GlucoMen Areo blood glucose meter:

Accuracy Evaluation to New ISO 15197:2013 with Specification and Technical Data

GlucoMen® areo

Reference Book, November 2014

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System accuracy evaluation of GlucoMen Areo according to the INTERNATIONAL STANDARD ISO 15197:2013

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1 Introduction to New ISO 15197:2013

New accuracy criteria for blood glucose meters have been published in the new EN ISO 15197:2013 guidelines. The new minimum acceptable accuracy criteria for results produced by a glucose monitoring system are as follows:

Accuracy Requirement A:

At glucose concentrations <5.55 mmol/L (100 mg/dL), ninety five percent (95%) of the individual glucose results shall fall within ± 0.83 mmol/L (15 mg/dL) of the results of the reference measurement.

At glucose concentrations ≥5.56 mmol/L (100 mg/dL), ninety five percent (95%) of the individual glucose results shall fall within ± 15% of the results of the reference measurement

Accuracy Requirement B:

Ninety nine percent (99%) of individual glucose results shall fall within zones A and B of the Consensus Error Grid (CEG).

In addition to the changed criteria, the system accuracy evaluation must include data from three different reagent system lots (three test strip lots), each with 100 fresh capillary blood samples.

Haematocrit Interference Evaluation:

Evaluation of haematocrit (packed cell volume) effect upon accuracy must be carried out with a minimum of five haematocrit levels at each of three glucose concentrations.
This evaluation is detailed separately, on pages 7 to 8 of this report

2. Objective of Accuracy Study

To investigate the blood glucose measuring accuracy of the GlucoMen Areo system, compared to the established laboratory reference method YSI 2300 STAT Plus. Evaluation was carried out to the accuracy requirements of ISO 15197:2013.

3. Method

This evaluation follows the revised procedures and requirements of the new ISO 15197:2013, including the following:

1 Data from three tested lots is included in the evaluation. For each strip lot, 200 measurements were collected. These measurements were performed using two different GlucoMen Areo meters for each lot (a total of 6 meters and 100 measurements per meter).

2 The distribution from low to high glucose concentrations obtained ensured that the correct percentages of samples (%) fall within defined glucose concentrations (mmol/L).

ISO category	Percentage of samples (%)	ISO and Study Glucose Concentration (mmol/L)
1	5	≤ 2.8
2	15	> 2.8 to 4.4
3	20	> 4.4 to 6.7
4	30	> 6.7 to 11.1
5	15	> 11.1 to 16.7
6	10	> 16.7 to 22.2
7	5	> 22.2

Samples were assigned to the respective category according to their glucose concentration as measured with the YSI 2300 STAT PLUS.

In accordance with ISO 15197:2013, where it was not possible to fill the categories from the patient group available, heparinised venous blood samples were obtained from subjects and manipulated in-vitro by IDT Laboratory staff to achieve the desired blood glucose levels.

Acceptable ranges and calculation procedures are all in line with the new ISO 15197:2013.

4. Results: Accuracy Requirement A - Bias

Bias plots for each test strip lot are shown separately opposite,

At glucose levels < 5.6mmol/L, 100% of results are within ± 0.83mmol/L of laboratory results.

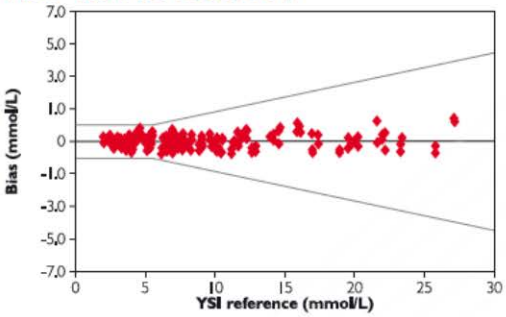
At glucose levels ≥ 5.6mmol/L, 99.8% of results are within ± 15% of laboratory results.

Combined system accuracy was 99.8%

Conclusion: GlucoMen Areo exceeds ISO 15197:2013 requirement of 95% within ± 0.83mmol/L and ± 15% of laboratory results respectively.

Figure 1. Bias Plot for GlucoMen Areo with data for 3 test strip lots reported separately as required by ISO 15197:2013

Lot 1: H1S1308001



Accuracy results for glucose < 5.5 mmol/L, n = 180

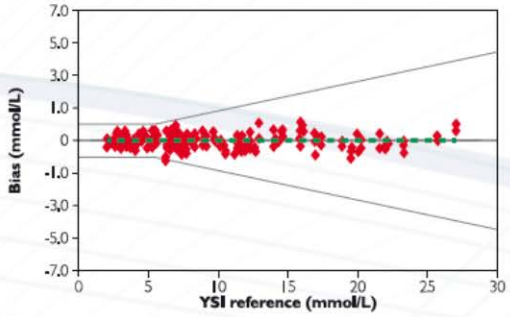
Within ± 0.28 mmol/L	Within ± 0.56 mmol/L	Within ± 0.83 mmol/L
44 (66)) 69.7%	65 (66) 98.5%	66 (66) **100%**

Accuracy results for glucose ≥ 5.55 mmol/L

Within ± 5%	Within ± 10%	Within ± 15%
112 (134) 78.9%	133 (134) 88.8%	134 (134) **100%**

Within ± 0.83mmol/L and ±15%	
200/200	**100%**

Lot 2: H1S1308002



Accuracy results for glucose < 5.55mmol/L

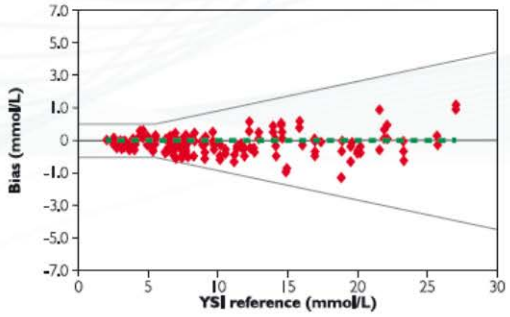
Within ± 0.28 mmol/L	Within ± 0.56 mmol/L	Within ± 0.83 mmol/L
48 (66)) 72.7%	65 (66) 98.5%	66 (66) **100%**

Accuracy results for glucose ≥ 5.55 mmol/L

Within ± 5%	Within ± 10%	Within ± 15%
112 (134) 78.9%	131 (134) 97.8%	133 (134) **99.3%**

Within ± 0.83mmol/L and ±15%	
199/200	**99.5%**

Lot 3: H1S1308003



Accuracy results for glucose < 5.55mmol/L

Within ± 0.28 mmol/L	Within ± 0.56 mmol/L	Within ± 0.83 mmol/L
52 (66)) 78.8%	65 (66) 98.5%	66 (66) **100%**

Accuracy results for glucose ≥ 5.55 mmol/L

Within ± 5%	Within ± 10%	Within ± 15%
93 (134) 78.9%	129 (134) 97.8%	134 (134) **100%**

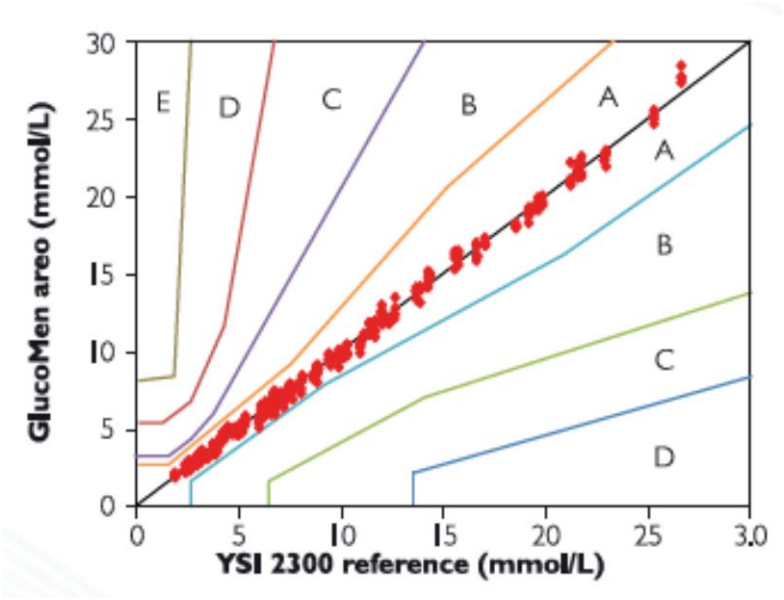
Within ± 0.83mmol/L and ±15%	
200/200	**100%**

Results: Accuracy Requirement B – Concensus Error Grid

100% of results are within Zone A of the Consensus Error Grid.

Conclusion: GlucoMen Areo exceeds ISO 15197:2013 requirement of 99% of results within zones A and B of the Consensus Error Grid.

Figure 2. Consensus Error Grid Plot for GlucoMen Areo



	Test Results		
Test Strip Lot	Zone A	Zone B	Zone A & B
H1S1308001	200	0	200
H1S1308002	200	0	200
H1S1308003	200	0	200
Total	**600**	**0**	**600**
Within %	100%	0%	100 %

The Consensus Error Grid (CEG) represents the results of a survey of 100 endocrinologists attending the American Diabetes Association Annual Meetinf 1994. The CEG is divided into five zones, which are defined by estimated risk to the patient if a result falls in a given zone. The risk levels defined by the CEG's zones are classified as:

Risk Level / CEG Zone	Risk to diabetic patient
A	No effect on clinical action
B	Altered clinical action - little or no effect on clinical outcomes
C	Altered clinical action - likely to affect clinical outcomes
D	Altered clinical action - could have significant medical risk
E	Altered clinical action - could have dangerous consequences

Haematocrit Interference Evaluation, ISO 15197:2013

Background

Varying haematocrit: is a potential source of error in blood glucose monitoring

Abnormal haematocrit levels interfere with glucose readings of patient self-testing blood glucose meters and are potentially a very significant source of inaccuracy.

How commonly will haematocrit levels vary from the normal level of approximately 42%?

A recent investigation, analysing data from 15,108 community patients has reported haematocrit ranging from 20 to 60% [(1)].
Such deviations from normal haematocrit levels of approximately 42% can be induced by lifestyle interventions (e.g. smoking or prolonged exercise), environmental conditions (e.g. altitude or seasonal variations), demographic factors (e.g. age) and disease and drug related conditions (e.g. haematological disorders, hypermenorrhea, pregnancy or renal disease). [(1)]
Within subject variability also exists, indicated by a 15% relative change [(2)].

Why can varying haematocrit dramatically affect a blood glucose test?

Haematocrit that is lower than normal can lead to overestimation of glucose values and haematocrit that is higher than normal can lead to underestimation of glucose values. The impact of abnormal haematocrit on blood glucose testing may be explained by a change in diffusion kinetics, and / or increased packed red cell volume and displacement of plasma volume leading to insufficient plasma volume for accurate testing. The impact of abnormal haematocrit will vary depending upon the technology of the blood glucose monitoring system.

Requirement: Haematocrit Interference Evaluation

The haematocrit operating range described within the test strip insert must be such that:

At glucose concentrations <5.55 mmol/L (100 mg/dL), the difference between the average measured value at each haematocrit level and the average measured value at the mid-level haematocrit should not exceed 0.55 mmol/L.

At glucose concentrations ≥5.56 mmol/L (100 mg/dL), the difference between the average measured value at each haematocrit level and the average measured value at the mid-level haematocrit should not exceed ± 10%.

The study described on the following page has been carried out to evaluate the potential effect of haematocrit level upon the accuracy of GlucoMen Areo.

References:

1. Lyon ME, Lyon AW. Patient acuity exacerbates discrepancy between whole blood and plasma methods through error in molality to molarity conversion: “Mind the gap!”. Clin Biochem. 2011;44(5-6):412–7.
2. Thirup P. Haematocrit: within-subject and seasonal variation. Sports Med. 2003;33(3):231–43.

Haematocrit Interference Evaluation: GlucoMen Areo

Aim of Study:

The performance of GlucoMen Areo was evaluated in accordance with the requirements of ISO15197:2013. This states that such investigation should include five haematocrit levels across the range specified in the labeling of the blood glucose monitoring system. As such this study measured the effect on system accuracy at five haematocrit levels across the operating range of 20% to 70% specified in the labeling of GlucoMen Areo.

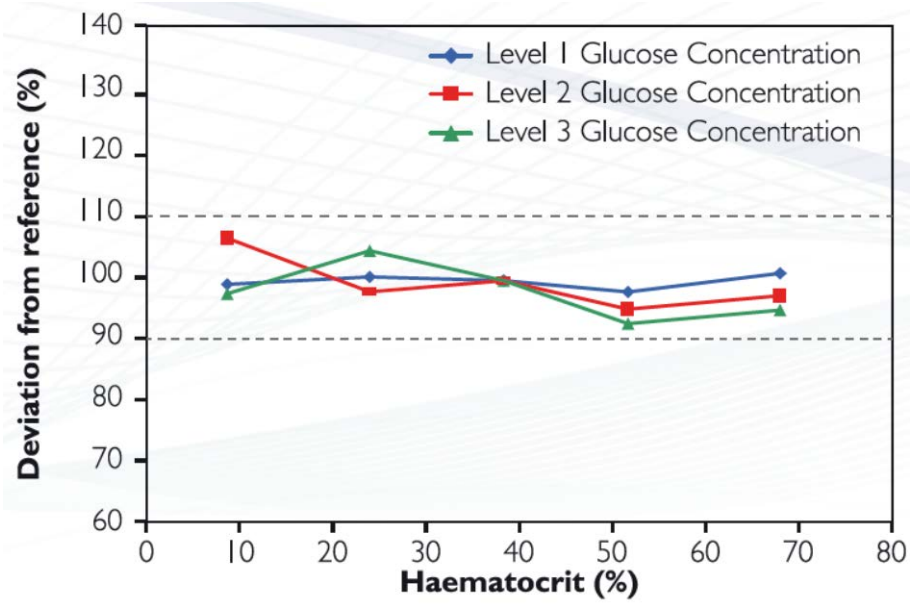
Acceptance criteria:

At all glucose concentrations (3 levels) and all haematocrit concentrations, bias from the result at an haematocrit of 42% ±2% must fall within ±10%.

Method:

Venous heparinised blood was manipulated to three different blood glucose concentrations, 2.2 mmol/L, 7.2 mmol/L, and 16.7 mmol/L, and five different haematocrit levels from 10% to 70%, a total of fifteen samples.
Each sample was used to perform 10 glucose tests on the GlucoMen Areo.
The reference analyser used to determine the glucose level of samples was the YSI 2300.

Results: GlucoMen Areo exhibits an haematocrit interference effect of <10% at all levels.



Conclusion: GlucoMen Areo exceeds ISO 15197:2013 requirements.

Precision Data: Final report

Background

Repeatability is evaluated by a series of measurements using the same blood sample, meter and test strip lot.

Method

Ten tests are performed on each of 10 meters, using the same blood sample. This is repeated using five blood glucose samples with concentrations ranging from low to high. Each meter is assigned a lot of test strips and a total of 3 lots must be used during the study.

ISO15197:2013 doesn't specify a separate acceptability criteria for precision. The manufacturer must establish acceptance criteria within the study protocol. In the GlucoMen Areo evaluation this was:

- Standard Deviation (SD) ≤ 0.25mmol/L at glucose concentration < 5.55mmol/L
- Coefficient of Variation (CV) ≤ 5% at glucose concentrations ≥ 5.55mmol/L

Results

The average glucose value for each sample must be reported along with standard deviation (SD) and coefficient of variation (CV) for each glucose concentration ≥ 5.55mmol/L, and standard deviation (SD) for for each glucose concentration < 5.55mmol/L

		Level 1	Level 2	Level 3	Level 4	Level 5
Lot 1	Mean	2.9	4.1	7.3	12.4	18.9
	SD	**2.2**	**2.2**	2.9	5.3	5.7
	CV	NA	NA	**2.2%**	**2.4%**	**1.7%**
Lot 2	Mean	3.0	4.2	7.3	12.5	18.9
	SD	**2.1**	**2.0**	3.2	5.1	5.3
	CV	NA	NA	**2.4%**	**2.2%**	**1.6%**
Lot 3	Mean	2.9	4.0	7.4	12.4	18.8
	SD	**2.0**	**2.0**	3.1	4.9	6.2
	CV	NA	NA	**2.4%**	**2.2%**	**1.8%**
All Lots	Mean	2.9	4.1	7.3	12.4	18.9
	SD	**2.1**	**2.0**	3.1	5.1	5.7
	CV	NA	NA	**2.3%**	**2.3%**	**1.7%**

Conclusion: GlucoMen Areo exhibits excellent precision and test repeatability at all levels.

Technical and Analytical

General Specification:

Contactless Download	GlucoMen Areo automatically downloads meter memory to a smartphone or tablet for the maintenance of an electronic logbook. Results can be emailed to healthcare professionals for closer diabetes management at necessary times
No Coding	No coding procedure is needed with GlucoMen Areo
Enzyme specificity	Glucose Oxidase is specific for β D-glucose, it does not react with any other sugars e.g. Maltose (safe in peritoneal renal dialysis)
Maltose independent	Glucose Oxidase is specific for β D-glucose and independent of all other sugars
Calibration	GlucoMen Areo blood glucose meter is plasma calibrated to allow the easy comparison of results with laboratory methods (see below for further details)
Blood Volume Control	The meter detects when enough blood has been applied to the test strip to enable a test (prevents under / over application)
Strip Expiry Date:	24 months shelf life 6 months after first opening vial
Test Range:	1.1 to 33.3 mmol/L
Test Time:	5 seconds
Sample Volume:	0.5 µl
Memory:	730 results with date and time; 1, 7, 14, 30, 60 & 90 day averages
Operating Temperature:	5 - 45°C
Haematocrit Range	10 - 70%
Operating Humidity:	10 - 90% Relative Humidity
Power Source:	2x 3V Lithium Battery CR2032, available free to users
Battery Life:	Approximately 1000 tests

Testing for Endogenous and Exogenous Interfering Substances:

General Requirements

ISO 15197:2013 lists a number of substances that could be present in the blood and have previously been found to interfere with a glucose measurement procedure.
Evaluation of potentially interfering substances must be carried out at 2 glucose concentrations, one within 2.8 to 5.5mmol/l and one within 13.9 to 19.4mmol/l.
At least 10 meter tests are carried out on each sample to arrive at an average that is compared to the reference glucose value.

Performance criteria – Interfering substances

A substance is considered an interferent if the average difference between the test sample and the control sample exceeds :

- 0.55mmol/l for the glucose concentration <5.55mmol/L, or
- 10% for the glucose concentration ≥5.55mmol/L

Performance – GlucoMen Areo Interference Testing

Maltose Independence:	Glucomen Areo test strips (Glucose Oxidase enzyme) react specifically with β D-glucose and do not react with any other sugars that may be in the blood.
Lipaemic Samples:	Cholesterol up to 13.0 mmol/L and Triglycerides up to 38.0 mmol/L do not significantly affect test results.

Testing was carried out as described by the Clinical Laboratory Standards Institute CLSI – EP7 – P Vol. 6 No. 13. Interference testing in clinical chemistry

All 30 substances have been tested at two levels of glucose (3.3 mmol/L and 17.8 mmol/L) and found **not to interfere with the performance of the system at physiological or therapeutic levels**.

Substance tested	Substance Concentration	Bias with glucose 2.8 to 5.5 mmol/l	Bias with glucose 13.9 to 19.4 mmol/l
Acetominaphen	10mg/dL	0.23	-1.0%
L-DOPA	3mg/dL	0.07	0.9%
Tolbutamide	25mg/dL	-0.24	-2.0%
Dopamide	0.1mg/dL	-0.30	-2.1%
Ibuprofen	40mg/dL	-0.24	-3.6%
Acetylsalicylic acid	40mg/dL	-0.32	-3.8%
Methyl-Dopa	15mg/dL	-0.12	2.0%
Tetracycline	1.5mg/dL	-0.31	0.3%
Ephedrine	0.05mg/dL	-0.41	-5.0%
Mannitol	30mg/dL	-0.29	-2.5%
Mannose	5.5mg/dL	-0.53	-7.1%
Sorbitol	0.2mg/dL	-0.30	-4.4%
Tolazamide	23mg/dL	0.29	2.9%
Ascorbic acid	6mg/dL	0.06	-0.4%
Maltose	50mg/dL	-0.37	-8.0%
EDTA	0.5mg/dL	-0.34	-5.3%
Lactose	25mg/dL	-0.44	0.3%
Heparin	3000U/L	-0.31	-1.5%
Maltotriose	240mg/dL	-0.30	-0.9%
Maltotetraose	120mg/dL	-0.38	-3.5%
Xylitol	0.12mg/dL	-0.39	-3.3%
Xylose	30mg/dL	-0.47	-3.2%
Gentisic acid	2mg/dL	-0.17	-3.9%
Paralidoxime Iodide (PAM)	50mg/dL	0.34	5.8%
Icodextrin	75mg/dL	0.23	3.1%
Fructose	20mg/dL	-0.35	-2.9%
Hemoglobin	200mg/dL	-0.49	-6.2%
Creatinine	5mg/dL	-0.26	-4.1%
Uric acid	15mg/dL	-0.43	-3.0%
Cholesterol	200mg/dL	-0.35	-4.3%
BILIRUBIN	30mg/dL	-0.28	8.6%
triglyceride	500mg/dL	0.21	8.8%
Galactose	15mg/dL	-0.39	-4.8%
Glutathione	1.5mmol/l	0.16	7.5%

GlucoMen Areo blood glucose meter:

Accuracy Evaluation to New ISO 15197:2013 with Specification and Technical Data

For more information please call 0800 243 667
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The Diabetes Diagnostics Company