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Repeatability precision measurement evaluation of the system for self-monitoring of blood glucose GL 44 following DIN EN ISO 15197:2015

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Abbreviations: CE: Conformite Europeene; ISO: International Organization for Standardization; SMBG: Self-Monitoring of Blood Glucose.

Introduction

Ongoing standardized verification of the repeatability precision measurement of blood glucose meter systems for self-monitoring post-launch is important clinically and helps confirm appropriate continues performance of self-monitoring blood glucose (SMBG) – systems [1]. In addition, publication of such studies is increasingly becoming a component of evidence-based purchase decision making. ISO 15197:2015, [2] for which mandatory compliance is recommended for SMBG systems by 2015, [3] has tighter accuracy requirements than ISO 15197:2003, [4-6]

In the present study, a postmarketing evaluation of the CE-marked GL44 system for repeatability precision were performed in accordance with ISO 15197:2015 protocols and requirements. The GL44 system were supplied in Germany from the Beurer GmbH, Germany.

Venous blood from a test person was sampled in Lithium-Heparine tubes (Vacutainer, Saarstedt, Germany). After well mixing, the blood was aliquoted into five samples of 300 µl each with glucose concentrations in 5 different ranges as revealed by measurements with the YSI 2300 STAT PLUS reference device: Hematocrit values of all samples used were between 43% and 44% and therefore in the required range, given in the user manual, between 35% and 50% (Table 1).

Test devices: In the study, ten glucose monitors with different serial numbers were used. Serial number and study code of the glucose monitors (Beurer GL44) (Table 2):

Test strip lots: In total, 600 test strips from each of the 3 lots were available. The following lots were included into the tests (Table 3):

The control measurements, done before the blood tests, were performed using three glucose control solutions with the following characteristics (Table 4):

Table 1. Self-monitoring blood glucose

Range	Actually measured blood glucose values
1: 30 - 50 mg/dl	41 mg/dl
2: 51 - 110 mg/dl	91 mg/dl
3: 111 - 150 mg/dl	123 mg/dl
4: 151 - 250 mg/dl	169 mg/dl
5: 251 - 400 mg/dl	281 mg/dl

Table 2. Serial number and study code of the glucose monitors

Study code	Serial number
GC 1	GL44T1
GC 2	GL44T2
GC 3	GL44T3
GC 4	GL44T4
GC 5	GL44T5
GC 6	GL44T6
GC 7	GL44T7
GC 8	GL44T8
GC 9	GL44T9
GC 10	GL44T10
GC 11	GL44T11 (not used)

Table 3. Lot numbering and expiration date

Test strips		
Numbering	**Lot No.**	**Expiration date**
Lot 1	A10/1	2017/03
Lot 2	A10/3	2017/03
Lot 3	A10/5	2017/03

Table 4. Control measurements, done before the blood tests

Control solution	Lot Number	Expiration date	Target range (mg/dl)
Level high	A04/3	2016/07	308-386
Level normal	A04/3	2016/12	124-154
Level low	A04/3	2016/08	65-81

For setting glucose concentrations between 30 – 50 mg/dl, the blood was stored at 37 °C.

To set the higher concentrations of glucose (> 120 mg/dl) the Lithium-heparin blood samples (300 µl each) were spiked with a glucose solution (Glucose 40 %, B. Braun, Melsungen, Germany). Before the measurements were started in the above-mentioned ranges, a 100 µl aliquot was separated from each 300 µl blood sample. These 100 µl samples were taken to separate plasma for the reference measurements" before". After the test measurements, the plasma was separated from

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the remaining blood sample volume and it was used for the reference measurements "after" the tests.

After reference sample separation, drops of blood were placed on the designated area of the test strip by means of a pipette (10 glucose monitors were handled in parallel). For each of the three included test lots, ten measurements on the ten monitors each were performed.

Results

The statistical analysis for each test lot and each glucose meter within the five glucose concentration ranges are given in Table 5.

Analysis of mean, standard deviation (SD) und coefficient of variation (CV) for each test lot and each glucose meter in the 5 glucose concentration ranges of 41 mg/dl, 91 mg/dl, 123 mg/dl, 169 mg/dl and 281 mg/dl, respectively.

Analysis of pooled mean values, pooled standard deviation (SD) and pooled coefficient of variation (CV)in summary of the 3 test lots (Table 6) in the 5 glucose concentration ranges of 41 mg/dl, 91 mg/dl, 123 mg/dl, 169 mg/dl and 281 mg/dl.

The pooled coefficient of variation was less than 5% for all test Lots and in all glucose concentration ranges of >100 mg/dl. Highest single coefficient of variation in the concentration ranges >100 mg/dl for a glucose meter was found to be 6.4%. At glucose concentrations of <100 mg/dl the pooled standard deviation did not exceeded the 95% confidence interval.

Table 5. Statistical analysis for each test lot and each glucose meter within the five glucose concentration ranges

Lot 1				**Lot 2**				**Lot 3**			
41 mg/dl											
meter	mean	SD	CV	meter	mean	SD	CV	meter	mean	SD	CV
1	35	1.7	4.9	1	33	1.2	3.6	1	30	1.6	5.3
2	37	1.1	3.0	2	34	1.9	5.6	2	31	2.1	6.8
3	39	1.0	2.6	3	34	1.7	5.0	3	33	1.9	5.8
4	37	1.5	4.1	4	34	1.5	4.4	4	32	1.3	4.1
5	38	1.2	3.2	5	34	1.8	5.3	5	32	1.6	5.0
6	38	0.9	2.4	6	34	1.8	5.3	6	31	1.2	3.9
7	38	1.9	5.0	7	36	1.4	3.9	7	31	1.7	5.5
8	36	1.2	3.3	8	35	1.4	4.0	8	33	1.2	3.6
9	34	1.8	5.3	9	33	1.4	4.2	9	31	2.7	8.7
10	33	1.4	4.2	10	32	1.2	3.8	10	30	0.9	3.0
mean	37	1.4	3.8	mean	34	1.5	4.5	mean	32	1.6	5.1
91 mg/dl											
meter	mean	SD	CV	meter	mean	SD	CV	meter	mean	SD	CV
1	101	2.1	2.1	1	90	1.7	1.9	1	92	3.6	3.9
2	97	3.7	3.8	2	97	2.6	2.7	2	91	2.1	2.3
3	96	3.6	3.8	3	95	2.6	2.7	3	90	2.1	2.3
4	95	3.3	3.5	4	100	2.0	2.0	4	92	1.6	1.7
5	97	4.8	4.9	5	95	3.0	3.2	5	91	3.3	3.6
6	98	1.6	1.6	6	96	2.2	2.3	6	95	2.5	2.6
7	98	4.7	4.8	7	96	2.3	2.4	7	95	2.0	2.1
8	91	4.3	4.7	8	97	3.8	3.9	8	88	4.3	4.9
9	96	4.2	4.4	9	94	3.9	4.1	9	91	1.9	2.1
10	96	2.3	2.4	10	93	3.1	3.3	10	91	1.1	1.2
mean	96	3.5	3.6	mean	95	2.7	2.8	mean	92	2.4	2.6
123 mg/dl											
meter	mean	SD	CV	meter	mean	SD	CV	meter	mean	SD	CV
1	122	2.5	2.0	1	124	4.7	3.8	1	120	2.3	1.9
2	127	3.0	2.4	2	127	3.0	2.4	2	124	3.7	3.0
3	127	2.5	2.0	3	126	2.3	1.8	3	122	1.8	1.5
4	124	5.7	4.6	4	129	2.8	2.2	4	129	2.3	1.8
5	129	5.5	4.3	5	126	4.7	3.7	5	122	3.0	2.5
6	125	2.3	1.8	6	129	4.0	3.1	6	123	3.9	3.2
7	128	2.8	2.2	7	126	2.2	1.7	7	126	4.1	3.3
8	125	4.8	3.8	8	128	8.2	6.4	8	119	3.8	3.2
9	128	6.5	5.1	9	121	1.9	1.6	9	121	1.7	1.4
10	124	6.6	5.3	10	120	4.0	3.3	10	119	1.6	1.3
mean	126	4.2	3.3	mean	125	3.8	3.0	mean	122	2.8	2.3
169 mg/dl											
meter	mean	SD	CV	meter	mean	SD	CV	meter	mean	SD	CV
1	174	3.2	1.8	1	166	4.6	2.8	1	162	2.3	1.4
2	172	5.6	3.3	2	169	3.3	2.0	2	168	3.3	2.0
3	174	3.8	2.2	3	165	3.2	1.9	3	168	4.2	2.5
4	173	5.9	3.4	4	167	5.2	3.1	4	169	5.8	3.4

5	172	5.8	3.4	5	171	3.0	1.8	5	168	3.2	1.9
6	173	4.9	2.8	6	165	5.1	3.1	6	166	1.9	1.1
7	173	2.9	1.7	7	172	3.2	1.9	7	170	2.8	1.6
8	172	3.5	2.0	8	171	2.8	1.6	8	163	5.3	3.3
9	174	3.6	2.1	9	168	2.9	1.7	9	165	4.8	2.9
10	170	4.6	2.7	10	176	3.8	2.2	10	164	2.9	1.8
mean	173	4.4	2.6	mean	169	3.7	2.2	mean	166	3.6	2.2
281 mg/dl											
meter	mean	SD	CV	meter	mean	SD	CV	meter	mean	SD	CV
1	284	5.8	2.0	1	283	5.6	2.0	1	281	6.8	2.4
2	283	8.7	3.1	2	284	5.3	1.9	2	283	5.0	1.8
3	285	12.0	4.2	3	285	6.9	2.4	3	290	11.4	3.9
4	291	8.7	3.0	4	292	3.8	1.3	4	286	8.0	2.8
5	295	6.8	2.3	5	289	7.1	2.5	5	292	3.6	1.2
6	302	6.1	2.0	6	297	5.6	1.9	6	284	4.9	1.7
7	298	6.7	2.2	7	296	5.2	1.8	7	293	7.0	2.4
8	291	4.6	1.6	8	299	4.7	1.6	8	283	4.1	1.4
9	297	9.3	3.1	9	289	2.0	0.7	9	286	9.0	3.1
10	293	9.9	3.4	10	291	5.5	1.9	10	288	5.5	1.9
mean	292	7.9	2.7	mean	291	5.2	1.8	mean	287	6.5	2.3

Table 6. Summary of lot 1, 2 and 3

Summary of lot 1, 2 and 3		**System**	**Beurer GL44**				
Blood Conc. Level		N	41 mg/dl	91 mg/dl	123 mg/dl	169 mg/dl	281 mg/dl
Mean	Lot #1	100	36	96	126	172	292
	Lot #2	100	34	95	125	169	290
	Lot #3	100	31	92	122	166	287
Pooled mean		300	34	94	125	169	290
SD	Lot #1	100	1.4	3.5	4.2	4.4	7,9
	Lot #2	100	1.5	2.7	3.8	3.7	5,2
	Lot #3	100	1.6	2.4	2.8	3.6	6,5
Pooled SD		300	1,5	2.9	3.6	3.9	6.5
CV (%)	Lot #1	100	3.8	3.6	3.3	2.5	2,7
	Lot #2	100	4.5	2.8	3.0	2.2	1,8
	Lot #3	100	5.1	2.7	2.3	2.2	2,3
Pooled CV (%)		300	4,5	3.0	2.9	2.3	2.3
Blood Conc. Level		N	41 mg/dl	91 mg/dl	123 mg/dl	169 mg/dl	281 mg/dl
pooled mean		300	34	94	125	169	290
pooled SD		300	1.5	2.9	3.6	3.9	6.5
pooled CV (%)		300	4.5	3.0	2.9	2.3	2.3

The validation of the glucose meter system Beurer GL44 was revealed in all concentration ranges according norm EN ISO 15197:2015, the intra-assay precision was expressed as pooled CV≤ 5% and pooled standard deviation within the 95% confidence interval. The pooled coefficient of variation and the pooled standard deviation with a confidence interval of 95 % represent appropriate and conclusive criteria for assessing the quality of the test system. The generated data demonstrate accurate and reliable results for the tested device.

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Conflicts of interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All authors are employees of the Institute of Diabetes, Karlsburg, Germany, which carries out studies evaluating blood glucose meter systems on behalf of various companies.

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