GlucoMen GM blood glucose meter:

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

GlucoMen® Gm

Reference Book, July 2013

Contents:

Page

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

Institut für Diabetes -Technologie Forschungs – und Entwicklungsgesellschaft mbH an der Universität Ulm. Data obtained during study IDT-BB-0905

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 6 to 7 of this report

2. Objective of Accuracy Study

To investigate the blood glucose measuring accuracy of the GlucoMen GM system, compared to the established laboratory reference method YSI 2300 STAT Plus. Evaluation was carried out to the accuracy requirements of ISO 15197:2013. Haematocrit Interference Evaluation is the subject of a separate study – see pages 8 of this report.

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 GM meters for each lot (a total of 6 meters, with 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

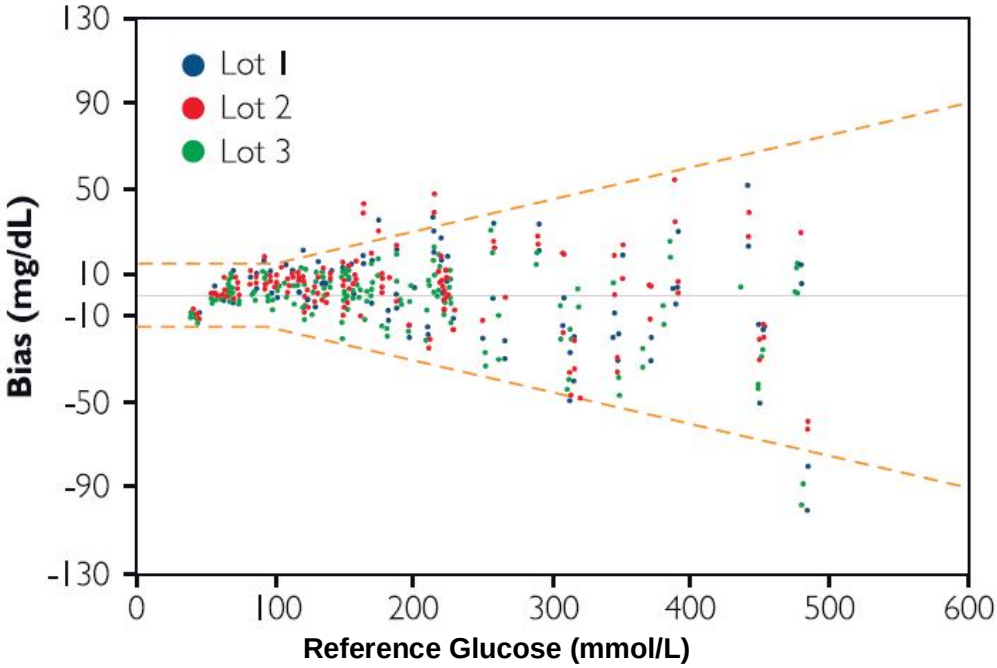
At glucose levels < 5.6mmol/L, 98% of results are within ± 0.83mmol/L of laboratory results.

At glucose levels ≥ 5.6mmol/L, 97% of results are within ± 15% of laboratory results.

Combined system accuracy was 97.2%

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

Figure 1. Bias Plot for GlucoMen GM



System accuracy results for glucose concentrations < 5.55mmol/L		
Within ± 0.28mmol/L	Within ± 0.56mmol/L	**Within ± 0.83mmol/L**
94 / 180 (52%)	154 / 180 (86%)	**177 / 180 (98%)**

System accuracy results for glucose concentrations ≥ 5.55mmol/L		
Within ± 5%	Within ± 10%	**Within ± 15%**
204 / 420 (49%)	347 / 420 (83%)	**406 / 420 (97%)**

Combined system accuracy results (absolute and relative deviations)

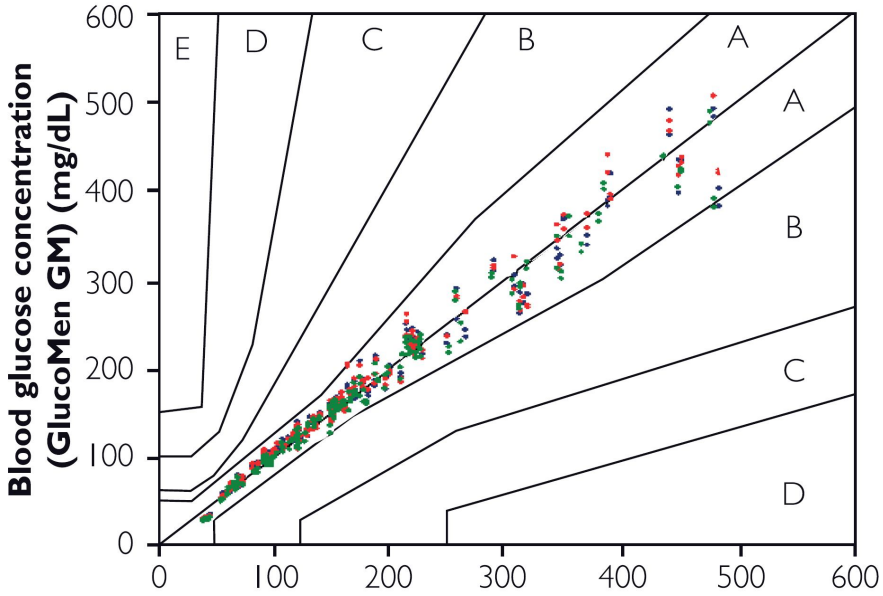
Within ± 0.83mmol/L and 15%
583 / 600 (97.2%)

Results: Accuracy Requirement B – Error Grid

100% of results are within Zone A and B of the Consenses Error Grid, with 99.5% in Zone A

Conclusion: GlucoMen GM 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 GM



Zone	A	B	C	D	E
Cases	597	3	0	0	0
Percentage	99.5	0.5	0	0	0

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, analyzing 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 GM.

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 GM

ARKRAY Laboratory, Science Park, Kyoto, Japan

Aim of Study:

To evaluate the performance of GlucoMen GM at different haematocrit levels, in accordance with the requirements of ISO15197:2013.

This study measured the effect on system accuracy of varying haematocrit (HCT%) levels, across five haematocrit levels within operating range of 30% to 55% haematocrit.

The study is in line with ISO 15197:2013, which states that such investigation should include the range of haematocrit values specified in the labeling of the blood glucose monitoring system.

Acceptance criteria:

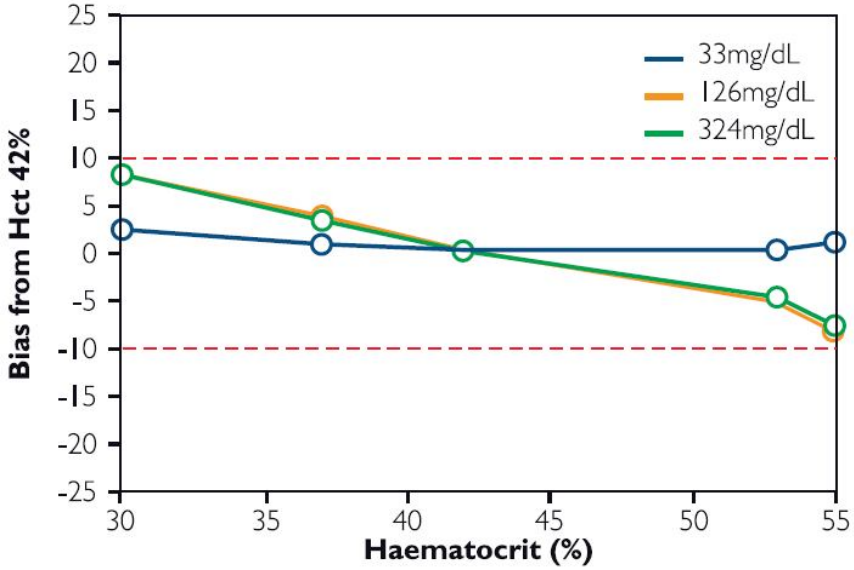
At all glucose concentrations (3 levels), bias from the result at an haematocrit of 42% must fall within ±10%.

Method:

Venous heparinised blood was manipulated to three different blood glucose concentrations, 1.8 mmol/L (33 mg/dL), 7.0 mmol/L (126 mg/dL), and 18.0 mmol/L (324 mg/dL), and five different haematocrit levels (30%, 37%, 42%, 53%, 55%), a total of fifteen samples.
Each sample was used to perform 10 glucose tests on the GlucoMen GM.
The reference analyser used to determine the glucose level of samples was the GA -1150.

Results:

GlucoMen GM exhibits an haematocrit interference effect of <10% at all levels.



Conclusion:

GlucoMen GM exceeds ISO 15197:2013 requirements.

Precision Data: Final report

Background:

ISO 15197:2013 sets out the protocol and evaluation procedure for evaluation of measurement precision (repeatability), which requires a series of measurements within a short interval of time, by a single laboratory technician, using the same meter and reagent lot.

Method:

In a laboratory study, the precision (repeatability) evaluation was carried out following the ISO 15197:2013 procedure. The precision of GlucoMen® GM was analysed using blood samples at five glucose concentrations across the operating range, performing 20 repeated tests with each sample.

Results:

ISO 15197:2013 requires that the average blood glucose value, the standard deviation and the coefficient of variation (CV) shall be calculated at each glucose concentration > 5.5 mmol/L, and that CV is not required for concentrations ≤ 5.5 mmol/L.

ISO 15197:2013 does not specify separate criteria for minimum acceptable precision and bias. The system accuracy requirements, as described on page 1, are designed to verify acceptability of the combined effects of precision and bias for the blood glucose monitoring system.

Ref. mmol/L	2.3	5.4	8.1	12.7	18.1
Average (mmol/L)	2.4	5.7	8.5	12.7	18.1
SD	0.1	0.1	0.2	0.3	0.5
CV%	-	2.3	2.8	2.7	2.5

Conclusion:

GlucoMen GM exhibits excellent precision across the range of blood glucose concentrations.

GlucoMen GM exceeds the accuracy requirements of ISO 15197:2013 which are designed to verify acceptability of the combined effects of precision and bias.

Technical and Analytical

General Specification:

No Coding	No coding procedure is needed with GlucoMen GM
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 GM blood glucose meter is plasma calibrated to allow easy comparison of results with laboratory methods (see below for further detail)
Blood Volume Control	The meter detect 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:	0.6 to 33.3mmol/L
Test Time:	7 seconds
Sample Volume:	0.5 µl
Memory:	250 results with date and time; 14, 30 day averages
Operating Temperature:	5 to 45°C
Haematocrit Range	30 – 55%
Operating Humidity:	10 to 90% Relative Humidity
Power Source:	3V Lithium Battery CR2450, available free to users
Battery Life:	Approximately 2000 Tests
Weight:	39g approximately
Size:	80 x 65 x 16mm approximately

Test Principle:

GlucoMen GM utilizes electrochemical test technology. Glucose in the blood sample mixes with reagent (glucose oxidase) on the test strip and is converted to gluconolactone. The electrons generated in this reaction are detected by conductors and the meter measures the level of electrical current to calculate the corresponding glucose level.

Reagent Composition:

The GlucoMen GM test strip enzyme is glucose oxidase (Aspergillus Niger), and the mediator is hexaammineruthenium (III) chloride.

Calibration / Traceability:

GlucoMen GM blood glucose meter is plasma calibrated to allow easy comparison of results with laboratory methods.

The GlucoMen GM system is calibrated versus venous plasma values determined using a Yellow Springs 2300 analyser (YSI). The YSI analyser is calibrated (as secondary reference measurement procedure) using a series of NERL standards; the NERL standards (primary calibrators) are referenced directly to the NIST (National Institute of Standards and Technology, USA).

Testing for Endogenous and Exogenous Interfering Substances:

Maltose Independence:	Glucomen GM 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.

All of the 30 substances listed below (page 12) could be present in the blood of intended users and could theoretically interfere with glucose measurement, many have been found to interfere with one or more glucose measurement procedures.

Testing was carried out as described by the Clinical Laboratory Standards Institute CLSI – EP7 – P Vol. 6 No. 13. Interference testing in cliniccl 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	3.3 mmol/L	17.8 mmol/L	COMMENT
4-Acetamidophenol	OK	OK	20 mg/dL CLSI test level
Acetylsalicylate	OK	OK	Up to 65 mg/dL - CLSI high test level 30 mg/dL
Ascorbic Acid	OK	OK	Up to 3 mg/dL CLSI test level
Bilirubin - Conjugated	OK	OK	Up to 40 mg/dL - CLSI high test level 30 mg/dL
Bilirubin - Unconjugated	OK	OK	Up to CLSI high test level 20 mg/dL
Cholesterol	OK	OK	Upto CLSI pathological test level 500 mg/dL
Creatinine	OK	OK	Up to 5 mg/dL CLSI test level
L-DOPA	OK	OK	OK till 10x therapeutic dose
Dopamine	OK	OK	OK to 0.1 mg/dL therapeutic dose
EDTA	OK	OK	Up to 1000 mg/dL (Equiv 5 x monovette)
Ephedrine	OK	OK	100x peak plasma therapeutic conc.
Fructose	OK	OK	Up to CLSI high test level 30 mg/dL
Galactose	OK	OK	Up to CLSI high test level 60 mg/dL
Gentisic Acid	OK	OK	CLSI recommended test level 1.8mg/dL
Glutathione	OK	OK	Up to 2 mg/dL - 14x typical plasma conc.
Hemoglobin	OK	OK	Up to 735 mg/dL
Hemolysis	OK	OK	Within Hct% 30-55%
Heparin	OK	OK	Up to 100,000 U/mL
Ibuprofen	OK	OK	Up to 50 mg/dL - >10X CLSI high therapeutic level
Lactose	OK	OK	Up to 30 mg/dL (10 x blood conc.)
Maltose	OK	OK	Up to 450 mg/dL - 2.5X CLSI test level
Maltotetraose	OK	OK	Up to 450 mg/dL
Maltotriose	OK	OK	Up to 240 mg/dL
Mannitol	OK	OK	Up to 800 mg/dL
Mannose	OK	OK	>10X lower normal serum (16 mg/dL)
Methyl - L - Dopa	OK	OK	Up to 1.5 mg/dL (3 x high physiological)
Oxygen	OK	OK	Within the range 5.4 - 20.1 KPa
Salicylic Acid	OK	OK	Up to 100 mg/dL. CLSI test level 3 x high therapeutic
Sodium Citrate	OK	OK	Up to 190 mg/dL
Sodium Fluoride	OK	OK	Up to 1250 mg/dL. CLSI test level 1000 mg/dL
Sodium Oxalate	OK	OK	Up to 1000 mg/dL. CLSI test level 800 mg/dL
Sorbitol	OK	OK	10 mg/dL. 3 x max plasma concentration
Tetracycline	OK	OK	Up to 1.5 mg/dL - >3 X CLSI therapeutic level
Tolazamide	OK	OK	8.4 mg/dL. 3 x peak therapeutic level
Tolbutamide	OK	OK	64 mg/dL. CLSI Toxic level
Triglyceride	OK	OK	Up to 3300 mg/dL.CLSI high test level 3000 mg/dL
Urea	OK	OK	280 mg/dL (7.4 x high normal)
Uric Acid	OK	OK	20 mg/dL CLSI test level
Warfarin	OK	OK	1 mg/dL CLSI high therapeutic level
Xylitol	OK	OK	50 mg/dL (>2000 x high serum conc)
Xylose	OK	OK	80 mg/dL (>high normal)

For more information please call 0800 243 667

Or email

glucomen@menarinidiag.co.uk

For more information please call 0800 243 667

Or email

glucomen@menarinidiag.co.uk

GlucoMen® Gm

GlucoMen®
The Diabetes Diagnostics Company