Validation Report

Evaluation of

System Accuracy

of the Blood Glucose Monitoring System

GlucoCheck XL

Compliant with DIN EN ISO 15197:2015

Sponsor:

aktivmed GmbH
Oldenburger Straße 17
48429 Rheine, Germany

This study was conducted at:

Institut für Diabetes Karlsburg GmbH
Greifswalder Straße 11e
17495 Karlsburg, Germany

Study director:

Dr. Eckhard Salzsieder
Greifswalder Straße 11e
17495 Karlsburg, Germany

oversight and disclosure:

ethical review board approval number :
BB 205-21
clinicaltrials.gov ID:
NCT05219526

date of realization:

07.09.2022 - 18.10.2022

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report no.:

report_system-accuracy_ISO_2021_006_aktivmed_GlucoCheck-XL_2

changes to previous version:

p20: typo

This Report was authored by:

Karlsburg, 02.11.2022

Dr. Matthes Kenning

Head of Laboratory

Institute für Diabetes Karlsburg GmbH

Greifswalder Straße 11e

17495 Karlsburg, Germany

Content and format of this report have been reviewed and approved:

Karlsburg, 02.11.2022

Dr. Eckhard Salzsieder

Study Director

Institute für Diabetes Karlsburg GmbH

Greifswalder Straße 11e

17495 Karlsburg, Germany

Contents

I. Disclaimer

Ambit

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

Decision rule

Measurement uncertainties (see V.7) are not taken into account for statements on conformity. The requirement is considered fulfilled if the measured value is less than or equal to the tolerance limit or the limit value (adequate for lower limit values). Analytical values that do not conform to agreed specifications are indicated accordingly on this report.

II. Summary

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

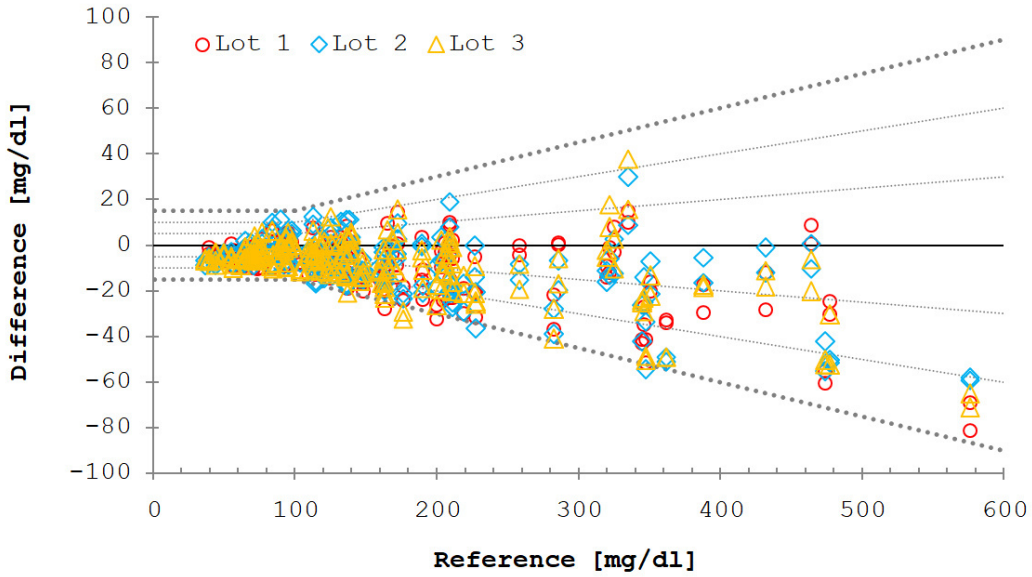

Fig. 1 | Bland-Altman Diagram for all tested Lots. 593 out of 600 measurements (98.8 %) show deviations <15 mg/dL / <15% for glucose concentrations <100 mg/dL and ≥ 100 mg/dL, respectively.

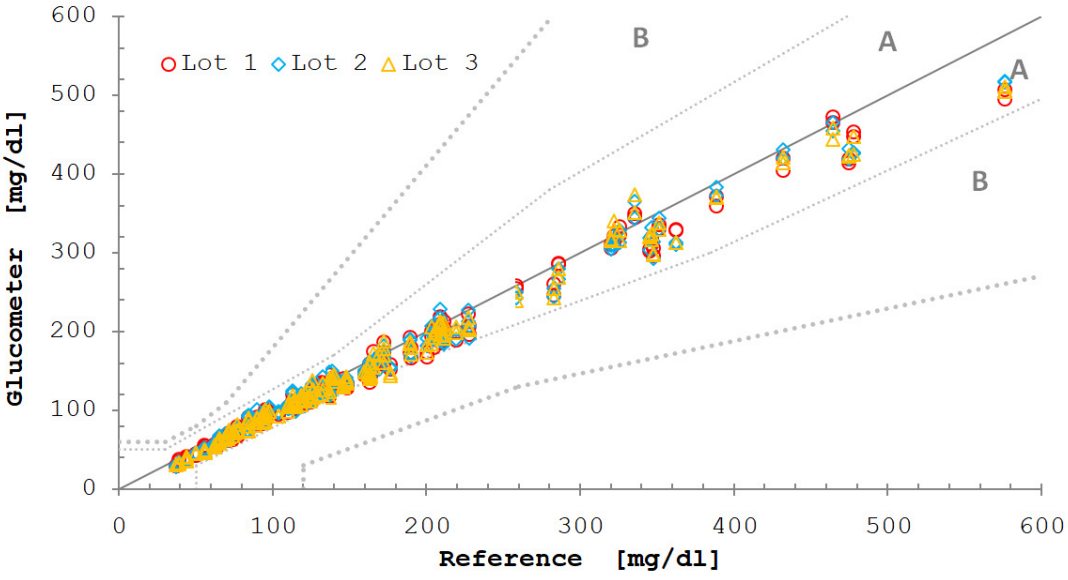

Fig. 2 | CEG of all tested Lots. All measurements (100%) reside within zone A and B.

III. Aim of the study

The present study evaluated the system accuracy of the BGM GlucoCheck XL 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 hyperglycaemia
- 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 XL, mg/dL
Manufacturer/Distributor:	aktivmed GmbH
Blood sample:	capillary whole blood
Sample volume:	0.5 µl
Glucose measurement range:	20 – 600 mg/dL (1.1 – 33.3 mmol/L)
Measuring time:	5 sec
Working temperature:	+10 °C – +40 °C
Relative humidity:	10 – 85 % rH n.c.
Hematocrit:	0 % - 70%
Enzyme:	GDH-FAD

For the evaluation, 3 blood glucose monitors GlucoCheck XL 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
427712000000003A	GC1	x
427712000000005C	GC2	x
4277120000000018	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]
Lot 1	TD22C207-B0R	07.03.2024	61	46	76
			150.5	128	173
			343	292	394

Numbering	Lot No.	Expiration date	Target [mg/dL]	Target area	[mg/dL]
Lot 2	TD22C919-B0R	19.03.2024	61	46	76
			150.5	128	173
			343	292	394
Lot 3	TD22D925-B0R	25.04.2024	61	46	76
			150.5	128	173
			343	292	394

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 LOTs 52502704, 515306 Precicontrol ClinChem Multi 2 LOTs 41007607, 525131

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 (Tab.8).

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 %.

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 September 9th 2022 until October 18th 2022.

VI.2. Environmental conditions

During the study the ambient room temperature ranged between 24.4°C and 25.7°C, the relative humidity ranged between 36% and 48% 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 met.

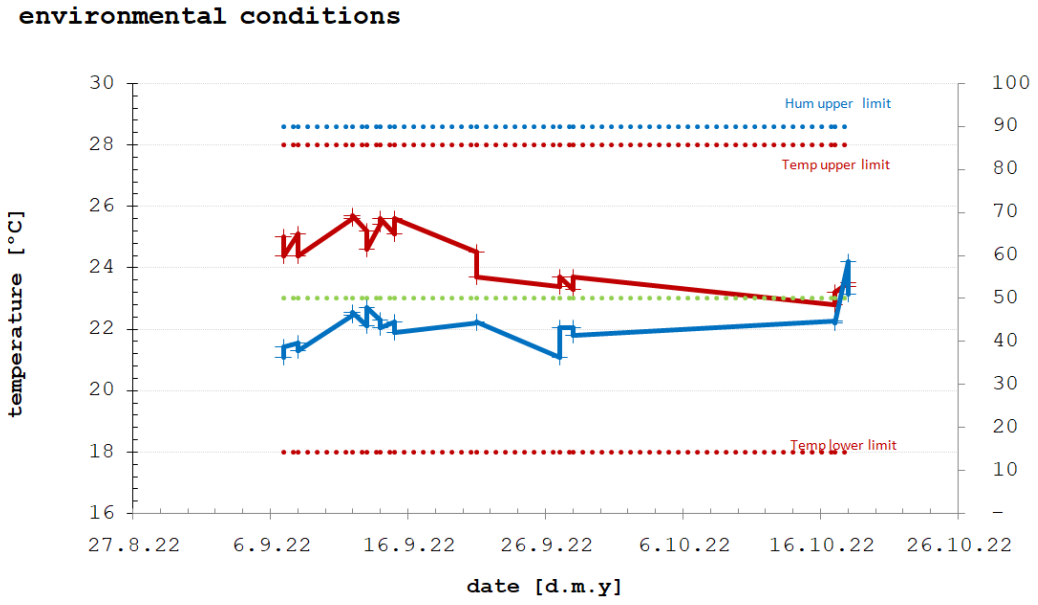

Fig. 3 | Environmental conditions during the evaluation.

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 - TD22C207-B0R. Measurements in mg/dL.

day	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***11***
high	***mean***		347.9	***SD***		*10.2*	***CV***	*2.9%*			
GC 1	342	345	348	345	357	351	350	352	326	368	354
GC 2	340	340	347	357	351	350	355	350	324	340	361
normal	***mean***		***152***	***SD***		*3.2*	***CV***	*2.1%*			
GC 1	153	158	155	154	149	152	151	147	150	160	155
GC 2	152	148	152	148	149	152	150	154	153	151	151
low	***mean***		*62.7*	***SD***		*3.1*	***CV***	*4.9%*			
GC 1	60	64	59	69	62	64	63	65	62	56	62
GC 2	62	62	63	69	63	63	65	64	63	57	63

Tab. 6 | Results of control measurements Lot 2 - TD22C919-B0R. Measurements in mg/dL.

day	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***11***
high	***mean***		*345.3*	***SD***		*8.4*	***CV***	*2.4%*			
GC 1	339	334	352	359	350	339	355	342	346	347	355
GC 2	327	341	345	357	343	334	337	353	346	342	353
normal	***mean***		*149.6*	***SD***		*3.4*	***CV***	*2.3%*			
GC 1	151	149	151	154	147	156	149	144	153	151	156
GC 2	152	147	151	148	146	147	150	146	146	146	152
low	***mean***		*61.6*	***SD***		*1.4*	***CV***	*2.2%*			
GC 1	62	61	62	61	60	61	62	62	63	63	62
GC 2	63	61	62	63	60	58	63	62	61	64	60

Tab. 7 | Results of control measurement Lot 3 - TD22D925-B0R. Measurements in mg/dL.

day	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***11***
high	***mean***		*349.1*	***SD***		*9.5*	***CV***	*2.7%*			
GC 1	348	345	347	356	349	344	345	347	349	353	375
GC 2	342	333	346	360	347	331	348	350	350	349	367

normal	***mean***		*151.2*	***SD***		*4.2*	***CV***	*2.8%*			
GC 1	152	150	153	151	150	149	153	150	147	162	161
GC 2	151	146	149	148	148	149	150	147	150	153	158
low	***mean***		*63.0*	***SD***		*2.2*	***CV***	*3.4%*			
GC 1	63	60	63	64	63	62	62	62	66	67	66
GC 2	63	60	62	65	62	62	62	61	61	68	62

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**
07.09.2022	before	106.0	238.7	204.6
	after	104.2	238.6	
08.09.2022	before	104.7	235.9	202.3
	after	103.4	232.7	
12.09.2022	before	105.5	237.2	201.8
	after	104.7	237.4	
13.09.2022	before	104.6	232.3	202.6
	after	103.9	233.8	
14.09.2022	before	105.8	234.9	201.3
	after	105.3	234.9	203.4
15.09.2022	before	105.3	235.0	204.9
	after	104.5	235.3	
21.09.2022	before	106.1	234.6	203.0
	after	104.0	234.8	
27.09.2022	before	104.8	234.4	201.5
	after	104.5	236.9	
28.09.2022	before	106.6	240.0	203
	after	105.5	241.0	201
17.10.2022	before	104.1	236.4	204.1
	after	103.3	240.9	
18.10.2022	before	104.4	242.4	202.0
	after	103.5	242.0	
mean [mg/dL]		104.7	236.8	202.7
SD		0.9	2.9	1.2
Dev to target [%]		1.7 %	-1.3 %	0.4 %
CV [%]		0.9 %	1.2 %	0.6 %

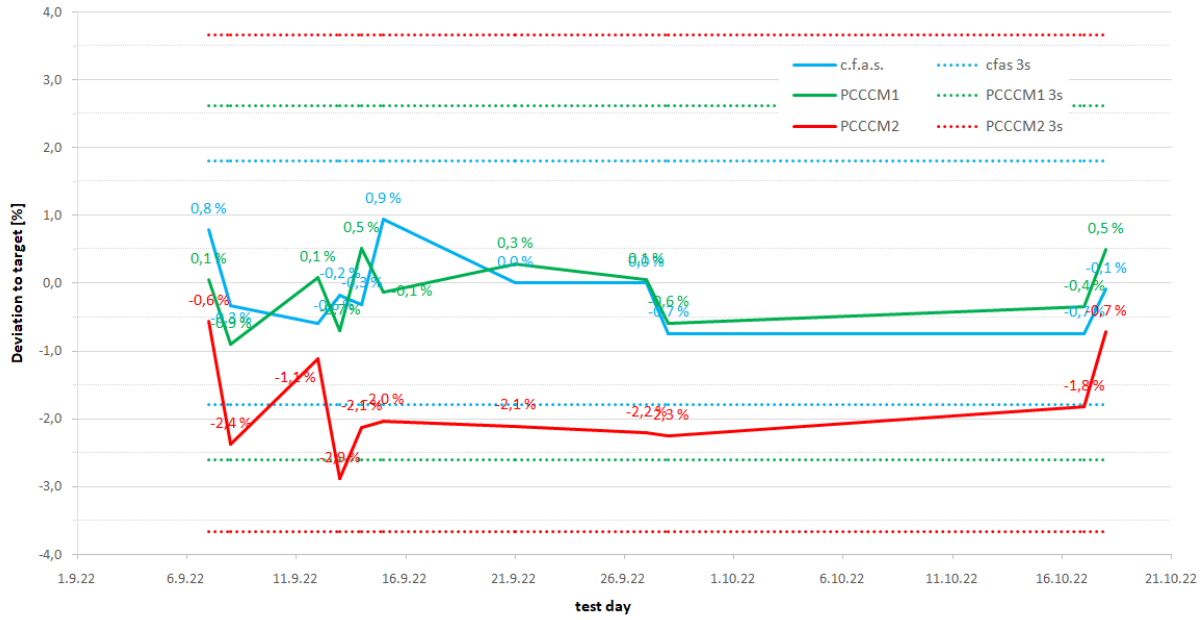

Fig. 4 | Control measurements reference device. Deviation of PreciControl ClinChem Multi 1 (PCCCM1, green), PreciControl ClinChem Multi 2 (PCCCM2, red) and calibrator for automated systems (c.f.a.s., cyan) to respective target for each test day (solid lines) and ± 3s acceptability levels (dotted lines).

VI.5. System accuracy measurements

In Lot 1 (TD22C207-B0R), 62 of 62 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 136 of 138 (98.6%) of measurements showed deviations of less than 15% to reference measurements for glucose concentrations ≥ 100 mg/dL (Tab.9).

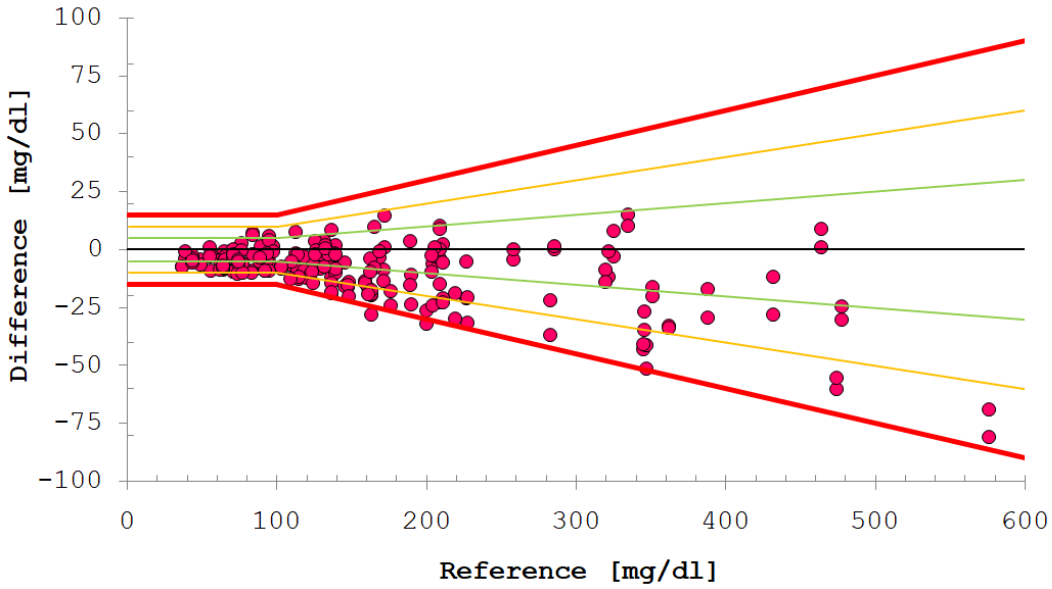

Fig. 5 | *Bland-Altman diagram for Lot 1* - TD22C207-B0R. *Thresholds of 5%, 10% and 15% indicated by green, orange and red solid line, respectively.*

Tab. 9 | *Results of system accuracy measurements Lot 1* - TD22C207-B0R.

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
62	33	53.2%	59	95.2%	62	100%

glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
138	57	41.3%	99	71.7%	136	98.6%

Tab. 10 | *Results of system accuracy measurements combined glucose Lot 1* - TD22C207-B0R.

System accuracy for combined glucose concentrations LOT 1: within ± 15mg/dL or ± 15%	
198 / 200	99.0%

In Lot 2 (TD22C919-B0R), 62 of 62 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 136 of 138 (98.6%) of measurements showed deviations of less than 15 % to reference measurements for glucose concentrations ≥ 100 mg/dL.

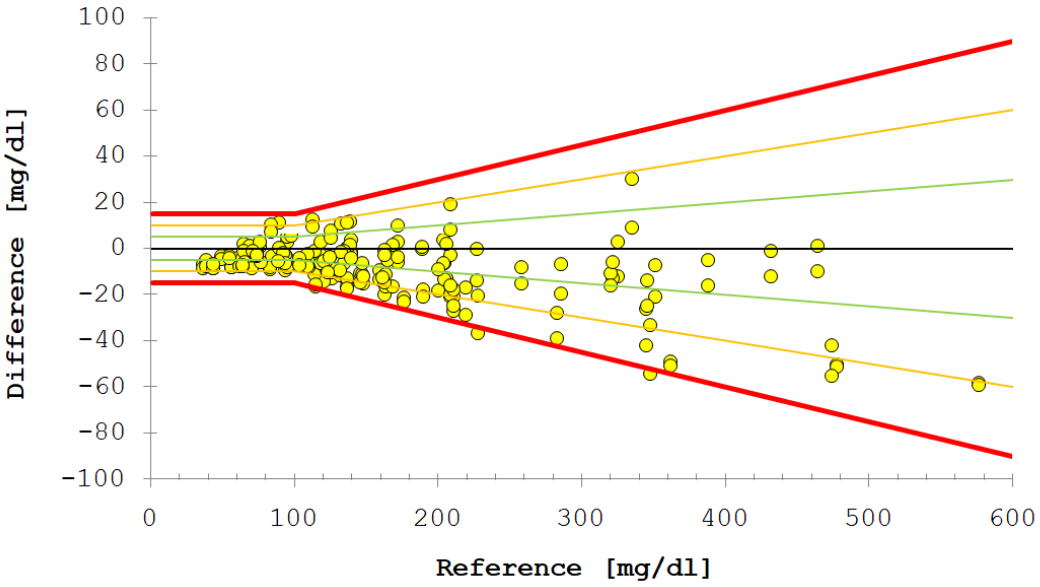

Fig. 6 | *Bland-Altman diagram for Lot 2* - TD22C919-B0R. *Thresholds of 5%, 10% and 15% indicated by green, orange and red solid line, respectively.*

Tab. 11 | *Results of system accuracy measurements Lot 2* - TD22C919-B0R.

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
62	30	48.4%	60	96.8%	62	100%

glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
138	54	39.1%	108	78.3%	136	98.6%

Tab. 12 | *Results of system accuracy measurements combined glucose Lot 2* - TD22C919-B0R.

System accuracy for combined glucose concentrations LOT 2: within ± 15mg/dL or ± 15%	
198 / 200	99.0%

In Lot 3 (TD22D925-B0R), 62 of 62 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 135 of 138 (97.8%) of measurements showed deviations of less than 15 % to reference measurements for glucose concentrations ≥ 100 mg/dL.

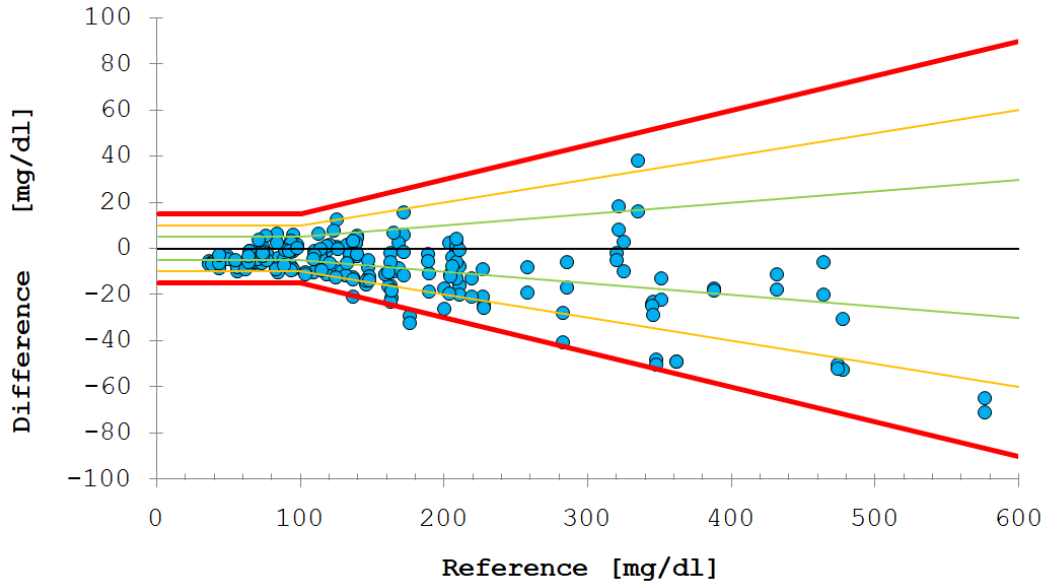

Fig. 7 | *Bland-Altman diagram for Lot 3* - TD22D925-B0R. *Thresholds of 5%, 10% and 15% indicated by green, orange and red solid line, respectively.*

Tab. 13 | *Results of system accuracy measurements Lot 3* - TD22D925-B0R.

glucose concentrations < 100 mg/dL						
N	**within ± 5 mg/dL**		**within ± 10 mg/dL**		**within ± 15 mg/dL**	
62	30	48.4 %	60	96.8%	62	100%

glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
138	59	42.8%	112	81.2 %	135	97.8%

Tab. 14 | *Results of system accuracy measurements combined glucose Lot 3* - TD22D925-B0R.

.System accuracy for combined glucose concentrations LOT 3: within ± 15mg/dL or ± 15%	
197 / 200	98.5%

Across all Lots, 186 of 186 (100%) measurements showed deviations of less than 15 mg/dL for glucose concentrations < 100 mg/dL, and 407 of 414 (98.3%) 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**	
186	93	50.0%	179	96.2%	186	100%

glucose concentrations ≥ 100 mg/dL						
N	**within ± 5%**		**within ± 10%**		**within ± 15%**	
414	170	41.1%	319	77.1%	407	98.3%

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

combined glucose concentrations				
between	38.6 mg/dL	**and**	576.2 mg/dL	
within ± 15 mg/dL or 15%				
593 / 600			98.8%	

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

VI.6. Exclusions

A total of 112 subjects were enlisted in order to obtain a data set of 100 measurements. 672 BGM measurements were performed in the evaluation. Seventy two measurements were excluded from the analysis and had to be replaced due to the following reasons: noncompliance with exclusion criteria (n=18), oversampling of glucose ranges (n=54).

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

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

VII. Conclusions

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

Across all Lots and concentrations, 593 of 600 (98.8%) measurements showed clinically acceptable deviations of less than 15 mg/dL or 15%, respectively. In each Lot between 98.5% 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.*