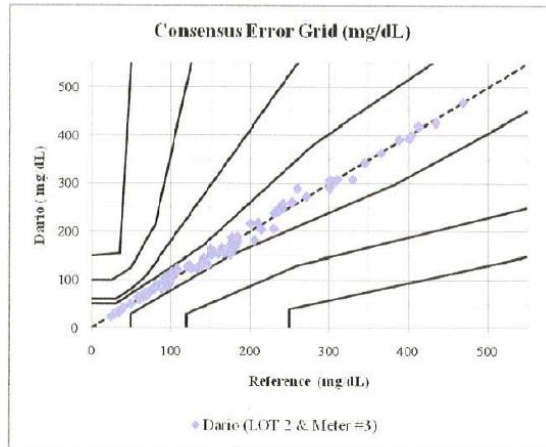
Table 3: Regression analysis result

Strip Meter	Dario(LOT 1)		Dario(LOT 2)		Dario(LOT 3)	
	Meter #1	Meter #2	Meter #3	Meter #4	Meter #5	Meter #6
N	100	100	100	100	100	100
Interval of measured glucose value	24-473	26-479	24-468	25-466	26-465	28-465
Slope	0.993	0.996	0.991	0.992	0.991	0.992
Y-intercept	2.313	2.372	2.109	2.588	3.869	3.443
R	0.9992	0.9993	0.9965	0.9966	0.9993	0.9992
R ²	0.9985	0.9986	0.9929	0.9932	0.9986	0.9984
N	200		200		200	
Interval of measured glucose value	24-479		24-468		26-465	
Slope	0.994		0.991		0.992	
Y-intercept	2.343		2.348		3.656	
R	0.9993		0.9965		0.9993	
R ²	0.9985		0.9931		0.9985	
N	600					
Interval of measured glucose value	24-479					
Slope	0.992					
Y-intercept	2.782					
R	0.9983					
R ²	0.9967					

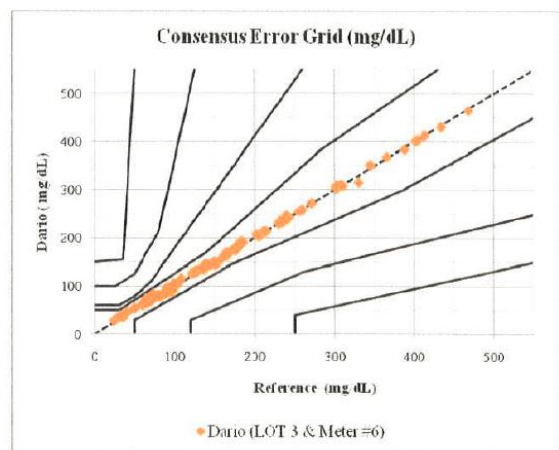
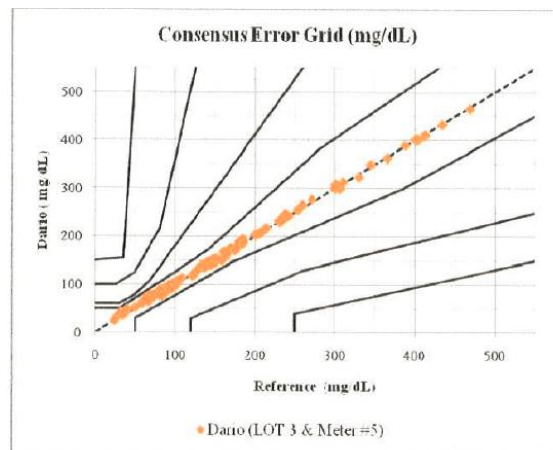
Figure 1 Consensus Error Grid (mg/dL)
Lot 1



Lot 2



Lot 3



6. Conclusions

The Performance Evaluation was performed according to the ISO 15197:2013, 6.3 System accuracy. According to the result analysis of this evaluation, the Dario™ BGMS showed excellent correlation coefficient ($R= 0.9993, 0.99965, 0.9993$) with YSI reference method. The results fell within the acceptance criteria of ISO15197:2013 for system accuracy requirements:

"Ninety-five percent (95%) of the measured glucose values shall fall within either $\pm 15\text{mg/dL}$ of the average measured values of the reference measurement procedure at glucose concentrations $< 100\text{mg/dL}$ or within $\pm 15\%$ at glucose concentrations $\geq 100 \text{ mg/dL}$ ", and– "99% of individual glucose measured values shall fall within zones A and B of the Consensus Error Grid (CEG) for type 1 diabetes". Additionally, 100% of individual glucose measured values were within zones A of the Consensus Error Grid (CEG) for type 1 diabetes.

The results of this Performance Evaluation study together with the results of the independent study performed in Germany and the user performance study all support the conclusion that the Dario™ BGMS meets the accuracy requirements of EN ISO15197:2013.