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Clinical Study Report

For the Blood Glucose Monitoring System

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Meter Model Number：	TD-4116
Strip Model Number：	TD-4392

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Date: 2021.09.23 15:05:14 EEST
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Location: Moldova

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For TD-4116 Blood Glucose Monitoring System

Abstract

Objective:

The aim of the study was to assess the accuracy and reliability of blood glucose monitoring system in the clinical studies according to international standard ISO 15197: 2013(E) and EN ISO 15197: 2015 criteria and more stringent guidelines.

Methods:

The study sample was collected from 160 subjects comprised 12 patients with types 1 diabetes and 114 patients with types 2 diabetes, and 34 people with type unknown. The study sampled blood specimens via fingertip stick from participants with diabetes in multiple sites. Three reagent lots of test strips were used.

Results:

The evaluated devices meet the ISO total error criteria. For 97.1% of the fingertip blood samples, the difference between meter and laboratory measurements of glucose be 15% when the laboratory glucose value is ≧5.5mmol/L (≧100mg/dL) and 0.83mmol/L (15mg/dL) of the laboratory glucose value when the glucose concentration is <5.5mmol/L (<100mg/dL) according to both the CLSI and ISO recommendations.

Conclusion:

The studies verify currently available devices of blood glucose monitoring exceeded the minimum acceptable accuracy when compared test results with laboratory methods based on standard guideline.

1. Introduction

Diabetes is a chronic illness that requires complex and continuous medical care. According to the International Diabetes Federation (IDF) analysis the prevalence of diabetes mellitus and impaired glucose tolerance (IGT) showed 366 million people have diabetes in 2011, and estimated the number will have risen to 552 million[1]. Diabetes care is complex and requires multi factorial risk reduction strategies beyond glycemic control. Clinical evidences have shown the importance of tight blood glucose control for diabetes patients[2].

A medical device is any article including software, intended to be used by humans for the diagnosis, prevention or monitoring of a disease such as blood glucose meters [in vitro diagnostics (IVD)]. Early development of health informatics deal with the resources,

devices, and methods required to optimize the acquisition, storage, retrieval, and use of information in health care.

Currently, a growing number of software applications are being developed for use on mobile platforms, which include smart phone, tablet computers, and personal digital assistants. As these mobile platforms become more user friendly, computationally powerful, and readily available, innovators have begun to develop mobile apps of increasing complexity to leverage the portability mobile platforms can offer. Some of these new mobile apps are specifically targeted to assisting individuals in their own health and wellness management[3, 4].

2. Study Objectives

This study was conducted to evaluate system accuracy and reliability of glucose monitoring devices in clinical and laboratory studies. The study was conducted on blood glucose meters to verify proper functioning prior was available for health providers and patients in the clinical.

3. Background

The portable glucose meter with test strips is a system that is used to test the level of glucose in capillary blood. A portable glucose meter is a handy tool for diabetics can easy to control their blood glucose variation that provide a convenient selection for diabetics to manage their blood glucose concentration at home or anywhere. The blood glucose monitoring system also offered a rapid and accurate means let health care professionals can easy to track patient's conditions.

This system of blood glucose monitoring has a good technology of electronic-chemic reaction with the enzyme structure of glucose oxidase (GOD) enzyme. The system took the enzyme (GOD) for test strips to perform clinical trial for measuring blood glucose concentration in this study. The advantage could be reduced material interference as oxygen saturation, hematocrit etc. to gain the correct test results.

The clinical accuracy study was conducted according to the analytical requirements of ISO 15197: 2013(E) and EN ISO 15197: 2015 [5,6,15]. This International Standard specifies requirements are intended for blood glucose monitoring systems used by lay persons and health care professionals. All systems are designed to meet the individual needs of various people with diabetes, and therefore have different types of features.

4. Selection of Study Population

4.1 Inclusion Criteria

The study recruited adult people over 18 years of age, and the participants can be people with diabetes type 1 or diabetes type 2, people with the metabolic disease or healthy people with family history of diabetes have high risk symptom as either hyperglycemia or hypoglycemia history. Patients did not take any other substances which could influence glucose measurement of the blood glucose meters, as high dosages of vitamin C, salicylate etc. Hematocrit levels were within normal range.

4.2 Exclusion Criteria

4.2.1 The blood sample have occurred coagulation in test process, or severe acute disease.

4.2.2 Requirements according to ISO 15197: 2013(E) and EN ISO 15197: 2015[6.15], results from the reference method were evaluated to verify sample stability. If the change between first and last reference values indicate glucose instability in the sample based on predetermined criteria considering that reference values differ by >4% at glucose ≧ 100mg/dL (≧ 5.55mmol/L) or >4mg/dL (>0.22mmol/L) at glucose <100mg/dL (<5.55mmol/L) then results for that sample have to be rejected.

5. Material and Methods

5.1 Study Design and Good Clinical Practice Conformity

This trial was a prospective, comparison, and multicenter study. This trial consisted of one visit and was conducted at three investigational sites. This trial conducted in accordance with the principles of the Declaration of Helsinki and the applicable guidelines for Good Clinical Practice whichever provided the greater protection of the individual. Prior to study participation was obtained individual assent or agreement to participate in this study. The investigation study was performed in 2013.

5.2 Study Subjects

The study consisted of 160 subjects, 22 to 84 years of age, patients with type 1 and 2 diabetes and intended users. Patients did not take any other substances which could influence glucose measurement. The study comprised 12 with types 1 diabetes and 114 with types 2 diabetes, and 34 people with type unknown. Mean age, and medium age were 54.1 years, and 55.5 years. Hematocrit levels were within normal range (median 42.5%, range 31%-54%). Patients participated in a study on accuracy and safety of a new implantable glucose biosensor.

5.3 Study Devices

Manufacturer: TaiDoc technology

Technology and Features (Table 1)

Blood sampling	**Capillary whole blood**
Sample volume	0.7μL
Measuring range	10–600mg/dL (0.6–33.3mmol/L)
Analysis time	7 seconds
Operating temperature	10-40°C
Operating humidity	<85% R.H.
Hematocrit range	30 - 55%
Measurement technology	glucose oxidase (GOD)
Calibration	Plasma

Meters (Table 2)

Serial number (S1)	Serial number (S2)	Serial number (S3)
411611234000001A – 6A	411611234000007A – 12A	411611234000014A – 20A

Test strips (Table 3)

Test strips:					
Lot number	Expiry	Lot number	Expiry	Lot number	Expiry
TD13A105-C0E	2014-07	TD13C111-B0E	2014-09	TD13D217-C0B	2014-10

Control solutions (Table 4)

Control solutions:					
Level 1 (Y1)	Expiry	Level 2 (G2)	Expiry	Level 3 (R3)	Expiry
YA13E001	2015-05	GA13B001	2015-02	RA13D001	2015-04

5.4 Reference Equipment

The study was used as the reference laboratory method using the glucose oxidase method – Yellow Springs 2300. YSI 2300 manufactured by YSI incorporated (Yellow Springs, OH) that chemistry using the glucose oxidase method. Another reference laboratory method in this study was used the Hexokinase method.

The calibration accuracy of the YSI analyzer at each study site was validated by testing National Institute of Standards and Technology (NIST) secondary reference material SRM 965a which consists of four levels of glucose concentrations.

The glucose reference measurement procedure is the aliquots of the sample shall be centrifuged immediately after collection to obtain plasma. Glucose reference values shall

be the average of at least duplicate measurements.

5.5 System Accuracy

System accuracy capability shall be evaluated with fresh blood samples by comparing glucose measurements from the blood-glucose monitoring system to reference glucose values. Ambient temperature shall be maintained at 23 °C ± 5 °C.

The minimum blood specimens must evaluate from 100 different patients with diabetes that blood glucose concentration distributed into seven intervals between 20 and 600mg/dL. The material for this study prepared six devices with three reagent lots of test strips. Each reagent lot measured twice and shall be measured three reagent lots of test strips, which six data of blood glucose were analyzed.

Table 5 the samples distribution of glucose concentrations were for system accuracy evaluation

Percentage of samples (%)	Glucose concentration (mg/dL)	Glucose concentration (mmol/L)
5	≦50	≦2.77
15	>50 to 80	>2.77 to 4.44
20	>80 to 120	>4.44 to 6.66
30	>120 to 200	>6.66 to 11.10
15	>200 to 300	>11.10 to 16.65
10	>300 to 400	>16.65 to 22.20
5	>400	>22.20

5.6 Study Procedure

The study was carried out at the diabetes centers of the clinic and hospital. The blood glucose measurements were used whole blood both of fingertips or venous for assessing the accuracy and reliability of blood glucose monitoring devices to meeting the international standards.

At the study sites, health care professionals tested subject's blood specimens via a fingertip stick apply to the blood glucose monitoring devices and the laboratory method. Each blood specimen was tested with three different lots for a total six readings per sample and tested in duplicate on the YSI analyzer/laboratory equipment of Hexokinase method. The samples were collected by health care professionals and patients with diabetes using a spring-loaded sterile lancet.

Accuracy evaluation for blood glucose meters collected a fresh blood sample from participants' finger stick in the clinical testing. Subjects also agreed to provide a fresh blood sample for hematocrit measurement, and duplicate reference glucose tests were performed

using YSI 2300 analyzer. Eighteen blood glucose meters were included in the clinical testing along with three reagent lots of test strips. All reagent system units for a sample shall be taken from the same vial.

Health care professional obtained a capillary blood sample was tested immediately used six different devices, and approximately 200µl of additional blood was collected into heparinized micro-collection tube duplicate reference glucose tests were performed using the YSI analyzer at each trial site.

In the user performance studies, lay users performed fingertip test on their own after reading the instructions for use. Participants attended this glucose test evaluation when finished it that participant filled in a questionnaire about their using evaluation evaluated this test system and user guide.

6. Statistical Analysis

6.1 Data Analysis and Results Presentation

6.1.1 Determination of System Accuracy Acceptability

The minimum acceptable system of accuracy criteria specified according to first and second edition of ISO 15197 standard guidelines (Table 6).

	Maximum deviation from glucose reference value	
EN ISO 15197: 2003	**At glucose levels <75 mg/dL (<4.2 mmol/L)**	**At glucose levels ≧75 mg/dL (≧4.2 mmol/L)**
	±15 mg/dL (0.83mmol/L)	±20%
ISO 15197: 2013(E)	**At glucose levels <100 mg/dL (<5.5 mmol/L)**	**At glucose levels ≧100 mg/dL (≧5.5 mmol/L)**
EN ISO 15197: 2015	±15 mg/dL (0.83mmol/L)	±15 %

	Presentation of results for system accuracy	
EN ISO 15197: 2003	**At glucose levels <75 mg/dL (<4.2 mmol/L)**	**At glucose levels ≧75 mg/dL (≧4.2 mmol/L)**
	Within ± (5 mg/dL, 10 mg/dL, 15 mg/dL) Within ± (0.28mmol/L, 0.56mmol/L, 0.83mmol/L)	Within ± (5%, 10%, 15%, 20%)
ISO 15197: 2013(E)	**At glucose levels <100 mg/dL (<5.5 mmol/L)**	**At glucose levels ≧100 mg/dL (≧5.5 mmol/L)**
EN ISO 15197: 2015	Within ± (5 mg/dL, 10 mg/dL, 15 mg/dL) Within ± (0.28mmol/L, 0.56mmol/L, 0.83mmol/L)	Within ± (5%, 10%, 15%)

6.1.2 Minimum System Accuracy Performance Criteria

The blood glucose monitoring system shall meet both of the following minimum criteria of ISO 15197 for acceptable system accuracy.

6.1.2.1 95% of the measured glucose values shall fall within either ±15mg/dL (±0.83 mmol/L) of the average measured values of the reference measurement procedure at glucose concentrations <100mg/dL (<5.55mmol/L) or within ±15% at glucose concentrations ≧100mg/dL (≧5.55mmol/L).

6.1.2.2 99% of individual glucose measured values shall fall within zones A and B of the Consensus Error Grid (CEG) for type 1 diabetes.

For this study using calculation tool was in Microsoft Office Excel were performed statistical analysis. According to the device labeling, glucose oxidase is the reference method in this study. The limits of glucose concentration categories are according to as the criterions in EN ISO 15197 version.

6.2 Bias Analysis

For reference analyzer glucose values less than 100mg/dL (<5.5mmol/L) subtract the reference value from the monitor value.

Meter Value (mg/dL/mmol/L) – Reference Value (mg/dL/mmol/L) = Difference (mg/dL)

For reference analyzer glucose values greater than or equal to 100mg/dL (≧5.55mmol/L) subtract the reference value from the monitor value. Divide the difference by reference value. Multiply the result by 100 to obtain the % difference.

$$\frac{\text{Meter Value (mg/dL/mmol/L)} - \text{Reference Value (mg/dL/mmol/L)}}{\text{Reference Value (mg/dL/mmol/L)}} \times 100 = \%\ \text{Difference}$$

6.3 Linear Regression Analysis

Regression analysis can be performed using any of a number of statistical analysis Excel software packages. Perform a linear regression of the data according to the software instructions, placing the reference data on the x-axis and the monitor/meter data on the y-axis. Calculate the correlation coefficient (r), slope and Y intercept.

6.4 Consensus Error Grid Analysis

This second edition of ISO 15197: 2013(E) and EN ISO 15197: 2015 adopts a risk based approach to the requirements for accuracy of glucose meter results using the Consensus Error Grid (CEG) developed for type I diabetes. Stricter system accuracy criteria were required 99% of all results to be in zones A and B of the Consensus Error Grid. The CEG is divided into five zones which are defined by estimated risk to the patients. Based on the consensus of the survey participants, glucose results in zones A and B lead to little or no effect on clinical outcome, whereas results in zones C to E lead to increasing risk of an

adverse outcome.

6.5 Evaluation User Performance

Objectives of this study were an examination of the relative accuracy using capillary blood, reproducibility with control solutions, and an evaluation under everyday conditions. Participants with type 1 or 2 diabetes aged 22 to 84 years old with a long-term experience used blood glucose meter monitored own glucose concentration. This study had recruited 160 patients who used the blood glucose monitoring system to test their own blood glucose. About 107 patients are from the clinic and 53 patients are from the hospital.

7. Results

Characteristics of the 160 participants (80 males and 80 females) was as follow mean age 54.1 (SD ±15.1) years, type 1 diabetes (n=12), type 2 diabetes (n=114). The detailed statistical interpretation of the results of glucose concentration was shown in the Figures. The analysis results of system accuracy evaluation were given in the Tables which followed from the Figures.

For the patients, the value of the readings from the devices was calculated. Results of the Consensus Error Grid analysis are graphically displayed for the blood glucose meters in Figure. Table shows a numerical approach represented an evaluated glucose meter into five regions. For system accuracy, the results used analysis method of the Consensus Error Grid analyzed have achieved 100% values within region A and with no results in region B, C, D, or E.

Table 7 the samples distribution of glucose concentrations were for system accuracy evaluation.

Percentage of samples (%)	Glucose concentration		Quantity of subjects distribution
	mg/dL	mmol/L	
5	≦50	≦2.77	8
15	>50 - 80	>2.77- 4.44	24
20	>80 - 120	>4.44- 6.66	32
30	>120 - 200	>6.66- 11.10	48
15	>200- 300	>11.10- 16.65	24
10	>300- 400	>16.65- 22.20	16
5	>400	>22.20	8

7.1 Subject Demographic Data

The number of patients was assessed at the three study sites; location 1, N=52(32.5%), location 2, N=53(33.1%); and location 3, N=55(34.4%). In this study, 7.5% subjects had type 1 diabetes, 71.25% had type 2 diabetes, and 21.25% did not have diabetes.

Table 8 summarizes the subject demographic information.

Demographic information /Location		Total	Site 1	Site 2	Site 3
Number of subjects (N=)		160	52	53	55
Gender (%)	**Male**	80 (50.00%)	32 (61.54%)	26 (49.06%)	22 (40.00%)
	Female	80 (50.00%)	20 (38.46%)	27 (50.94%)	33 (60.00%)
Age (mean, ranges)		54.11 (22–84)	55.85 (25–76)	54.06 (22–81)	52.51 (22–84)
Diabetes type	**Type I**	12 (7.50%)	1 (1.92%)	8 (15.09%)	3 (5.45%)
	Type II	114 (71.25%)	41 (78.85%)	40 (75.47%)	33 (60.00%)
	None	34 (21.25%)	10 (19.23%)	5 (9.43%)	19 (34.55%)
Treatment	**Oral medicine**	91 (56.88%)	34 (65.38%)	32 (60.38%)	25 (45.45%)
	Insulin	32 (20.00%)	5 (9.62%)	16 (30.19%)	11 (20.00%)
	None	37 (23.13%)	13 (25.00%)	5 (9.43%)	19 (34.55%)

7.2 Incidence of Adverse Events

No hypo- or hyperglycemia events were reported. No bruising or other adverse events were noted at the finger test sites. No other adverse events were reported for the venous. The collections of blood specimens are very common. During a blood test, a small amount of blood is taken from human body. It's usually drawn from a vein in the arm using a thin needle. A finger prick with a sterile lancet which is usually a proper method obtains capillary blood samples. Blood tests have few risks. A variety of adverse complications may be encountered during the blood collection process. These complications are minor and go away shortly after blood specimen collection.

7.3 System Accuracy Analysis

Table 9 System accuracy criteria. Compliance of the blood glucose monitoring system versus the YSI reference device according to ISO 15197: 2003 criteria

Glucose meter	Subjects (N=)	Test results of the blood glucose device fulfilling specified error limits at glucose concentration < 75mg/dL (4.2mmol/L)				Test results of the blood glucose device fulfilling specified error limits at glucose concentration ≧ 75mg/dL (4.2mmol/L)				
		Test results (n=)	Within ±			Test results (n=)	Within ±			
			5 mg/dL (0.28 mmol/L)	10 mg/dL (0.56 mmol/L)	15 mg/dL (0. 83 mmol/L)		5%	10%	15%	20%
Capillary blood sampling										
BGMs	160	150	99 (66.0%)	146 (97.3%)	150 (100%)	810	411 (50.7%)	694 (85.7%)	779 (96.2%)	810 (100%)
Overall BGMs	160	960	**Glucose concentration between 20mg/dL (1.11mmol/L) and 600mg/dL (33.33mmol/L)**			**Within ±15mg/dL or ±15% (Within ±0.83mmol/L or ±15%)**			929 (96.8%)	

● **BGMs: Blood Glucose Meters**

Table 10 System accuracy criteria (Three reagent Lots of test strips). Fulfillment of the blood glucose monitoring systems using the glucose threshold of 100mg/dL required according to the ISO 15197: 2013(E) and EN ISO 15197: 2015.

Glucose meter with test strips	Overall		Test results of the blood glucose device fulfilling specified error limits at glucose concentration < 100mg/dL (5.5mmol/L)				Test results of the blood glucose device fulfilling specified error limits at glucose concentration ≧ 100mg/dL (5.5mmol/L)			
	Within ±									
	n	±15mg/dL or ±15% (±0.83mmol/L or ±15%)	n	5mg/dL (0.28mmol/L)	10mg/dL (0.55mmol/L)	15mg/dL (0.83mmol/L)	n	5%	10%	15%
Capillary blood sampling (Subjects, N=160)										
BGMs (3 Lots)	960	932 (97.1%)	252	158 (62.7%)	239 (94.8%)	251 (99.6%)	708	364 (51.4%)	603 (85.2%)	681 (96.2%)
BGMs (Lot 1)	320	311 (97.2%)	84	54 (64.3%)	80 (95.2%)	84 (100%)	236	117 (49.6%)	198 (83.9%)	227 (96.2%)
BGMs (Lot 2)	320	309 (96.6%)	84	48 (57.1%)	80 (95.2%)	84 (100%)	236	131 (55.5%)	202 (85.6%)	225 (95.3%)
BGMs (Lot 3)	320	312 (97.5%)	84	56 (66.7%)	79 (94.0%)	83 (98.8%)	236	116 (49.2%)	203 (86.0%)	229 (97.0%)

Table 11 an analysis of the distribution of glucose concentration for capillary blood

Glucose concentration / Location	Glucose concentration of capillary blood mg/dL (mmol/L)			
	Total	Site 1	Site 2	Site 3
Range	29.2–522.0 (1.62-29.00)	39.5–509.0 (2.19-28.28)	30.6–510.0 (1.70-28.33)	29.2–522.0 (1.62-29.00)
Median	138.0 (7.67)	159.5 (8.86)	125.0 (6.94)	135.0 (7.50)
Mean	174.8 (9.71)	171.9 (9.55)	182.7 (10.15)	169.9 (9.44)

7.4 Bias Analysis

According to Bland and Altman, the analysis of test reading were done with analyze it for Microsoft Excel. A plot of test results from an evaluation of glucose monitoring system is illustrated in Figure.

Figure 1 System accuracy plot. Measurement bias of capillary blood glucose obtained with blood glucose monitoring systems versus the laboratory reference device of Yellow Spring Instrument 2300. The lines represent ±15 mg/dL (0.83mmol/L) for glucose concentrations <75mg/dL (4.2mmol/L) and ±20% for glucose concentration ≧ 75mg/dL (4.2mmol/L).

Figure 1 System accuracy plot- Capillary Blood (mmol/L)

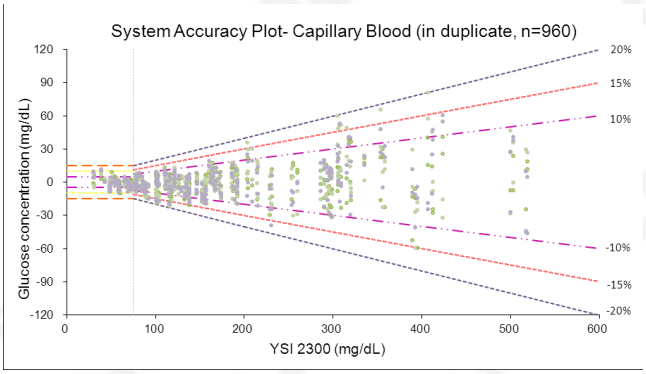
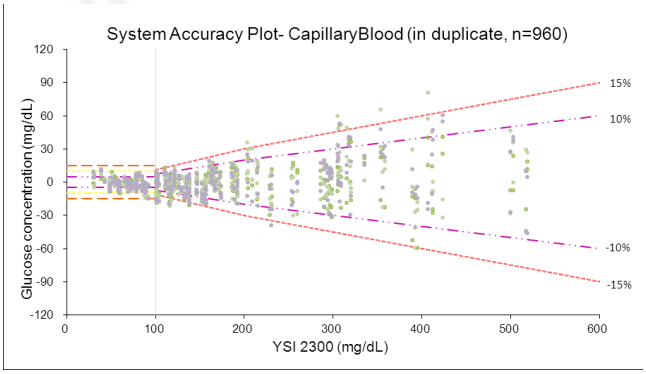


Figure 2 System accuracy plot. Measurement bias of capillary blood glucose obtained with blood glucose monitoring systems versus the laboratory reference device of Yellow Spring Instrument 2300. The lines represent ±15mg/dL (0.83mmol/L) for glucose concentrations <100mg/dL (5.5mmol/L) and ±15% for glucose concentration ≧ 100mg/dL (5.5mmol/L).

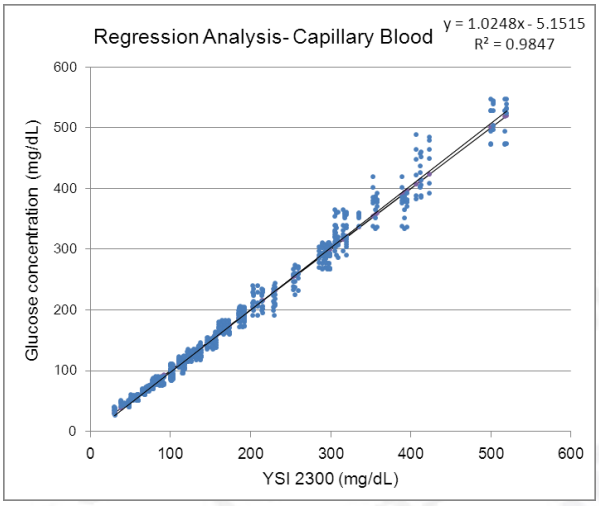
Figure 2 System accuracy plot- Capillary Blood (mmol/L)



7.5 Regression Analysis

According to Passing and Bablok, the analysis of test reading were done with analyze it for Microsoft Excel. A regression plot an evaluation on the capillary sampling for glucose monitoring system is illustrated in Figure.

Figure 3 Regression plot- Capillary Blood (mmol/L)



7.6 Error Grid Analysis

According to ISO 15197 new accuracy criteria, that adopts a risk based approach to the requirements for accuracy of glucose meter results using the Consensus Error Grid (CEG) developed for type 1 diabetes. The analysis of test reading were done with analyze it for Microsoft Excel. In the accuracy study, the analyses of the Consensus Error Grid showed 100% of test results were within zone A and zone B compared to the Yellow Spring 2300 reference method. (100% of test results were within zone A, while 0% was within zone B, with no results in zones C, D, or E).

Figure 4 Error grid analysis of the Consensus Error Grid- Capillary Blood (mmol/L)

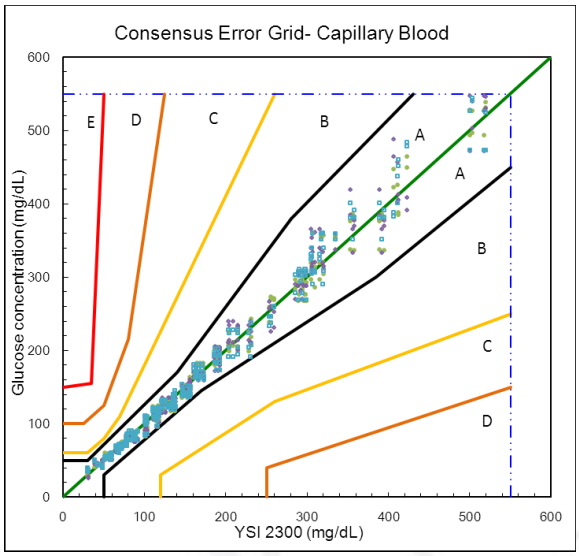


Table 12 Definitions of the Error Grid Zones (CEG)

Risk level (CEG zone)	Percentage	Risk to diabetic patient
100%	A	No effect on clinical action.
0%	B	Altered clinical action – little or no effect on clinical outcome.
0%	C	Altered clinical action – likely to affect clinical outcome.
0%	D	Altered clinical action – could have significant medical risk.
0%	E	Altered clinical action – could have dangerous consequences.

7.7 Evaluation User Performance

Evaluating intended users can operate and obtain correct results using device instruction to be provided. 154 lay users at three study centers completed a questionnaire rating the blood glucose monitoring system for ease of use (Figure 5-7).

Table 13 Difference plot

Test results of the blood glucose device fulfilling specified error limits at glucose concentration < 100mg/dL (5.5mmol/L)					
Glucose meter	Subjects (N=)	Test results (n=)	Within ±		
			5 mg/dL (0.28 mmol/L)	10 mg/dL (0.55mmol/L)	15 mg/dL (0. 83 mmol/L)
BGMs	154	36	22 (61.1%)	33 (91.7%)	36 (100%)
Test results of the blood glucose device fulfilling specified error limits at glucose concentration ≧ 100mg/dL (5.5mmol/L)					
Glucose meter	Subjects (N=)	Test results (n=)	Within ±		
			5%	10%	15%
BGMs	154	118	47 (39.8%)	89 (75.4%)	115 (97.5%)
Overall BGMs					
Glucose meter	Subjects (N=)	Test results (n=)	Within ±		
			15mg/dL or ±15% (0.83mmol/L or ±15%)		
BGMs	154	154	151 (98.1%)		

Figure 5 Accuracy plot (mmol/L)

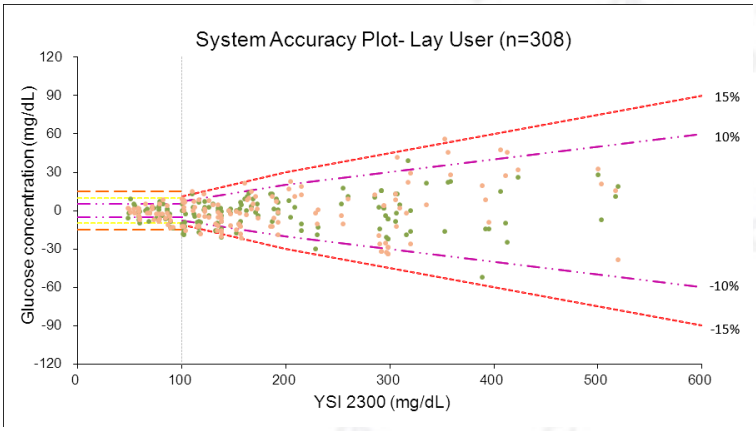
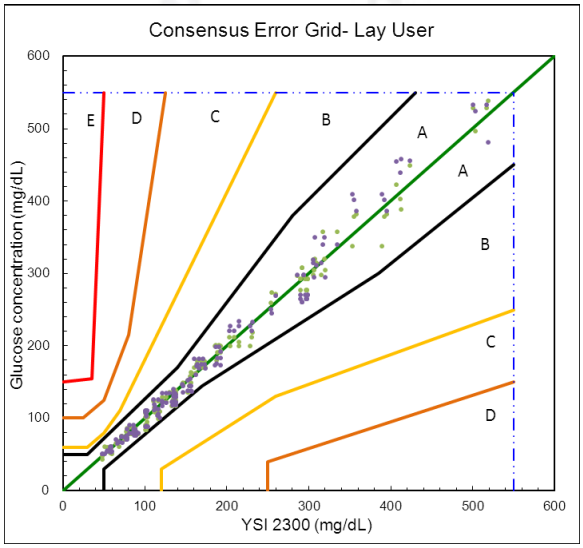


Table 14 Regression Analysis

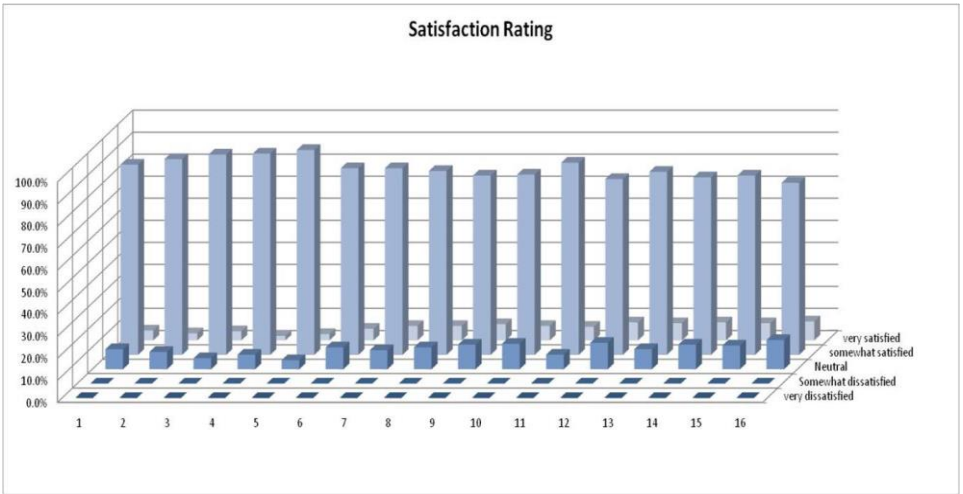
Regression equation	Y= 1.0357x - 0.4005
Correlation coefficient	R^2 = 0.9818

Figure 6 Consensus Error Grid (mmol/L)



Risk level (CEG zone)	Percentage
100%	A
0%	B
0%	C
0%	D
0%	E

Figure 7 Questionnaire



7.7.1 User Performance Results for AST accuracy

Table 14 Overall results of alternative sites included the palm, forearm, and upper arm presented in table.

Blood glucose monitoring system	Overall	Test results of the blood glucose device fulfilling specified error limits at glucose concentration < 100 mg/dL (5.5 mmol/L)				Test results of the blood glucose device fulfilling specified error limits at glucose concentration ≧ 100 mg/dL (5.5 mmol/L)			
	Within ±								
	±15 mg/dL or ±15% (±0.83 mmol/L or ±15%)	n	5 mg/dL (0.28mmol/L)	10 mg/dL (0.55mmol/L)	15 mg/dL (0.83mmol/L)	n	5%	10%	15%
Lay user (Subjects, N=160)									
Palm	**159 (99.4%)**	57	23 (40.4%)	46 (80.7%)	57 (100%)	103	36 (35.0%)	73 (70.9%)	102 (99.0%)
Forearm	**157 (98.1%)**	57	13 (22.8%)	44 (77.2%)	57 (100%)	103	24 (23.3%)	70 (68.0%)	100 (97.1%)
Upper arm	**155 (96.9%)**	57	17 (29.8%)	48 (84.2%)	57 (100%)	103	22 (21.4%)	61 (59.2%)	98 (95.1%)

A. Palm capillary blood sampling

Figure 8 Bias analysis (mg/dL)

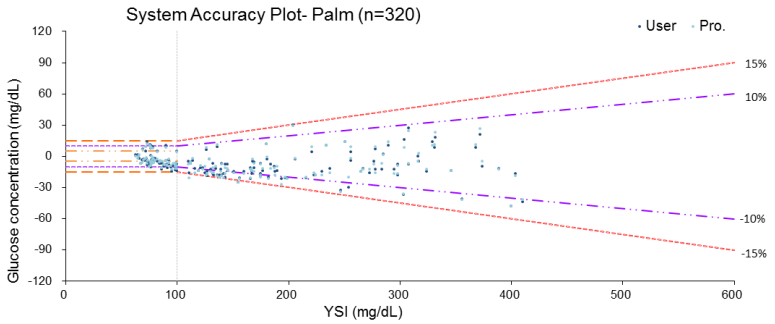
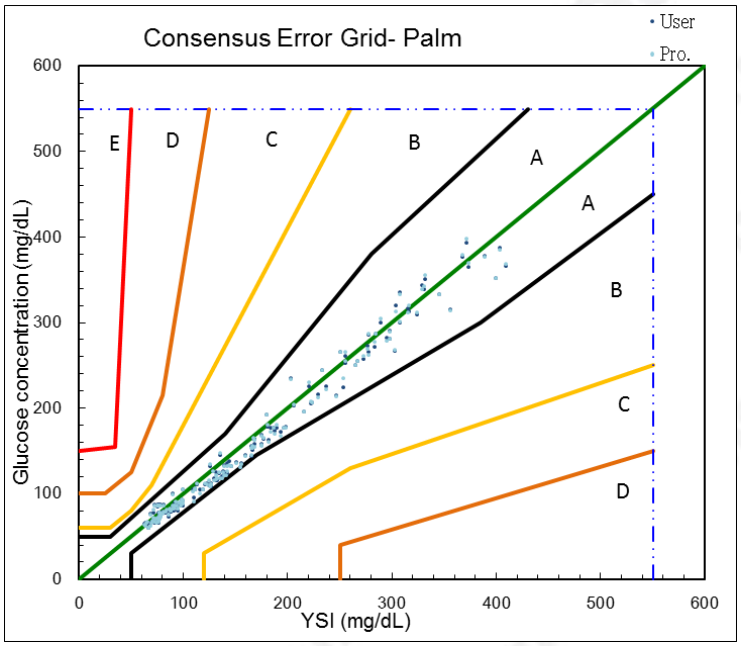


Table 15 Regression Analysis

Regression equation	y = 0.9825x – 4.6997
Correlation coefficient	R^2 = 0.9831

Figure 9 Consensus Error Grid (mg/dL)



Risk level (CEG zone)	Percentage
A	100
B	0
C	0
D	0
E	0

B. Forearm capillary blood sampling

Figure 10 Bias analysis (mg/dL)

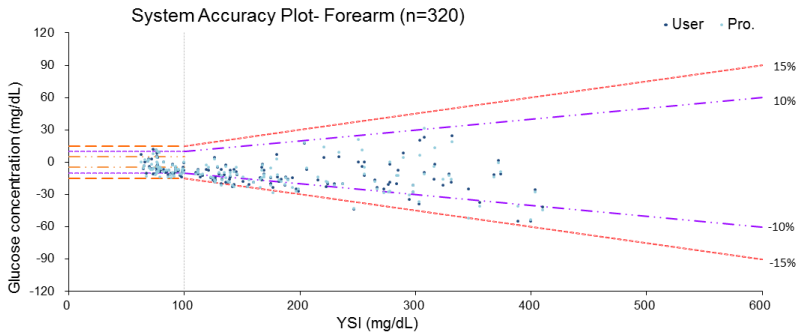
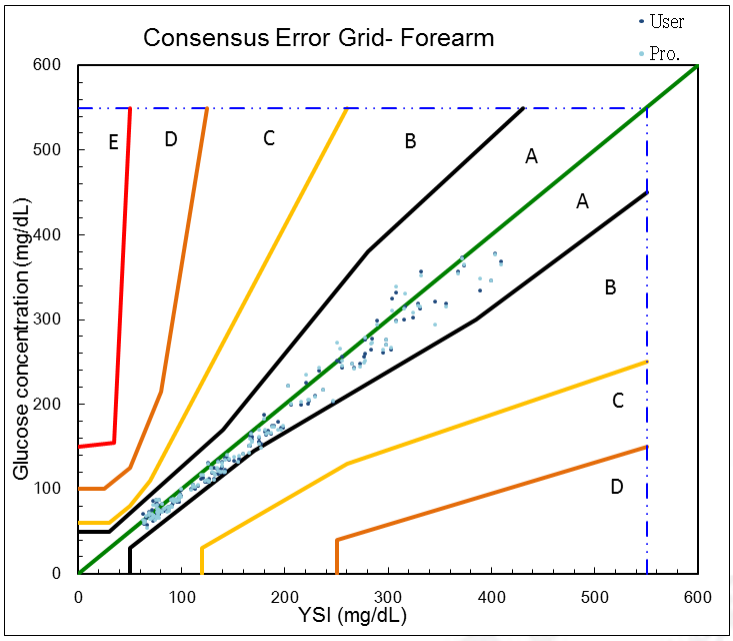


Table 16 Regression Analysis

Regression equation	y = 0.9506x – 2.6905
Correlation coefficient	R^2 = 0.9832

Figure 11 Consensus Error Grid (mg/dL)



Risk level (CEG zone)	Percentage
A	100
B	0
C	0
D	0
E	0

C. Upper arm capillary blood sampling

Figure 12 Bias analysis (mg/dL)

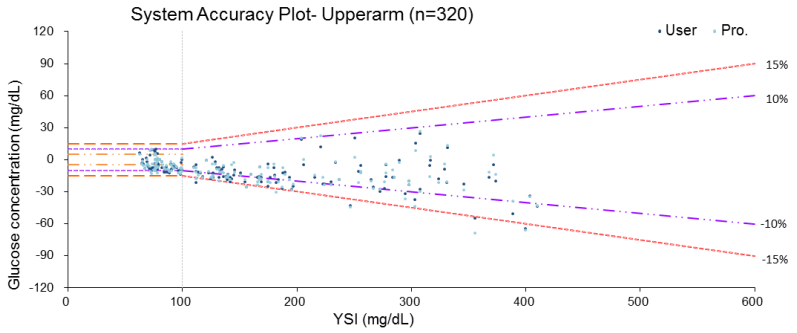
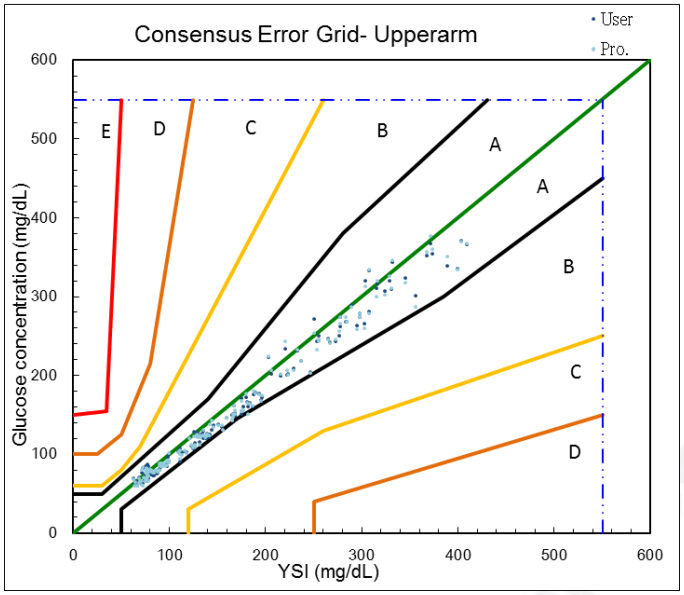


Table 17 Regression Analysis

Regression equation	y = 0.9377x – 1.5015
Correlation coefficient	R^2 = 0.9831

Figure 13 Consensus Error Grid (mg/dL)



Risk level (CEG zone)	Percentage
A	100
B	0
C	0
D	0
E	0

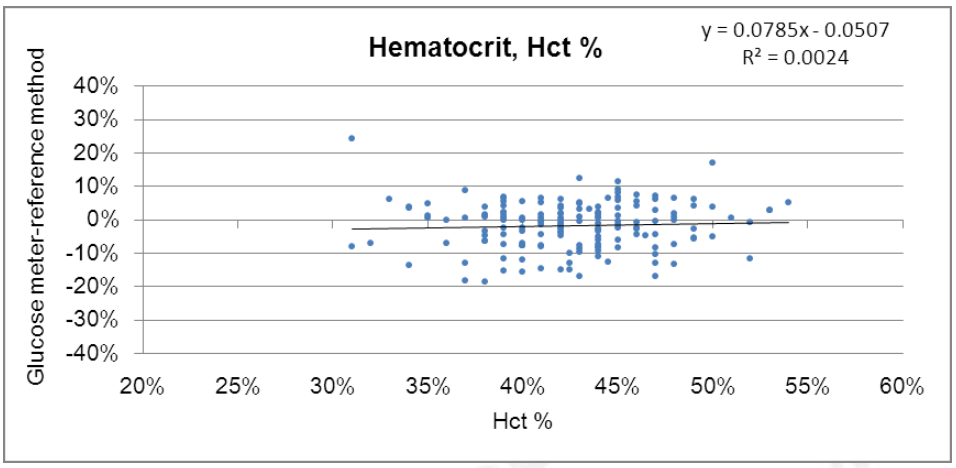
7.8 Human Factors Evaluation

Human factors reports on the blood glucose monitoring systems were to show that system fulfills all regulatory requirements particularly the usability standard IEC 62366, IEC 60601-1-11.

7.9 Influence of Hematocrit

The investigation of the effect is based on the measurement on the glucose meter of blood glucose meter under standardized and optimal measuring conditions. The hematocrit range was 31– 54%. The effect of hematocrit with a trend-line and a regression equation is shown in figure. The x-axis shows the hematocrit value in percent. The y-axis shows the difference in glucose concentration between blood glucose meter and the mean result of the comparison method in mg/dL (mmol/L).

Figure 14 The effect of hematocrit (n= 160)



8. Discussion and Conclusions

Subjects participating in this study were between 22 to 84 years old. Most patients have a history of diabetes for many years in different levels of education with conducted one or more times of a daily blood glucose measurement. The test of this study was done via the diabetics, the intended users, and trained healthcare professionals. The blood glucose monitoring system was evaluated with three reagent lots of test strips in this study to ensure representative performance would be obtained.

This study was done in the compliance with ISO 15197, which requires a specific distribution of the glucose values in predefined ranges. Evaluating system accuracy was plotted and analyzed a plot of the difference between individual data from glucose monitoring system. Blood glucose monitoring system readings were plotted against the results of the reference measurements as shown in Figure. The summing up in the graph of consensus error grid shows that 100% of the results obtained the accuracy quality limits proposed in ISO 15197. The accuracy plot analysis also shows the number of results within fixed limits of 15% and 10%.

A numerical approach represented an evaluated glucose meter into five regions to quantify clinical accuracy of patients' blood glucose as compared to the blood glucose value obtained in their glucose meter.

The slope is not statistically significant different from zero. Glucose measurements in the evaluation were not affected by hematocrit values within the range 31 – 54%.

Participants attended this glucose test evaluation when finished that participant filled in a questionnaire about their using evaluation evaluated this test system and user guide. An overall ease of use rating of 4.0 was obtained when all response were averaged, indicating that the lay users found the new system easy to use.

9. References

1. 2013 International Diabetes Federation, the global burden. http://www.idf.org/diabetesatlas/5e/the-global-burden
2. American Diabetes Association. Standards of Medical Care in Diabetes 2013: Clinical Practice Recommendations. Diabetes Care, volume 36, supplements 1, January 2013.
3. Draft Guidance for Industry and Food and Drug Administration Staff: Mobile Medical Applications, 2007.
4. Draft Guidance for Industry and Food and Drug Administration Staff: Mobile Medical Applications, Draft Guidance 2011.
5. EN ISO 15197: 2003. In Vitro Diagnostic Test Systems - Requirements for Blood Glucose Monitoring Systems for Self-Testing in Managing Diabetes Mellitus
6. ISO 15197: 2013 (E) In Vitro Diagnostic Test Systems - Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.
7. MEDDEV. 2.7.1 Rev.3 Dec. 2009, Guidelines on Medical Devices Clinical Evaluation: A Guide for Manufacturers and Notified Bodies.
8. MEDDEV. 2.7/4 Rev.3 Dec. 2010, Guidelines on Medical Devices Clinical Evaluation: A Guide for Manufacturers and Notified Bodies.
9. Comelius T, Harald P, Thirmas B, Volkmar S, Marco G, Thomas F, Andreas P Accuracy Evaluation of Five Blood Glucose Monitoring Systems Obtained from the Pharmacy: A European Multicenter Study with 453 Subjects. Diabetes Technol Ther 2012 April; 14(4): 330-337
10. Evaluation of Precision performance of Quantitative measurement Methods; Approved Guideline-Second Edition; CLSI document EP5-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2004
11. IEC 62366, Medical devices – Application of usability engineering to medical devices
12. EN 13612, Performance evaluation of in vitro diagnostic medical device.

13. ISO 13485: 2003, Medical devices – Quality management systems – requirements for regulatory purposes.
14. IEC 60601-1-11: 2010 International Standard. Medical electrical equipment Part 1-11: General requirement for basic safety and essential performance.
15. EN ISO 15197: 2015 (E) In Vitro Diagnostic Test Systems - Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.