Supplementary Material for

Evaluation of system accuracy, precision, hematocrit influence and user performance of two blood glucose monitoring systems based on ISO 15197:2013/EN ISO 15197:2015

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Table S1: Demographic data of Participants

		User Performance Evaluation (n = 102)		System Accuracy Evaluation (n = 100)	Venous Accuracy Evaluation (n = 100)
		A	B		
Type of diabetes	**Type 1**	50 (49%)		48 (48%)	50 (50%)
	Type 2	52 (51%)		45 (45%)	45 (45%)
	No Diabetes	n.a.		7 (7%)	5 (5%)
Gender	**Female**	41 (40%)		43 (43%)	44 (44%)
	Male	61 (60%)		57 (57%)	56 (56%)
	Age	59.7 [22-83]	60 [22-83]	58.6 [21-83]	59.0 [21-82]
Highest education level	**Secondary education (9 years)**	17 (17%)	18 (18%)	n.d.	n.d.
	Secondary education (10 years)	43 (42%)		n.d.	n.d.
	University entrance diploma	22 (22%)	21 (21%)	n.d.	n.d.
	University degree	20 (20%)		n.d.	n.d.

Data provided as numbers and rate of occurrences, except for age which is given as mean and [range]. Abbreviations: n.a., not applicable; n.d., not documented
Highest education level was only documented for subjects who also participated in the user performance evaluation, but not those who only participated in the system accuracy evaluation.

Inclusion and Exclusion criteria:

Inclusion criteria:

- Signed informed consent form
- Minimum age of 18 years
- Subjects are legally competent and capable to understand character, meaning and consequences of the study.
- If blood glucose values < 80 mg/dl or > 300 mg/dl shall be measured after short term alteration in insulin therapy:
    - Male or female with type 1 diabetes and intensified insulin therapy or insulin pump therapy.
    - Signature of subjects to document consent with these procedures on informed consent form.

Exclusion:

- Pregnancy or lactation period if venous samples are needed
- Severe acute disease that compromises the subject's capability to participate in the study (at the study physician's discretion)
- Severe chronic disease with potential risk during the test procedures (at the study physician's discretion)
- Medical relevant anemia
- Suspected lack of compliance
- Dependence on investigator or sponsor
- If blood glucose values < 80 mg/dl shall be measured after short term alteration in insulin therapy:
- Pregnancy or lactation period

- Subjects with type 1 diabetes, suffering from
    - Coronary heart disease
    - Condition after myocardial infarction
    - Condition after cerebral events
    - Peripheral arterial occlusive disease
    - Hypoglycemia unawareness

For venous blood samples, we additionally ensured that the venous blood met the requirements indicated in the manufacturer's labelling, e.g., no interfering substances and the hematocrit to be within the indicated range.

System accuracy assessment, venous accuracy analysis and user performance evaluation with hexokinase reference method

The analyses were performed as described in the main text except that comparator values were determined in duplicate measurements with a Cobas Integra 400 Plus (Roche) analyzer using the hexokinase method on separated plasma samples. Glucose concentrations measured by the laboratory analyzer ranged from 37 to 468 mg/dL. A total of 22 measurements were not included in the analysis, reasons for that were: the concentration category was filled already (12x), sample stability could not be ensured (8x), no valid QC result of the comparator measurement (1x) and hemolysis in plasma sample for comparator analysis (1x).

For both systems 100% of BGMS results were within ± 15 mg/dL or ± 15% of the hexokinase comparator results for system accuracy analysis as well as user performance evaluation (Figure S1). A bias ranging from 1.3% to -1.9% for system A and from 1.2% to -0.3% for system B for system accuracy was found for all test strip lots (Table S2). The bias is the difference between the BGMS results and the comparator results divided by the mean of all.

In venous accuracy analysis of system B, glucose concentrations ranged between 35 mg/dL and 509 mg/dL. Here, 9 samples were excluded from analysis due to the following reasons: concentration category already filled (7x), sample stability could not be ensured (1x) and comparator sample was outside the borders used for CEG analysis (1x).
Venous accuracy analysis for system B revealed that for all lots between 98% and 100% of BGMS results were within ± 15 mg/dL or ± 15% of the hexokinase comparator results (Figure S1). Similar to system accuracy assessment, all measurement results from venous samples for system B fell in the clinically acceptable zone A of the CEG analysis.

For user performance evaluation with the Cobas Integra 400 Plus, one sample of each system A and B had to be rejected from analysis since there was no valid quality control (QC) measurement result of the comparator method.

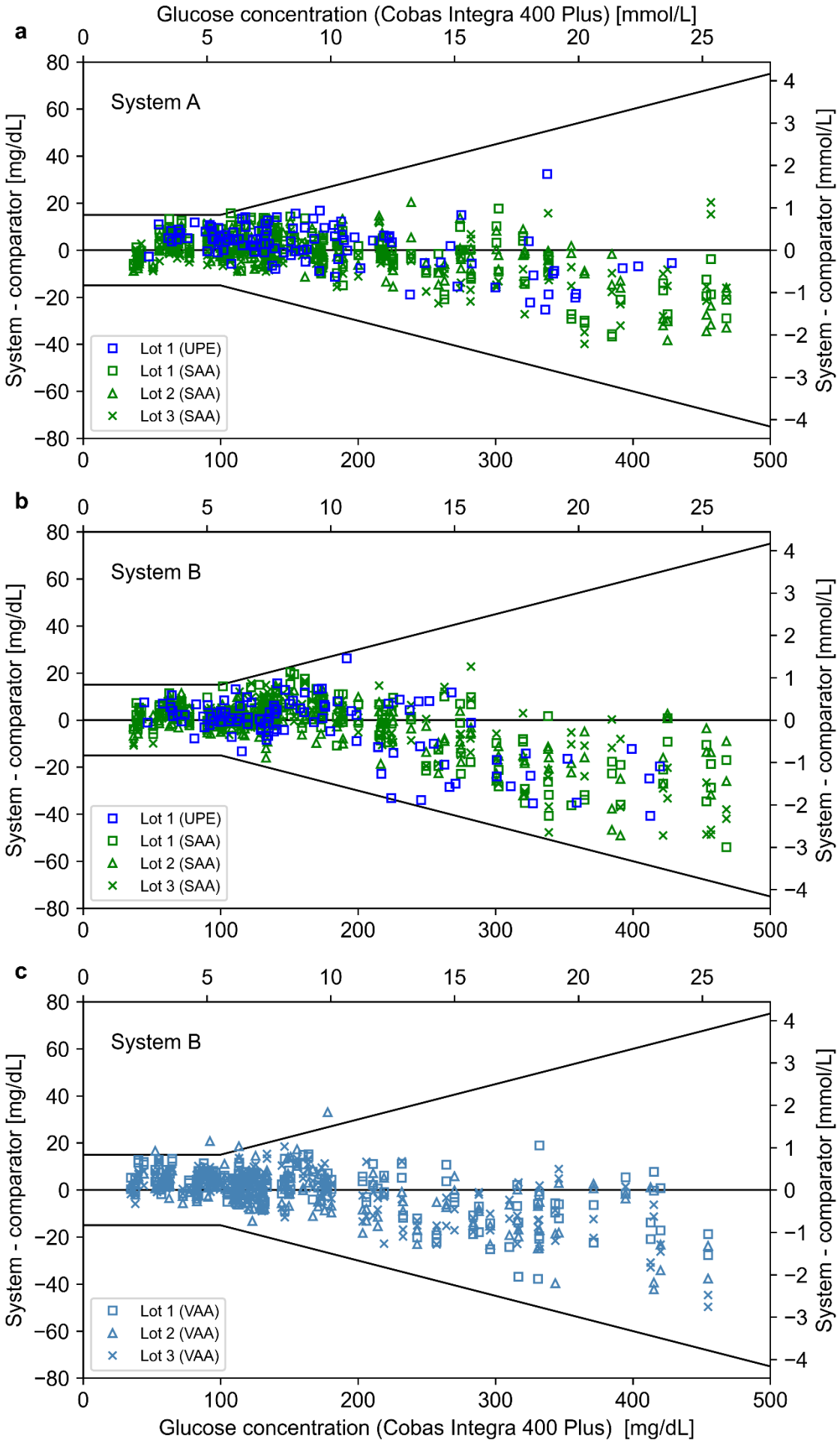
a
Glucose concentration (Cobas Integra 400 Plus) [mmol/L]
System A
System - comparator [mg/dL]
System - comparator [mmol/L]
Lot 1 (UPE)
Lot 1 (SAA)
Lot 2 (SAA)
Lot 3 (SAA)
b
System B
Lot 1 (UPE)
Lot 1 (SAA)
Lot 2 (SAA)
Lot 3 (SAA)
c
System B
Lot 1 (VAA)
Lot 2 (VAA)
Lot 3 (VAA)
Glucose concentration (Cobas Integra 400 Plus) [mg/dL]

Figure S1: Difference plots for the two investigated blood glucose monitoring systems. The upper two plots A and B show system accuracy analysis (SAA) in green and user performance evaluations (UPE) in blue of system A and B. In the lower plot C accuracy analysis of venous samples (VAA) for system B is depicted. The three investigated lots are displayed with different symbols.

Table S2: System Accuracy Results and Measurement Bias for the investigated BGMS

System	Lot	Within ±15 mg/dL or ±15%	Within ±10 mg/dL or ±10%	Within ±5 mg/dL or ±5%	CEG Zone A/B	Bias*
A	1	100% (200/200)	95.0% (190/200)	64.5% (129/200)	100%	1.3%
	2	100% (200/200)	99.0% (198/200)	72.0% (144/200)		0.1%
	3	100% (200/200)	99.0% (198/200)	77.0% (154/200)		-1.9%
B	1	100% (200/200)	93.0% (186/200)	66.5% (133/200)	100%	1.2%
	2	100% (200/200)	96.5% (193/200)	73.0% (146/200)		-0.3%
	3	100% (200/200)	93.5% (187/200)	67.0% (134/200)		0.3%

* Bias, the systematic measurement difference between the BGMS result and comparator method result divided by the mean of all, was calculated based on Bland and Altman (4).