Validation Report

Evaluation of

System Accuracy

of the Blood Glucose Monitoring System

GlucoCheck Gold

Compliant with DIN EN ISO 15197:2015

Sponsor:

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p20: typo

p10: correction of specifications of measurement conditions and measuring range

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Contents

I. Disclaimer

The results presented in this validation report report exclusively refer to the devices, test strip lots and control solutions specified in sections V.1 to V.3.

II. Summary

Evaluation of system accuracy of the BGM GlucoCheck Gold revealed that measurements obtained fulfill the acceptance criteria defined in DIN EN ISO 15197:2015.

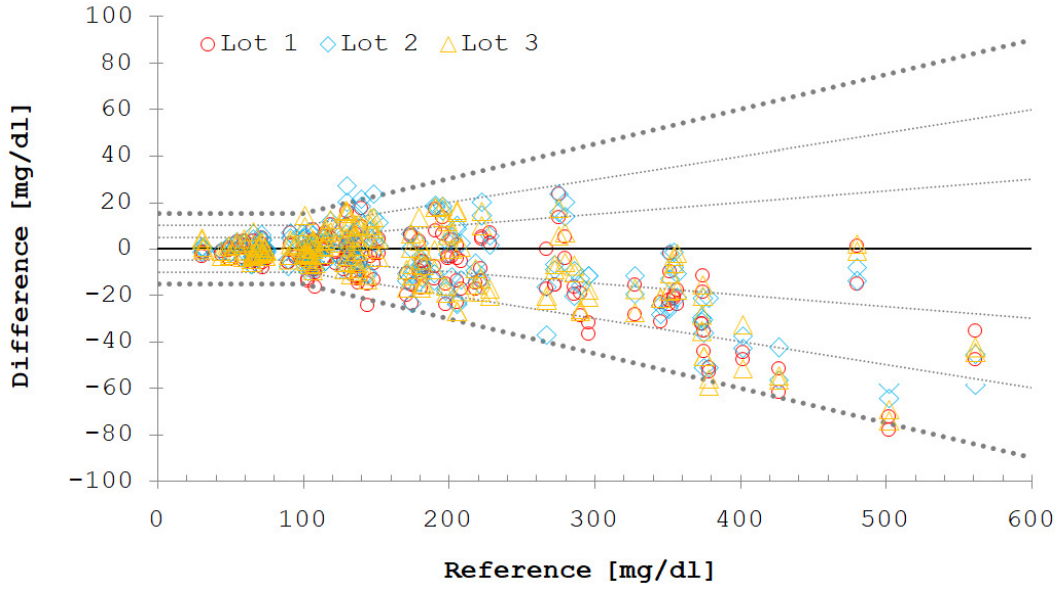

Fig. 1 | Bland-Altman Diagram for all tested Lots. 9 out of 600 measurements (1.5%) show deviations > 15 mg/dL / > 15% for glucose concentrations <100 mg/dL and ≥ 100 mg/dL, respectively.

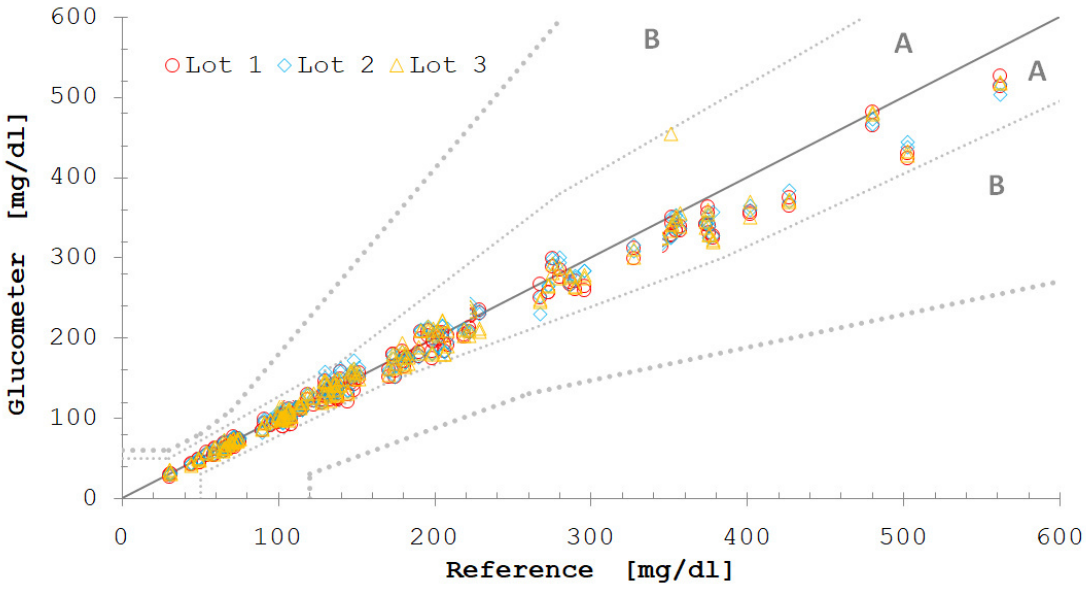

Fig. 2 | CEG of all tested Lots. All measurements (100%) reside within zone A and B.

III. Aim of the study

The present study evaluated the system accuracy of the BGM GlucoCheck Gold in accordance with the directive DIN EN ISO 15197 [1]: *In vitro diagnostic test systems - Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus*.

IV. Design of the study

IV.1. General considerations

System accuracy is evaluated in duplicate using fresh capillary blood samples (finger tip plasma) in order to obtain 100 evaluable data sets, using 3 reagent lots. The glucose concentrations have to cover the measurement intervals representing hypo-, eu-, and hyperglycemic conditions (Tab. 1). Blood samples are collected and processed according to the instructions of the blood glucose measurement system, including sample pre-treatment (if necessary; V.5). The blood glucose levels are measured in whole blood using the BGM (see V.1) and in plasma using the reference method Cobas c111 Analyzer (see V.4).

Tab. 1 | Blood glucose levels and proportion of samples for the evaluation of repeatability precision

Range	Glucose [mg/dL] / [mmol/L]	proportion of samples
1	≤ 50 / ≤ 2.77	5
2	> 50 – 80 / > 2.77 – 4.44	15 (8 unaltered)
3	> 80 – 120 / > 4.44 – 6.66	20 (all unaltered)
4	> 120 – 200 / > 6.66 – 11.10	30 (all unaltered)
5	> 200 – 300 / > 11.10 – 16.65	15 (all unaltered)
6	> 300 – 400 / > 16.65 – 22.20	10 (at least 5 unaltered)
7	> 400 / > 22.20	5

IV.2. Acceptance criteria

i. 95% of the measured glucose values must be within ± 15 mg/dL for glucose concentrations < 100 mg/dL of the mean values obtained by the reference measurement method

ii. 95% of the measured glucose values must be within ± 15 % for glucose concentrations ≥ 100 mg/dL of the mean values obtained by the reference measurement method

iii. 99% of individual glucose readings must reside within zones A and B of the consensus error grid (CEG, Parkes error grid) for type 1 diabetes

IV.3. Test persons

In order to obtain a potential subjects for the study, people were first informed about the objective, procedure, potential risks, and expected duration of the study. After declaration of willingness to participate in the study, a written and signed consent from the volunteer was requested. On the experimental day, good physical fitness was a prerequisite for blood sampling.

Inclusion criteria:

- Male or female patients with hypo-, eu- or hyperglycemia
- The written informed consent had to be signed
- The volunteers must be older than 18 years
- The volunteers have legal capacity and are able to understand meaning, nature and possible consequences of the procedures involved

Exclusion criteria:

- Pregnancy or lactation
- Acute or chronic diseases with the risk of aggravation by the measure
- A current constitution that does not allow participating in the study
- Participation in another study or activity with the blood glucose measuring system evaluated in the present study
- Application of substances listed in Appendix A of DIN EN ISO 15197:2015

The subject received an expense allowance of € 10.00.

IV.4. Sampling

The blood sampling takes 5 – 10 minutes and is executed by the trained and qualified medical personnel under strictly hygienic conditions, using sterile disposable material

only in order to minimize risks for the subjects. In case of discomfort of a subject, blood sampling is interrupted / aborted

IV.5. Experimental Procedure

All units of the reagent system for one sample are taken from the same package and are exchanged after 10 patients. All samples are applied to the reagent system unit as described in the instructions for use of the blood glucose measurement system. The evaluation is performed in the following order:

a. The packages are numbered and assigned to the BGM
b. A capillary blood sample of 200 µl is taken and glucose measurement is performed with the reference measurement method
c. The glucose concentration in the sample is measured using two blood glucose monitors (directly from the finger tip or see below)
d. If modified samples are used (see 4.e), they are applied in a manner that simulates the procedure specified in the instructions (i.e. using a pipette)
e. Immediately after the last measurement with the blood glucose measurement system, an aliquot of sample (b) is taken and glucose measurement is performed according to the reference measurement method
f. Both reference values are evaluated to verify sample stability:
    - Deviation of reference values of no more than 4 mg/dL for a glucose concentration < 100 mg/dL.
    - Deviation of reference values of no more than 4% for a glucose concentration ≥ 100 mg/dL.
        - If these results indicate an unacceptable shift in glucose concentration, the results from the respective subject are excluded, the sample is discarded, and replaced with another sample from the same glucose concentration range.
g. Steps (b) to (f) are repeated with the next subject

Residual blood samples are destroyed after completion of the test on the respective test day.

V. Material and methods

V.1. Test device

Data as provided by the manufacturer / operating instructions:

Blood Glucose Monitoring System:	GlucoCheck Gold, mg/dL
Manufacturer/Distributor:	aktivmed GmbH
Blood sample:	capillary whole blood
Sample volume:	0.5 µl
Glucose measurement range:	10 – 800 mg/dL (0.56 – 44.4 mmol/L)
Measuring time:	5 sec
Working temperature:	+8 °C – +45 °C
Relative humidity:	10 - 85 % rH n.c.
Hematocrit:	0 % - 70%
Enzyme:	GDH-FAD

For the evaluation, 3 blood glucose monitors GlucoCheck Gold mg/dL were provided by the manufacturer. Two devices were used during the tests (see Tab. 2).

Tab. 2 | Serial number and study code of blood glucose monitors

Serial number	Study code	devices used in the study
4289122230059991	GC1	x
428912223005997F	GC2	x
4289122230060007	GC3	

V.2. Test strips

Tab. 3 | Sensor strip lots included in the evaluation

Numbering	Lot No.	Expiration date	Target [mg/dL]	Target area [mg/dL]	
			47	32	62
Lot 1	WG22C921-BEE	19.03.24	140	125	155
			342	304	380

Numbering	Lot No.	Expiration date	Target [mg/dL]	Target area [mg/dL]	
			47	32	62
Lot 2	WG22C925-BEE	23.03.24	140	125	155
			342	304	380
			47	32	62
Lot 3	WG22E105-BEE	03.05.24	140	125	155
			342	304	380

V.3. Controls

Tab. 4 | Specifications of control solutions

Control solution	Lot No.	Expiration date
1 | low	YAA21E01	07.05.2023
2 | normal	WAA20L01	01.12.2022
3 | high	BAA21G01	02.07.2023

The measurements were performed according to the instructions by the manufacturer. Prior to and after test measurements, control measurements in each range and for each test strip lot and each monitor were performed.

V.4. Reference device

Analyzer:	Cobas c111 Analyzer
Manufacturer:	Roche Diagnostics Mannheim, Germany
Method:	Hexokinase, enzymatic photometric test
Sample:	Lithium-Heparin-Plasma from capillary blood
Sample volume:	2 µl
Glucose measurement range:	1.98–720 mg/dL / 0.11–40 mmol/L
Measuring time:	8 min
Working temperature:	15—32 °C
Relative humidity:	30—80 %
Calibration:	calibrator for automated systems, 202 mg/dL, LOT 53994501, exp 31.07.2023
Control:	Precicontrol ClinChem Multi 1 LOT 46149006, exp 28.02.2023

Precicontrol ClinChem Multi 2
LOT 41007607, exp 30.11.2023

Accuracy and Precision

The control of accuracy and precision was performed by use of Roche Diagnostics reference control materials with glucose concentrations of PCCCM1 103 mg/dL and PCCCM2 240 mg/dL, respectively. Quality controls were measured on each test day, before and after the test series.

Maintenance, adjustment and control procedures

For all the equipment used during the study, the control procedure has been implemented according to the manufacturer's instructions.

V.5. Blood sample acquisition and manipulation

In order to test blood samples in different glucose ranges (compare Tab. 1), the glucose concentration of a sample was adjusted by glucose supplementation or glycolysis following amended standard protocols:

- To reach the higher blood glucose concentrations, defined amounts of a 20 % glucose solution was added to 200 µl blood samples and safety mixed by shaking for 30 minutes at room temperature
- For blood glucose concentrations < 80 mg/dL, 200 µl blood samples were incubated at 37°C max in a shaking water bath for 1 to 4 hours

V.6. Determination of hematocrit

Determination of the hematocrit was performed in accordance with DIN 58933-1. Blood was sampled in micro-hematocrit capillaries and centrifuged at rcf 9.500 xg for 3 minutes. The hematocrit value was determined with an accuracy of ± 1 % by using a nomogram.

V.7. Measurement uncertainty

Expanded measurement uncertainty (k=2, 95%) was estimated in Jun. 2022 in accordance with ISO 11352 based on certified reference materials at ± 3.0 %.

No measurement uncertainties are taken into account for statements on conformity. The requirement is considered to be met if the measured value complies with acceptability levels. Analytical values that do not conform to specifications are displayed accordingly on this test report.

V.8. Data analysis

The analysis of data for the evaluation of system accuracy was performed in accordance with the instructions stated in DIN EN ISO 15197:2015. Glucose measurements were taken in plasma and displayed as plasma equivalents.

VI. Results

VI.1. Time of realization

The study took place in the period from July 25th 2022 until August 22nd 2022.

VI.2. Environmental conditions

During the study the ambient room temperature ranged between 23.7°C and 28.3°C, the relative humidity ranged between 35% and 55% rH (Fig. 3). The prescribed environmental conditions for BGM and reference systems as stated DIN EN ISO 15197:2015 (see characteristics in V.1 and V.4) were exceeded during the evaluation on August 15th. The evaluation was aborted, postponed until the prescribed conditions could be ensured, and was continued on August 22nd.

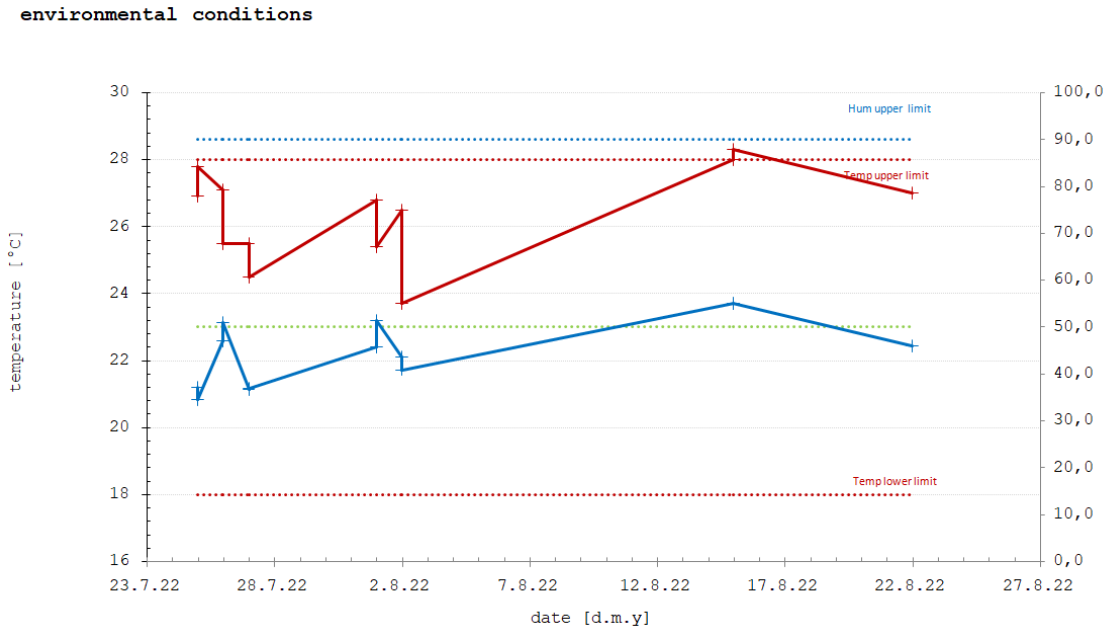

Fig. 3 | Environmental conditions during the evaluation.

VI.3. Control measurements BGM

All BGM performed according to their specifications and requirements with control measurements lying within the desired range for all levels (Tabs. 5 – 7). Therefore, no device was replaced.

Tab. 5 | Results of control measurements Lot 1 - WG22C921-BEE

day	***1***	***2***	***3***	***4***	***5***	***6***	***7***	
high	***mean***		348.4	***SD***		4.4	***CV***	1.3%
GC 1	349	344	347	348	340	346	345	
GC 2	355	352	350	351	344	350	356	
normal	***mean***		143.4	***SD***		1.9	***CV***	1.3%
GC 1	142	142	142	141	142	140	146	
GC 2	144	145	145	144	145	143	146	
low	***mean***		49.4	***SD***		1.3	***CV***	2.6%
GC 1	50	50	48	49	48	51	48	
GC 2	51	51	50	49	48	51	48	

Tab. 6 | Results of control measurements Lot 2 - WG22C925-BEE

day	***1***	***2***	***3***	***4***	***5***	***6***	***7***	
high		***mean***	347.9	***SD***		6.3	***CV***	1.8%
GC 1	345	351	337	346	343	342	347	
GC 2	355	363	348	353	347	346	347	
normal		***mean***	144.6	***SD***		1.7	***CV***	1.2%
GC 1	145	144	143	148	143	143	142	
GC 2	143	145	146	147	144	145	146	
low		***mean***	49.6	***SD***		0.8	***CV***	1.7%
GC 1	50	50	49	50	48	49	50	
GC 2	49	50	49	51	49	51	50	

Tab. 7 | Results of control measurement Lot 3 - WG22E105-BEE.

day	***1***	***2***	***3***	***4***	***5***	***6***	***7***	
high		***mean***	344.4	***SD***		5.7	***CV***	1.6%
GC 1	346	347	343	342	339	345	340	
GC 2	347	354	347	350	331	349	341	
normal		***mean***	142.7	***SD***		2.1	***CV***	1.5%
GC 1	143	141	141	142	142	140	141	
GC 2	143	145	141	147	144	142	146	
low		***mean***	49.6	***SD***		1.1	***CV***	2.2%
GC 1	50	49	49	48	48	51	51	
GC 2	50	50	49	49	49	51	51	

VI.4. Control measurements Reference

Tab. 8 | Results of control measurements – reference.

test day		**PCCCM1 Target: 103 mg/dL**	**PCCCM2 Target: 240 mg/dL**	**c.f.a.s. target: 202 mg/dL**
1	before	104.0	231.7	203.0
	after	105.2	241.1	
2	before	105.9	240.3	202.4
	after	107.6	243.0	
3	before	102.5	237.9	202.9

test day		PCCCM1 Target: 103 mg/dL	PCCCM2 Target: 240 mg/dL	c.f.a.s. target: 202 mg/dL
	after	104.0	234.2	
4	before	102.7	232.5	202.9
	after	102.0	232.8	
5	before	103.7	231.9	202.1
	after	103.5	233.1	
6	before	106.3	239.9	206.2
	after	105.2	239.4	
7	before	104.2	231.3	203.2
	after	103.6	235.5	
mean [mg/dL]		104.3	236.0	203.6
SD		1. 6	4.1	1.6
Dev to target [%]		-0.7 %	-1.7 %	0.3 %
CV [%]		1.5 %	1.7 %	0.8 %

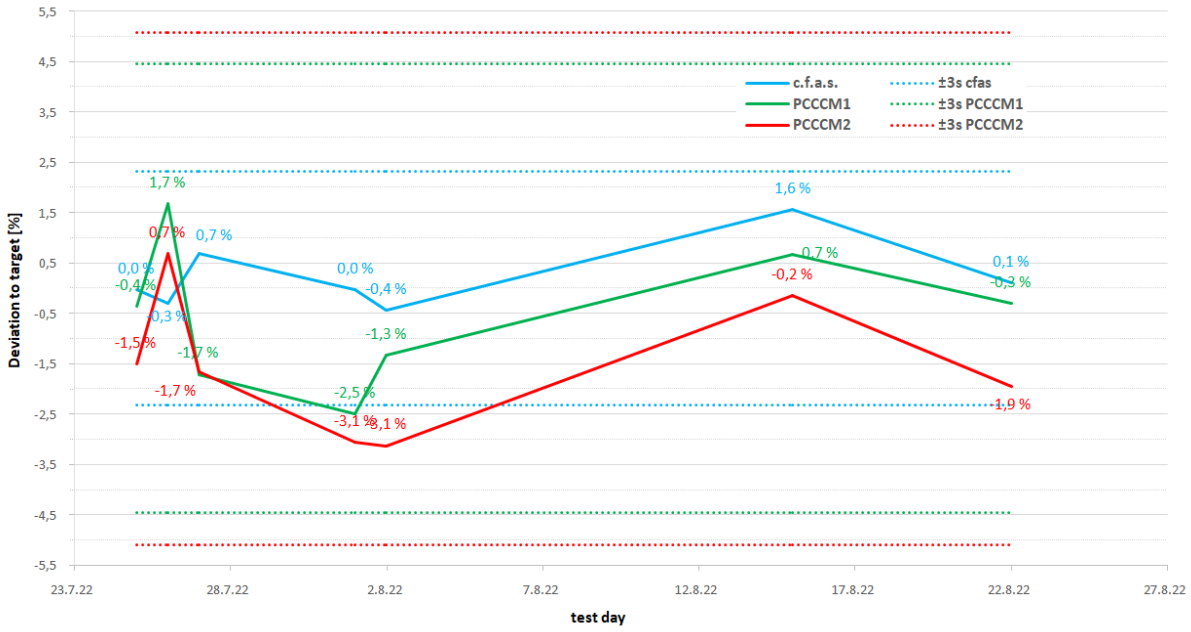

Fig. 4 | Control measurements reference device. Deviation of PreciControl ClinChem Multi 1 (green), PreciControl ClinChem Multi 2 (red) and calibrator for automated systems (cyan) to respective target for each test day (solid lines) and ± 3s acceptability levels (dotted lines).

VI.5. System accuracy measurements

In Lot 1 (WG22C921-BEE), 48 of 48 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 149 of 152 (98%) of measurements showed deviations of less than 15% to reference measurements for glucose concentrations ≥ 100 mg/dL (Tab.9).

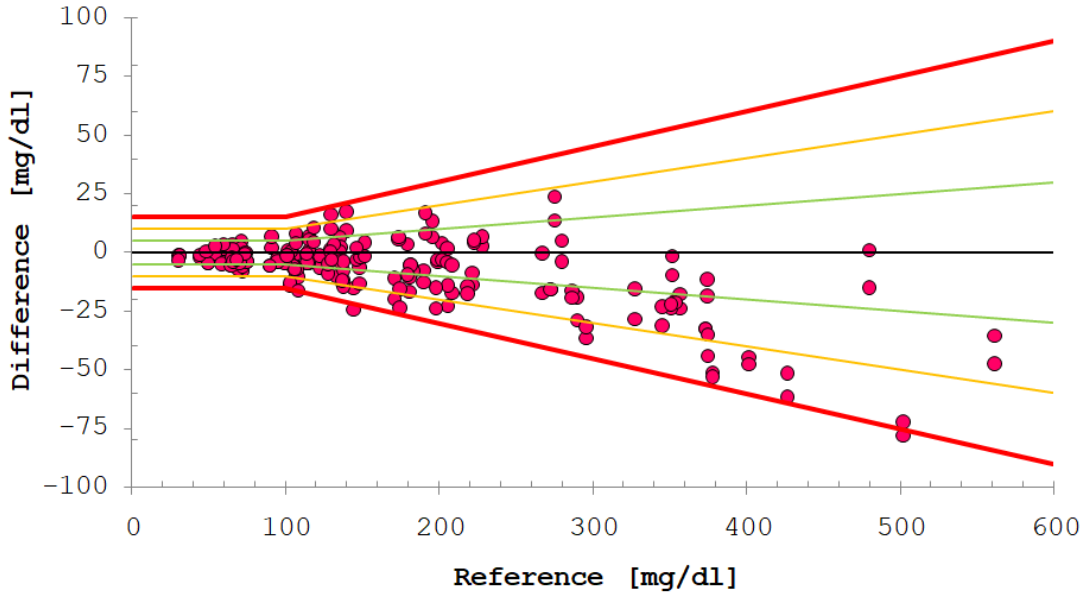

Fig. 5 | Bland-Altman diagram for Lot 1 - WG22C921-BEE. Thresholds of 5%, 10% and 15% indicated by green, orange and red solid line, respectively.

Tab. 9 | Results of system accuracy measurements Lot 1 - WG22C921-BEE.

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
48	40	83.3%	48	100%	48	100%

glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
152	73	48.0%	128	84.2%	149	98.0%

Tab. 10 | Results of system accuracy measurements combined glucose Lot 1 - WG22C921-BEE.

System accuracy for combined glucose concentrations LOT 1: within ± 15mg/dL or ± 15%	
197 / 200	98.5%

In Lot 2 (WG22C925-BEE), 48 of 48 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 148 of 152 (97.4%) of measurements showed deviations of less than 15 % to reference measurements for glucose concentrations ≥ 100 mg/dL.

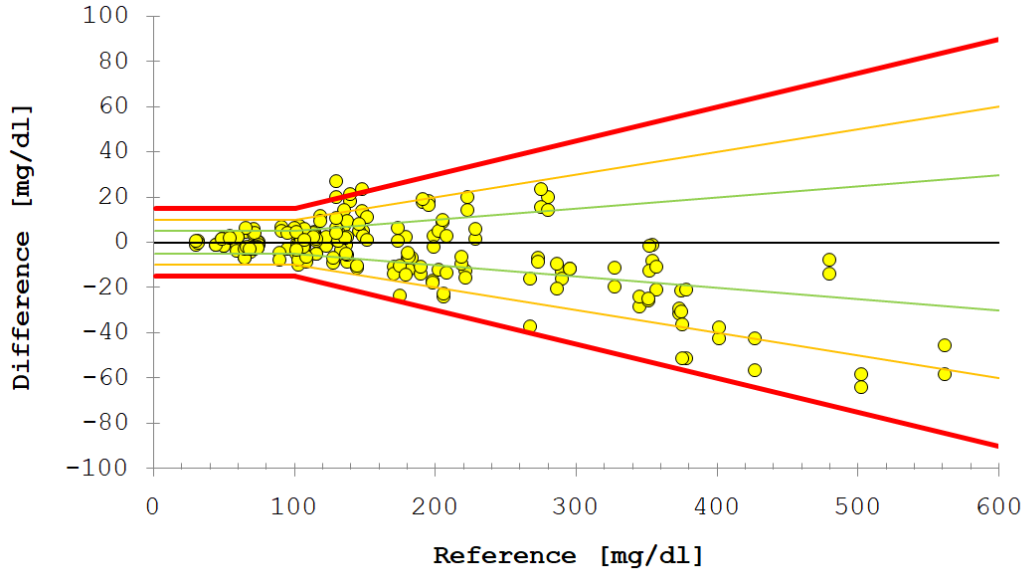

Fig. 6 | Bland-Altman diagram for Lot 2 - WG22C925-BEE. Thresholds of 5%, 10% and 15% indicated by green, orange and red solid line, respectively.

Tab. 11 | Results of system accuracy measurements Lot 2 - WG22C925-BEE.

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
48	41	85.4%	48	100%	48	100%
glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
152	74	48.7%	135	88.8%	148	97.4%

Tab. 12 | Results of system accuracy measurements combined glucose Lot 2 - WG22C925-BEE.

System accuracy for combined glucose concentrations LOT 2: within ± 15mg/dL or ± 15%	
196 / 200	98.0%

In Lot 3 (WG22E105-BEE), 48 of 48 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 150 of 152 (98.7%) of measurements showed deviations of less than 15 % to reference measurements for glucose concentrations ≥ 100 mg/dL.

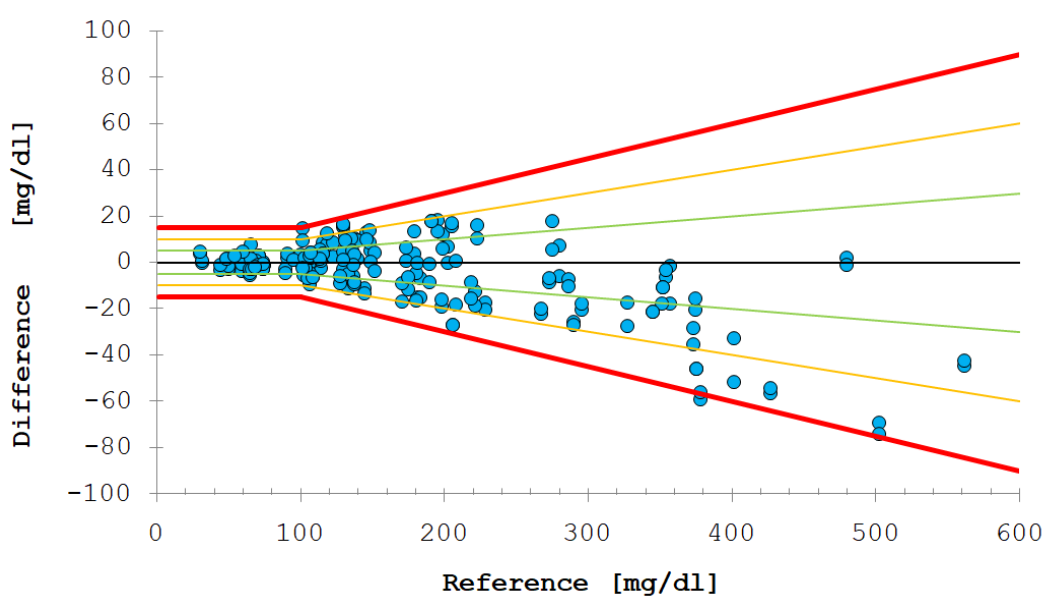

Fig. 7 | Bland-Altman diagram for Lot 3 - WG22E105-BEE. Thresholds of 5%, 10% and 15% indicated by green, orange and red solid line, respectively.

Tab. 13 | Results of system accuracy measurements Lot 3 - WG22E105-BEE

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
48	46	95.8%	48	100%	48	100%

glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
152	68	44.7%	135	88.8%	150	98.7%

Tab. 14 | Results of system accuracy measurements combined glucose Lot 3 - WG22E105-BEE

.System accuracy for combined glucose concentrations LOT 3: within ± 15mg/dL or ± 15%	
198 / 200	99.0%

Across all Lots, 144 of 144 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 447 of 456 (98.0%) of measurements showed deviations of less than 15 % to reference measurements for glucose concentrations ≥ 100 mg/dL.

Tab. 15 | Results of system accuracy measurements – all Lots.

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
144	127	88.2%	144	100%	144	100%
glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
456	215	47.1%	398	87.3%	447	98.0%

Tab.16 | Across-Lot summary of system accuracy of BGM GlucoCheck Gold across all glucose ranges.

combined glucose concentrations				
between	30.4 mg/dL	**and**	561.6 mg/dL	
within ± 15 mg/dL or 15%				
591 / 600			98.5%	

All measurements (100%) reside within zones A and B of the consensus error grid (Fig. 2)

VI.6. Exclusions

A total of 111 subjects were enlisted in order to obtain a data set of 100 measurements. 666 BGM measurements were performed in the evaluation. Sixty six measurements were excluded from the analysis and had to be replaced due to the following reasons: noncompliance with exclusion criteria; participation in study or activity with the blood glucose measuring system evaluated in the present study (n=6), application of substances listed in Appendix A of DIN EN ISO 15197:2015 (n=36), oversampling of glucose ranges (n=24).

VI.7. Adverse Device Effect , Adverse Event, Device Deficiencies

There were no incidents of adverse device effects, adverse events and/or device deficiencies, respectively.

VII. Conclusions

The blood glucose monitor GlucoCheck Gold was evaluated and determined to fully meet the requirements stipulated in DIN EN ISO 15197:2015.

Across all Lots and concentrations, 591 of 600 (98.5%) measurements showed clinically acceptable deviations of less than 15 mg/dL or 15%, respectively. In each Lot between 98% and 99% of measurements reached a clinically acceptable level of accuracy, meeting the requirements for acceptance criteria *i.* – *ii.* All measurements (100%) reside within zones A and B of the consensus error grid, complying with acceptance criterion *iii*.

VIII. References

1. *DIN EN ISO 15197:2015-12. In vitro diagnostic test systems - Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.*