C-EUBD
Committee Education in the
Use of Biomarkers in Diabetes

Report EurA1c 2017

HbA1c Trial
EQA organisers

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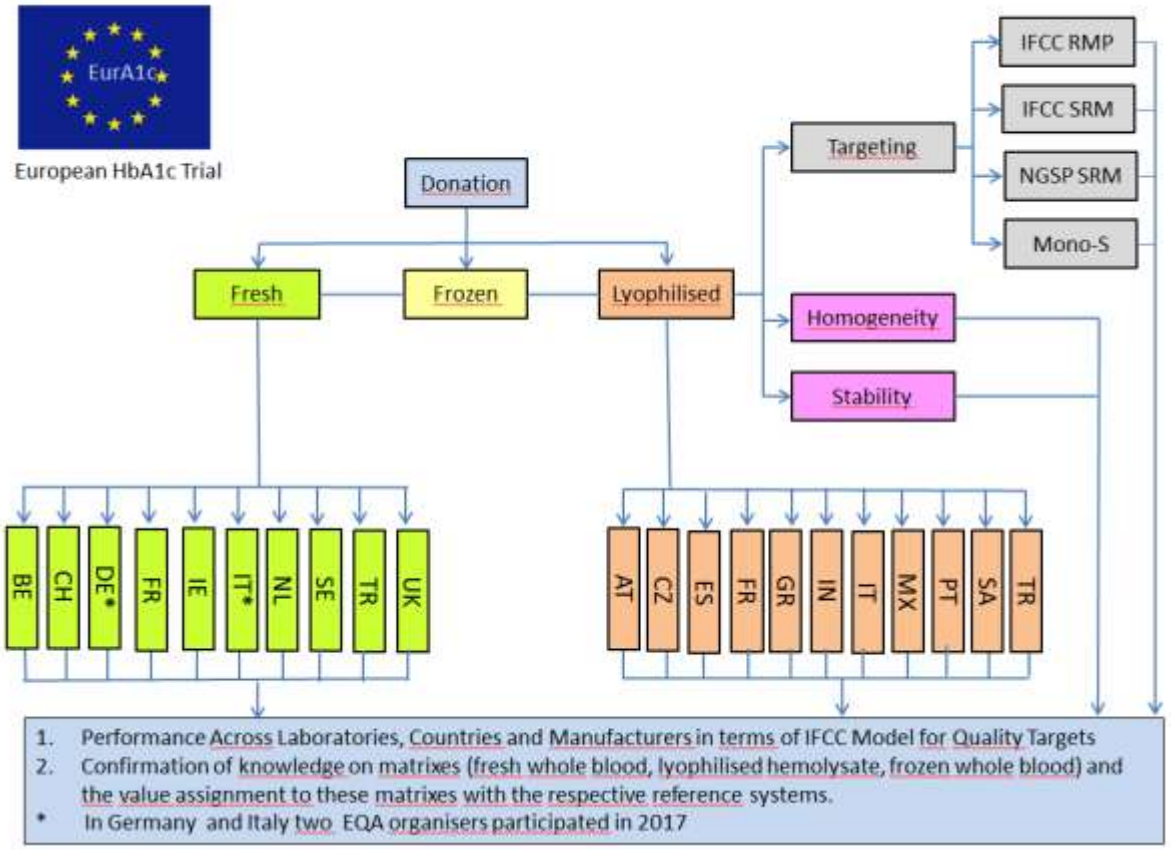
I Introduction and Overview of Results

Introduction
In 2017 twenty EQA organisers agreed to participate in the second “EurA1c” project. The design is shown in figure 1.

12 EQA organisers used fresh whole blood samples and 11 organisers used lyophilised samples (4 organisations used both fresh and lyophilised samples). In October 2017 the fresh whole blood samples were sent to the participants. From November 2017 up to April 2018 the lyophilised samples were assayed by the participants. This report is dealing with the results.

Figure 1. Design EurA1c Trial 2017



Confidentiality and Ownership
The results of the EurA1c project are owned by all EQA organisers. Previously we agreed that reports are confidential and will not be shared with participants and other third parties until there is the definite report.

The time schedule is:

13 July:	Draft report sent to all who are involved in EurA1c 2017. At the same time the invitation to participate in EurA1c 2018 is sent.
31 August:	Deadline for comments and remarks
30 September:	Final report sent to all who are involved. All who are involved are free to share results with third parties

Value Assignment
5 Approved IFCC Network Laboratories assigned the values to the samples with the IFCC Reference Measurement Procedure. For EurA1c 2017-1 the assigned value is 44.2 mmol/mol (expanded uncertainty 0.7 mmol/mol) and for EurA1c 2017-2 the assigned value is 58.0 mmol/mol (expanded uncertainty 0.8 mmol/mol).

Outliers
Outliers have been removed before calculation of the mean and between laboratory CV. Instead of using statistical criteria we only considered “blunders” as outliers. Criterion was a difference exceeding 25% of the target values. In our opinion these results are a relevant picture of “real life”. In this way 30 results (0.8%) have been excluded from the database of fresh whole blood samples and 18 results (1.1%) from the database of lyophilised hemolysates.

Methods
This is a point of consideration. The definition of the methods varied per EQA organiser and for quite a number of laboratories the method was not reported at all (113 of the 1809 laboratories using fresh whole blood; 24 of the 838 laboratories using lyophilised hemolysate). In the reports you will see this reflected. It is desirable that this is improved in future trials.

Units
In some cases results were reported in NGSP units. We converted them to SI (IFCC) units using the Master Equation (NGSP = 0.0915IFCC + 2.15) prior to calculation of means, SDs and making comparisons. All results in the report are in SI units.

Summary Results
Table 1 summarizes the results. The participating EQA organisers are ranked per country in alphabetical order. Results are given for the fresh whole blood and lyophilised hemolysate samples.

Table 1. Results of EurA1c 2017

Country	Fresh Whole Blood			Lyophilised Hemolysate		
	n	Mean Bias in mmol/mol	Between Laboratory CV	n	Mean Bias in mmol/mol	Between Laboratory CV
Austria				138	+0.6	5.1%
Belgium	135	+1.1	2.6%			
Czech Republic				208	0.4	4.4%
France	111	+0.4	3.0%	112	+0.1	5.7%
Germany Instand	637	+0.6	4.6%			
Germany RfB	74	+1.1	4.3%			
Greece				77	+0.8	6.5%
International*				66	+0.1	4.2%
Ireland	44	+1.1	3.5%			
Italy CRB	64	+1.1	3.8%	61	+0.6	4.8%
Italy Polymed	125	+0.6	4.4%			
Mexico				19	-0.3	12.7%
Netherlands	128	+0.8	3.2%			
Portugal				42	+0.4	5.1%
South Africa				3	-0.1	3.5%
Spain				71	+0.5	3.5%
Sweden	138	+0.3	3.7%			
Switzerland	155	+0.4	4.6%			
Turkey	53	+1.0	5.4%	41	2.1	5.7%
United Kingdom	145	+1.2	3.4%			
Overall	1809	+0.7	4.1%	838	+0.5	5.3%

** Individual laboratories of a number of countries*

In total 2647 laboratories participated in EurA1c 2017: 1809 used fresh whole blood samples and 838 used lyophilised hemolysates. The results are encouraging. The mean bias of all countries in the fresh whole blood programme is +0.7 mmol/mol and in the lyophilised hemolysate programme +0.5 mmol/mol. The between laboratory CV is also quite satisfying. The mean CV in both programmes is 4.1% and 5.3% respectively.

Differentiation Results
Results are differentiated by sample a) per country, b) per manufacturer, and c) per manufacturer per country in fresh whole blood (section II) and lyophilised hemolysates (section III).

II Results EQA Fresh Whole Blood samples

Table 2 shows the results per country for each sample. Tables 3 and 4 show the results per manufacturer for manufacturers with 6 or more participants (table 3) and those with 5 or less participants (table 4).

Table 2. Results per Country for Fresh Whole Blood

Country	EurA1c 2017-1 Target 44.2 mmol/mol				EurA1c 2017-2 Target 58.0 mmol/mol				Mean 2 Samples	
	n	Mean	Bias	CV %	n	Mean	Bias	CV%	Bias	CV%
Belgium	134	45.2	+1.0	2.7	135	59.1	+1.1	2.4	+1.1	2.6
France	111	44.7	+0.5	3.3	111	58.3	+0.3	2.6	+0.4	3.0
Germany Instand	635	44.8	+0.6	4.6	637	58.6	+0.6	4.6	+0.6	4.6
Germany RfB	74	45.3	+1.1	4.1	74	59.1	+1.1	4.5	+1.1	4.3
Ireland	44	45.3	+1.1	3.7	44	59.1	+1.1	3.2	+1.1	3.5
Italy CRB	64	45.4	+1.2	3.9	64	58.9	+0.9	3.6	+1.1	3.8
Italy Polymed	125	44.9	+0.7	4.6	125	58.6	+0.6	4.2	+0.6	4.4
Netherlands	127	45.0	+0.8	3.7	128	58.7	+0.7	2.6	+0.8	3.2
Sweden	139	44.4	+0.2	3.9	138	58.4	+0.4	3.4	+0.3	3.7
Switzerland	156	44.6	+0.4	4.7	155	58.5	+0.5	4.4	+0.4	4.6
Turkey	54	45.2	+1.0	5.8	53	59.0	+1.0	4.9	+1.0	5.4
UK	144	45.3	+1.1	3.3	145	59.2	+1.2	3.5	+1.2	3.4
Overall	1807	44.9	+0.7	4.2	1809	58.7	+0.7	4.0	+0.7	4.1

Table 3. Results per Manufacturer for Fresh Whole Blood (n>5)

Manufacturer	EurA1c 2017-1 Target 44.2 mmol/mol				EurA1c 2017-2 Target 58.0 mmol/mol				Mean 2 Samples	
	n	Mean	Bias	CV %	n	Mean	Bias	CV%	Bias	CV%
Abbott Architect	35	44.3	+0.1	3.9	35	58.4	+0.4	3.1	+0.2	3.5
Alere Afinion	165	44.1	-0.1	3.9	168	57.8	-0.2	3.6	-0.2	3.8
Beckman Coulter AU	32	44.8	+0.6	7.2	33	57.4	-0.6	6.1	0.0	6.7
Beckman Coulter UC DxC	17	45.0	+0.8	5.1	17	59.2	+1.2	5.0	+1.0	5.1
Bio-Rad D10	59	45.6	+1.4	4.7	60	59.5	+1.5	4.8	+1.5	4.8
Bio-Rad D100	19	44.1	-0.1	3.2	19	57.2	-0.8	2.5	-0.4	2.9
Bio-Rad Variant	112	45.4	+1.2	3.9	112	59.2	+1.2	3.0	+1.2	3.5
Medinor	10	44.7	+0.5	8.3	10	58.0	0.0	6.9	+0.3	7.6
Menarini (ARKRAY) HA 8160	76	45.3	+1.1	3.1	76	58.9	+0.9	2.6	+1.0	2.9
Menarini (ARKRAY) HA 8180	100	45.1	+0.9	3.2	100	58.7	+0.7	2.7	+0.8	3.0
Not Known	113	44.9	+0.7	5.6	111	58.0	0.0	6.6	+0.3	6.1
Roche Diagnostics	319	44.0	-0.2	3.8	318	58.4	+0.4	3.5	+0.1	3.7
Sebia Capillarys 2	64	44.3	+0.1	2.9	64	57.7	-0.3	2.4	-0.1	2.7
Sebia Capillarys 3	13	44.7	+0.5	2.0	13	58.0	0.0	1.5	+0.3	1.8
Sebia Minicap	13	44.4	+0.2	3.1	13	57.8	-0.2	2.0	0.0	2.6
Siemens Advia	13	46.9	+2.7	6.8	14	61.0	+3.0	8.6	+2.9	7.7
Siemens DCA/Vantage	217	45.3	+1.1	4.3	217	59.6	+1.6	4.2	+1.4	4.3
Siemens Dimension	56	46.4	+2.2	3.9	56	58.3	+0.3	4.0	+1.3	4.0
Tosoh G7	31	45.6	+1.4	4.5	30	59.6	+1.6	3.2	+1.5	3.9
Tosoh G8	281	45.4	+1.2	2.7	281	59.3	+1.3	2.6	+1.3	2.7
Trinity Premier Hb9210	29	45.3	+1.1	3.7	29	59.5	+1.5	2.8	+1.3	3.3

Table 4. Results per Manufacturer for Fresh Whole Blood (n < 6)

Manufacturer	EurA1c 2017-1 Target 44.2 mmol/mol				EurA1c 2017-2 Target 58.0 mmol/mol				Mean 2 Samples	
	n	Mean	Bias	CV %	n	Mean	Bias	CV%	Bias	CV%
Abbott other	1	45.0	+0.8		1	58.0	0.0		0.4	
Beckman Coulter other	1	47.0	+2.8		1	61.0	+3.0		2.9	
Beckman Coulter P/ACE MDQ	1	41.0	-3.2		1	58.5	+0.5		-1.4	
Biokit ILAB 600	1	46.0	+1.8		1	60.0	+2.0		1.9	
Bio-Rad other	1	43.2	-1.0		1	59.6	+1.6		0.3	
DiaSys InnovaStar	2	47.4	+3.2	1.6	2	61.4	+3.4	7.7	3.3	4.7
Eurolyser Smart 700/340	3	45.0	+0.8	1.4	3	56.6	-1.4	5.9	-0.3	3.7
HemoCue HbA1c 501	1	45.0	+0.8		1	61.0	+3.0		1.9	
Hitado other	1	50.0	+5.8		1	64.0	+6.0		5.9	
Horiba Pentra	2	42.1	-2.1	7.3	2	55.6	-2.4	1.7	-2.3	4.5
Menarini (ARKRAY) HA 8140	2	46.5	+2.3	1.5	2	61.5	+3.5	1.1	2.9	1.3
Menarini (ARKRAY) other	3	45.3	+1.1	2.7	3	59.4	+1.4	3.4	1.3	3.1
Mindray	2	40.5	-3.7	5.2	2	55.0	-3.0	5.1	-3.4	5.2
Mono S	1	43.7	-0.5		1	56.9	-1.1		-0.8	
Ortho Clinical Diagnostics Vitros 5.1 FS	1	45.3	1.1		1	57.4	-0.6		0.2	
Recipe HPLC	1	43.2	-1.0		1	58.5	+0.5		-0.3	
Shimadzu Mono S	1	43.2	-1.0		1	57.0	-1.0		-1.0	
Tosoh G9	1	45.0	+0.8		1	61.0	+3.0		1.9	
Tosoh G10	2	46.0	+1.8	9.2	2	60.0	+2.0	7.1	1.9	8.2
Tosoh G11	1	45.0	+0.8		1	59.0	+1.0		0.9	
Tosoh GX	1	45.0	+0.8		1	59.0	+1.0		0.9	
Tosoh other	3	44.8	+0.6	1.2	3	58.5	+0.5	0	0.5	0.6

The results in tables 2 and 3 are consistent: for each of the samples low (nearly always positive) biases are seen per country and per manufacturer.
Also quite acceptable are the between laboratory CVs. Unfortunately quite a number (n=113) laboratories did not specify their method. These laboratories are in the group “Not Known”.

Table 5 shows the performance per manufacturer per country. Included are only manufacturers meeting 2 criteria: at least 6 participants per country and at least two countries with 6 participants. We marked high biases (>2 mmol/mol) and high between laboratory CVs >6%)

Table 5. Fresh Whole Blood Results per Manufacturer and Country (n>5)

Method	n	HbA1c Low		HbA1c High		Mean	
		Bias	CV	Bias	CV	Bias	CV
Abbott Architect							
Overall	35	+0.1	3.9	+0.4	3.1	+0.2	3.5
DE-Instand	15	+0.8	4.8	+1.3	3.7	+1.1	4.3
FR	8	-0.5	2.0	-0.5	1.6	-0.5	1.8
Alere Afinion							
Overall	165	-0.1	3.9	-0.2	3.6	-0.2	3.8
DE-Instand	31	+0.1	3.1	+0.3	2.9	+0.2	3.0
IE	11	+0.7	4.2	-0.2	2.0	+0.2	3.1
SE	42	-1.1	3.0	-0.8	2.5	-0.9	2.8
CH	69	+0.5	3.9	-0.1	4.3	+0.2	4.1
Bio-Rad D10							
Overall	59	+1.4	4.7	+1.5	4.8	+1.5	4.8
DE-Instand	37	+1.2	4.6	+1.5	4.8	+1.4	4.7
FR	6	+1.9	3.9	+1.9	3.6	+1.9	3.8
Bio-Rad Variant							
Overall	112	+1.2	3.9	+1.2	3.0	+1.2	3.5
DE-Instand	22	+1.2	5.2	+1.2	4.5	+1.2	4.9
DE-RfB	8	+1.7	3.6	+2.2	3.1	+2.0	3.4
FR	15	+1.2	3.2	+1.1	1.7	+1.2	2.5
IT-Polymed	27	+1.2	3.6	+1.1	2.9	+1.2	3.3
TR	10	+0.8	4.8	+1.0	3.1	+0.9	4.0
SE	15	+0.6	1.5	+0.8	1.6	+0.7	1.6
Menarini (ARKRAY) HA 8160							
Overall	76	+1.1	3.1	+0.9	2.6	+1.0	2.9
BE	26	+1.4	2.8	+1.4	2.6	+1.4	2.7
DE-Instand	7	+0.8	2.8	+1.2	2.0	+1.0	2.4
IT-CRB	17	+0.7	3.5	+0.4	3.2	+0.5	3.4
NL	15	+1.4	3.4	+0.8	1.9	+1.1	2.7
Menarini (ARKRAY) HA 8180							
Overall	100	+0.9	3.2	+0.7	2.7	+0.8	3.0
BE	36	+0.9	2.9	+0.8	2.4	+0.8	2.7
IE	6	+0.1	2.7	+0.2	2.0	+0.1	2.4
IT-CRB	14	+0.9	2.4	+0.7	2.1	+0.8	2.3
NL	20	+1.2	1.9	+0.7	1.3	+0.9	1.6
UK	12	+0.1	4.0	0.0	3.9	0.0	4.0
Roche							
Overall	319	-0.2	3.8	+0.4	3.5	+0.1	3.7
DE-Instand	203	-0.2	3.8	+0.4	3.6	+0.1	3.7
DE-RfB	13	+0.3	3.3	+0.8	3.6	+0.5	3.5
FR	7	0.0	3.2	+0.6	2.9	+-0.3	3.1
IT-CRB	6	+0.7	7.3	-0.2	8.1	+0.2	7.7
IT-Polymed	6	-0.8	4.6	-0.1	4.3	-0.5	4.5
NL	26	+0.1	3.0	+0.5	2.2	+0.3	2.6
TR	8	+0.4	3.4	+0.4	5.0	+0.4	4.2
UK	7	-0.6	5.5	+0.7	1.9	+0.1	3.7
SE	9	-1.7	2.7	-1.4	2.5	-1.6	2.6
CH	27	-0.1	3.2	+0.9	2.1	+0.4	2.7
Sebia Capillarys 2							
Overall	64	+0.1	2.9	-0.3	2.4	-0.1	2.7
BE	7	-0.3	2.1	-0.2	2.9	-0.3	2.5
DE-Instand	8	+0.2	4.0	-0.2	2.9	0.0	3.5
FR	27	-0.2	2.6	-0.6	2.4	-0.4	2.5
IT-Polymed	7	+0.2	2.5	-1.1	2.1	-0.5	2.3
UK	6	0.0	1.7	-0.3	1.4	-0.1	1.6

Table 5. Continued

Method	n	HbA1c Low		HbA1c High		Mean	
		Bias	CV	Bias	CV	Bias	CV
Siemens DCA/Vantage							
Overall	217	+1.1	4.3	+1.6	4.2	+1.4	4.3
DE-Instand	52	+0.5	4.0	+0.8	4.2	+0.6	4.1
DE-RFB	13	+1.4	3.4	+1.5	4.6	+1.5	4.0
IE	16	+1.6	3.7	+2.8	2.7	+2.2	3.2
NL	13	+0.7	4.7	+0.6	4.2	+0.6	4.5
UK	40	+1.6	3.8	+2.0	4.8	+1.8	4.3
SE	55	+1.2	3.7	+1.6	3.3	+1.4	3.5
CH	28	+1.3	6.2	+2.1	4.9	+1.7	5.6
Siemens Dimension							
Overall	56	+2.2	3.9	+0.3	4.0	+1.3	4.0
DE-Instand	36	+2.0	3.7	+0.0	4.2	+1.0	4.0
DE-RFB	6	+2.9	4.0	+1.5	3.7	+2.2	3.9
Tosoh G7							
Overall	31	+1.4	4.5	+1.6	3.2	+1.5	3.9
DE-Instand	8	+2.5	2.2	+2.7	2.7	+2.6	2.5
IT-PM	6	-0.6	7.2	+0.3	4.0	-0.2	5.6
Tosoh G8							
Overall	281	+1.2	2.7	+1.3	2.6	+1.3	2.7
BE	39	+1.2	2.3	+1.4	2.0	+1.3	2.2
DE-Instand	53	+1.0	2.7	+1.0	3.4	+1.0	3.1
DE-RFB	10	+1.2	1.5	+1.2	1.6	+1.2	1.6
FR	24	+0.6	2.0	+0.5	2.4	+0.5	2.2
IE	6	+1.8	1.9	+1.5	1.8	+1.7	1.9
IT-CRB	10	+1.5	2.3	+1.4	2.7	+1.5	2.5
IT-Polymed	43	+1.0	4.1	+1.3	3.1	+1.2	3.6
NL	29	+1.7	2.7	+1.6	2.1	+1.7	2.4
TR	9	+1.3	2.6	+1.6	2.2	+1.5	2.4
UK	47	+1.5	1.5	+1.7	1.5	+1.6	1.5
SE	10	+0.6	2.3	+0.6	2.3	+0.6	2.3
Trinity Premier Hb9210							
Overall	29	+1.1	3.7	+1.5	2.8	+1.3	3.3
FR	7	+1.1	3.8	+1.8	3.2	+1.5	3.5
UK	10	+1.5	3.5	+1.9	2.5	+1.7	3.0

III Results EQA Lyophilised Hemolysate samples

Table 6 shows the results per country for each sample. Tables 7 and 8 show the results per manufacturer for manufacturers with 6 or more participants (table 7) and 5 or less participants (table 8).

Table 6. Results per Country for Lyophilised Hemolysate

Country	EurA1c 2017-1 Target 44.2 mmol/mol				EurA1c 2017-2 Target 58.0 mmol/mol				Mean 2 Samples	
	n	Mean	Bias	CV %	n	Mean	Bias	CV%	Bias	CV%
Austria	138	45.2	+1.0	5.2	138	58.1	+0.1	4.9	+0.6	5,1
Czech Republic	208	45.2	+1.0	4.6	208	57.9	-0.1	4.1	+0.4	4,4
France	112	44.8	+0.6	6.1	111	57.7	-0.3	5.3	+0.1	5,7
Greece	77	45.6	+1.4	6.9	76	58.3	+0.3	6.0	+0.8	6,5
International*	66	44.7	+0.5	4.5	69	57.6	-0.4	3.9	+0.1	4,2
Italy CRB	61	45.4	+1.2	5.4	60	58.0	0.0	4.2	+0.6	4,8
Mexico	19	45.2	+1.0	12.7	17	56.4	-1.6	12.7	-0.3	12,7
Portugal	42	45.3	+1.1	5.2	43	57.8	-0.2	5.0	+0.4	5,1
South Africa	3	43.3	-0.9	3.5	3	58.7	+0.7	3.5	-0.1	3,5
Spain	71	45.1	+0.9	3.6	72	58.1	+0.1	3.4	+0.5	3,5
Turkey	41	46.9	+2.7	6.1	41	59.5	+1.5	5.3	+2.1	5,7
Overall	838	45.2	+1.0	5.2	838	58.0	0.0	5.0	+0.5	5.3

** Individual laboratories of a number of countries*

Table 7. Results per Manufacturer for Lyophilised Hemolysate (n>5)

Manufacturer	EurA1c 2017-1 Target 44.2 mmol/mol				EurA1c 2017-2 Target 58.0 mmol/mol				Mean 2 Samples	
	n	Mean	Bias	CV %	n	Mean	Bias	CV%	Bias	CV%
Abbott Architect	33	41.6	-2.6	6.8	34	53.8	-4.2	6.6	-3.4	6.7
Beckman Coulter AU	9	49.2	+5.0	7.1	9	61.4	+3.4	4.8	+4.2	6.0
Bio-Rad D10	39	43.6	-0.6	6.5	39	55.8	-2.2	4.5	-1.4	5.5
Bio-Rad D100	18	44.6	+0.4	2.6	18	57.4	-0.6	1.5	-0.1	2.1
Bio-Rad other	53	44.6	+0.4	4.4	53	57.6	-0.4	4.1	0.0	4.3
Bio-Rad Variant	37	46.6	+2.4	6.3	37	59.7	+1.7	3.9	+2.1	5.1
Menarini (ARKRAY) HA 8160	75	44.7	+0.5	4.6	74	57.6	-0.4	3.9	+0.1	4.3
Menarini (ARKRAY) HA 8180	78	45.2	+1.0	3.1	78	57.8	-0.2	3.2	+0.4	3.2
Menarini other	36	44.9	+0.7	3.5	36	57.3	-0.7	3.9	0.0	3.7
Not Known	24	47.7	+3.5	10.2	17	59.4	+1.4	9.5	+2.5	9.9
Roche Diagnostics	135	45.9	+1.7	5.0	135	59.4	+1.4	4.7	+1.6	4.9
Sebia Capillarys 2	59	45.1	+0.9	3.7	59	57.4	-0.6	2.6	+0.1	3.2
Sebia Capillarys 3	8	45.4	+1.2	2.1	8	57.5	-0.5	1.4	+0.3	1.8
Siemens DCA/Vantage	9	49.7	+5.5	5.1	9	62.9	+4.9	7.3	+5.2	6.2
Siemens Dimension	18	47.2	+3.0	4.3	19	58.6	+0.6	5.7	+1.8	5.0
Tosoh G7	15	45.9	+1.7	5.5	17	58.6	+0.6	4.5	+1.2	5.0
Tosoh G8	79	44.6	+0.4	3.7	79	57.7	-0.3	3.8	+0.1	3.8
Tosoh other	55	45.5	+1.3	3.5	55	57.9	-0.1	2.9	+0.6	3.2
Trinity Premier Hb9210	20	45.0	+0.8	2.2	21	58.0	0.0	2.4	+0.4	2.3

Remarkable biases are seen for Abbott Architect, Beckman Coulter AU and Siemens DCA/Vantage. For Siemens DCA/Vantage it is known that there is a matrix effect for lyophilised samples.
For the Abbott enzymatic test we investigated the phenomenon: fresh whole blood and lyophilised hemolysates were assayed on our Abbott instrument after manufacture of the samples and we did not find a difference in results. However, on storage in the refrigerator for 6 and 18 months we found a decrease in measured HbA1c which we did not see in the same samples stored in the freezer (see section on stability on page 13).
In both Austria and France the negative bias comes along with a very low between laboratory CV (see table 9). This suggests that there is a long term stability issue for Abbott when samples are stored in the refrigerator. We started a detailed stability study to investigate this.

Table 8. Results per Manufacturer for Lyophilised Hemolysate (n < 6)

Manufacturer	**EurA1c 2017-1 Target 44.2 mmol/mol**				**EurA1c 2017-2 Target 58.0 mmol/mol**				**Mean 2 Samples**	
	n	Mean	Bias	CV %	n	Mean	Bias	CV%	Bias	CV%
Abbott other	3	42.4	-1.8	6.4	5	56.2	-1.8	3.0	-1.8	4.7
Beckman Coulter	3	48.5	+4.3	1.5	3	61.4	+3.4	1.6	+3.9	1.6
Beckman Coulter P/ACE MDQ	1	44.0	-0.2		2	57.0	-1.0	2.5	-0.6	2.5
Beckman Coulter UC DxC	4	49.7	+5.5	1.0	4	61.8	+3.8	6.8	+4.7	3.9
Ceragem LabonaCheck A1c	2	43.0	-1.2	3.3	2	55.0	-3.0	5.1	-2.1	4.2
Erba Diagnostics other	3	45.2	+1.0	7.9	3	55.9	-2.1	6.4	-0.6	7.2
ISE S.r.l. Hemo One ISE HbA1c	1	49.7	+5.5		1	63.1	+5.1		+5.3	
Menarini (ARKRAY) HA 8140	1	45.0	+0.8		2	56.5	-1.5	1.3	-0.4	1.3
Mindray	2	43.4	-0.8	4.6	2	57.0	-1.0	2.5	-0.9	3.6
Randox RX Daytona	1	49.0	+4.8		1	63.0	+5.0		+4.9	
Randox other	1	45.3	+1.1		1	63.9	+5.9		+3.5	
Sebia Minicap	5	44.2	0.0	1.0	5	58.0	0.0	6.1	0.0	3.6
Sekisui CS T240	2	46.5	+2.3	4.6	2	57.5	-0.5	6.1	+0.9	5.4
Siemens Advia	4	48.3	+4.1	3.5	3	62.0	+4.0	5.6	+4.1	4.6
Siemens other	3	46.9	+2.7	4.6	3	59.8	+1.8	7.4	+2.3	6.0
Tosoh G11	1	45.0	+0.8		1	58.0	0.0		+0.4	
Tosoh GX	1	43.2	-1.0		1	55.2	-2.8		-1.9	

Table 9 shows results per manufacturer per country. Included are only manufacturers with 6 or more participants in at least 2 countries.
High biases (>2 mmol/mol) and high between laboratory CVs (>6%) are marked.

Table 9. Lyophilised Hemolysate Results per Manufacturer and Country (n>5)

Method	n	HbA1c Low		HbA1c High		Mean	
		Bias	CV	Bias	CV	Bias	CV
Abbott Architect							
Overall	33	-2.6	6.8	-4.2	6.6	-3.4	6.7
FR	8	-3.3	3.0	-5.0	2.5	-4.2	2.8
GR	6	-0.7	5.6	-1.7	4.8	-1.2	5.2
AT	11	-3.2	1.5	-4.9	2.0	-4.1	1.8
Bio-Rad D10							
Overall	39	-0.6	6.5	-2.2	4.5	-1.4	5.5
FR	10	-1.6	4.9	-3.1	5.0	-2.4	5.0
CZ	8	+0.9	8.6	-0.7	3.9	+0.1	6.3
Bio-Rad D100							
Overall	18	+0.4	2.6	-0.6	1.5	-0.1	2.1
AT	6	+0.5	1.2	-0.2	1.3	+0.1	1.3
ES	7	-0.1	3.8	-1.1	1.2	-0.6	2.5
Bio-Rad Variant							
Overall	37	+2.4	6.3	+1.7	3.9	+2.1	5.1
FR	11	+4.1	5.5	+3.2	3.7	+3.7	4.6
TR	9	+4.0	5.0	+2.5	3.6	+3.3	4.3
Menarini (ARKRAY) HA 8160							
Overall	75	+0.5	4.6	-0.4	3.9	+0.1	4.3
GR	13	-0.2	4.7	+0.1	3.4	-0.1	4.1
IT-CRB	16	-0.3	5.5	-1.1	2.4	-0.7	4.0
AT	8	+1.4	3.5	0.0	3.6	+0.7	3.6
PT	25	+1.0	4.0	-0.5	4.2	+0.3	4.1
CZ	6	+1.8	4.6	+2.1	5.8	+2.0	5.2
Menarini (ARKRAY) HA 8180							
Overall	78	+1.0	3.1	-0.2	3.2	+0.4	3.2
IT-CRB	10	+1.8	2.0	+0.6	2.2	+1.2	2.1
INT*	10	+0.8	1.8	-0.6	2.5	+0.1	2.2
AT	23	+0.6	2.7	-0.6	3.2	0.0	3.0
ES	30	+1.4	3.0	+0.4	2.5	+0.9	2.8
Roche Diagnostics							
Overall	135	+1.7	5.0	+1.4	4.7	+1.6	4.9
FR	9	+0.9	8.3	+1.8	5.0	+1.4	6.7
GR	21	+1.6	4.3	+0.6	6.5	+1.1	5.4
AT	62	+1.6	3.8	+1.3	3.4	+1.5	3.6
CZ	17	+2.2	5.4	+1.9	4.8	+2.1	5.1
TR	6	+4.3	3.1	+4.6	4.5	+4.5	3.8
Sebia Capillarys 2							
Overall	59	+0.9	3.7	-0.6	2.6	+0.1	3.2
FR	27	+1.0	3.8	-0.6	2.4	+0.2	3.1
INT*	14	+1.0	3.5	+0.1	3.2	+0.6	3.4
ES	6	+1.0	1.7	-1.2	2.1	-0.1	1.9
Tosoh G7							
Overall	15	+1.7	5.5	+0.6	4.5	+1.2	5.0
GR	5	+3.0	7.1	+2.4	5.0	+2.7	6.1
CZ	7	+0.9	5.0	-1.0	2.6	-0.1	3.8
Tosoh G8							
Overall	79	+0.4	3.7	-0.3	3.8	+0.1	3.8
FR	25	-0.2	2.4	-0.3	4.2	-0.3	3.3
IT-CRB	10	+1.3	7.0	-1.2	4.7	0.0	5.9
INT*	10	-0.1	2.3	-1.0	2.6	-0.6	2.5
AT	7	-0.8	2.6	+0.7	3.4	-0.1	3.0
ES	11	+0.9	2.9	-0.4	2.7	+0.3	2.8
CZ	6	+1.6	1.6	+0.7	1.4	+1.2	1.5
TR	8	+0.9	3.1	0.0	5.2	+0.4	4.2

** Group of Individual laboratories of a number of countries*

IV. Value Assignment (Targeting)

The samples in their respective matrices have been measured with the IFCC RMP, the IFCC SRLs, the US NGSP SRLs and the Swedish Mono S. Table 10 shows the results.

Table 10. Results of Reference Measurement Procedures

Matrix	**Low HbA1c (range 43.5 – 44.9 mmol/mol)**				**High HbA1c (range 57.2 – 58.8 mmol/mol)**			
	IFCC RMP	IFCC SRLs	US NGSP SRLs	Sweden Mono S	IFCC RMP	IFCC SRLs	US NGSP SRLs	Sweden Mono S
	n = 5	n = 8	n = 3	n = 1	n = 5	n = 8	n = 3	n = 1
Fresh Whole Blood	44.2	44.7	44.6	44.2	58.0	58.3	58.7	57.4
Lyophilised Hem	43.8	45.6	45.0	44.2	57.0	58.3	58.3	57.4
Frozen Whole Blood	44.3	44.6	44.9	44.7	58.2	58.1	58.3	57.4

1) US-NGSP and Sweden Mono-S results in % are converted to SI (IFCC) units with the respective Master Equations
2) Expanded Uncertainty (k=2) of the IFCC RMP in fresh whole blood are 0.7 mmol/mol in the low and 0.8 in the high sample.
3) In yellow: values outside the uncertainty range of the assigned values in fresh whole blood with the IFCC RMP

V. Homogeneity

Homogeneity testing of the samples EurA1c-2017-2, 4 and 6 is performed according to ISO 13528:2005 (Annex B) with the Menarini 8180V. The results in table 11 show that the samples are homogeneous.

Table 11. Homogeneity test of EurA1c 2017-2, 4 and 6

Vial	**Fresh Whole Blood**				**Lyophilised Hemolysate**				**Frozen Whole Blood**			
	EurA1c 2017-2				**EurA1c 2017-4**				**EurA1c 2017-6**			
	1	2	mean	Δ	1	2	mean	Δ	1	2	mean	Δ
1	59.0	59.1	59.05	0.1	59.3	58.8	59.05	0.5	57.9	57.9	57.90	0.0
2	59.3	58.7	59.00	0.6	59.1	58.8	58.95	0.3	58.0	57.9	57.95	0.1
3	59.1	59.3	59.20	0.2	58.8	59.0	58.90	0.2	57.7	57.9	57.80	0.2
4	59.3	58.5	58.90	0.8	59.1	59.0	59.05	0.1	57.7	57.9	57.80	0.2
5	58.7	59.3	59.00	0.6	59.3	59.3	59.30	0.0	57.7	57.7	57.70	0.0
6	58.7	58.8	58.75	0.1	59.1	59.3	59.20	0.2	57.3	57.7	57.50	0.4
7	58.7	59.0	58.85	0.3	59.3	59.3	59.30	0.0	57.5	57.9	57.70	0.4
8	59.1	58.8	58.95	0.3	59.4	59.3	59.35	0.1	57.5	57.9	57.70	0.4
9	58.7	59.1	58.90	0.4	59.3	59.0	59.15	0.3	57.9	57.7	57.80	0.2
10	59.0	58.8	58.90	0.2	59.3	59.1	59.20	0.2	57.9	57.7	57.80	0.2
11	59.1	58.7	58.90	0.4	59.0	59.1	59.05	0.1	57.5	57.9	57.70	0.4
12	59.0	58.7	58.85	0.3	59.0	59.1	59.05	0.1	57.5	57.9	57.70	0.4
average			58.9				59.1				57.8	
SD		0.000	0.115	0.292		0.091	0.144	0.157		0.000	0.116	0,201
0.3 x SD_{RL}			0.306				0.306				0.306	
Criterion			-0.306				-0.215				-0.306	
Homogeneity:			**Pass**				**Pass**				**Pass**	

VI Stability

Fresh Whole Blood

Fresh whole blood samples EurA1c 2017-2 (HbA1c 58.0 mmol/mol) were stored at room temperature and in the refrigerator at 2-8°C and measured after 1,2,3,4,5 and 8 days after storage. Results are expressed as the difference in measured HbA1c on day X and day 1 (table 12). It can be seen that on storage at room temperature results of three methods start to show differences. It can be concluded that at room temperature samples are stable for 5 and in the refrigerator for at least 8 days.

Table 12. Stability of Fresh Whole Blood at Room Temperature and in the Refrigerator*

Method	Day 1	Day 2	Day 3	Day 4	Day 5	Day 8
Storage at Room Temperature						
Menarini/ARKRAY HA 8180V	0	0	+1	0	-1	-3
Trinity Premier Hb9210	0	0	0	-1	-1	-2
Sebia Capillarys 2	0	0	+1	0	0	-2
Roche Cobas c513	0	0	-1	0	-1	0
Abbott Architect C4000	0	0	+1	+1	0	0
Tosoh G8	0	0	+1	0	0	-1
Storage Refrigerator						
Menarini/ARKRAY HA 8180V	0	0	+1	+1	0	+1
Trinity Premier Hb9210	0	0	0	0	0	0
Sebia Capillarys 2	0	-1	0	+1	0	0
Roche Cobas c513	0	+1	0	0	+1	0
Abbott Architect C4000	0	0	0	0	0	0
Tosoh G8	0	0	0	0	0	0

** Difference between Day X and Day 1 in mmol/mol*

Lyophilised Hemolysate

Lyophilised hemolysate samples EurA1c 2016-1 (HbA1c 42.3 mmol/mol) were stored in the refrigerator at 2-8°C and in the freezer at -20°C and measured after 6 and 18 months (results of EurA1c 2016 samples are chosen to show stability because of these samples long-term results are available). Results are shown in table 13. It can be seen that the results of the Abbott Architect enzymatic assay start to show differences after 6 months. This is a remarkable and unexpected result of this new test. This may explain why a negative bias is observed in the EurA1c trial in some countries. Further investigation of this is scheduled.

Table 13. Stability of Lyophilised Hemolysate in Refrigerator and Freezer -20°C*

Method	0 month	6 months	18 months
Storage Refrigerator			
Menarini/ARKRAY HA 8180V	0	-1	-1
Trinity Premier Hb9210	0	-1	-1
Sebia Capillarys 2	0	-1	-1
Roche Cobas c513	0	0	0
Abbott Architect C4000	0	-4	-6
Tosoh G8	0	+1	+1
Storage Freezer -20°C			
Menarini/ARKRAY HA 8180V	0	-1	0
Trinity Premier Hb9210	0	+1	0
Sebia Capillarys 2	0	-1	-1
Roche Cobas c513	0	+1	0
Abbott Architect C4000	0	0	+1
Tosoh G8	0	0	+1

** Difference between Month X and Month 0 in mmol/mol*

Frozen Whole Blood

Frozen whole blood samples EurA1c 2016-1 (HbA1c 42.3 mmol/mol) were stored in freezers at -20°C and -70°C and measured after 6 and 18 months (results of EurA1c 2016 samples are chosen to show stability because of these samples long-term results are available).

Results are shown in table 14. It can be seen that on storage at -20°C results start to differ from the originally measured HbA1c concentration.

Table 14. Stability of Frozen Whole Blood in Freezer -20°C and Freezer -70°C*

Method	**0 month**	**6 months**	**18 months**
Storage Freeze -20°C			
Menarini/ARKRAY HA 8180V	0	0	+3
Trinity Premier Hb9210	0	-2	-4
Sebia Capillarys 2	0	0	+1
Roche Cobas c513	0	0	0
Abbott Architect C4000	0	0	+2
Tosoh G8	0	0	-2
Storage Freezer -70°C			
Menarini/ARKRAY HA 8180V	0	0	0
Trinity Premier Hb9210	0	0	-1
Sebia Capillarys 2	0	0	-1
Roche Cobas c513	0	0	+1
Abbott Architect C4000	0	0	0
Tosoh G8	0	0	0

** Difference between Month X and Month 0 in mmol/mol*

VII Units and POCT meters

In the EurA1c Trial 2017 we asked information on units and POCT meters

Unit of measurement reported
Can you let us know how units are used/reported in your country

a. IFCC units measured by laboratories – IFCC units reported by you
b. NGSP units measured by laboratories – NGSP units reported by you
c. NGSP units measured by laboratories – converted to IFCC units by you and reported to us

POCT meters
Do you know the test setting for POCT meters: within-laboratory, operated by professionals with training in laboratory medicine, or in the vicinity of the patient by a non-laboratory professional?

a. I don't know
b. Majority by laboratory professionals
c. Majority by non-laboratory professionals

Table 15 shows your answers.

Table 15. Units and POCT meters

EQA organiser	Units			POCT		
	a IFCC IFCC	**b** NGSP NGSP	**c** NGSP to IFCC	**a** Don't know	**b** Lab prof.	**c** Non-Lab prof.
Total	14	4	1	10	2	6
Belgium						
Germany Instand						
Germany RfB	X			X		
France	X			X		
Greece						
International	X			X		
Ireland	X					X
Italy CRB	X			X		
Italy Polymed	X			X		
Mexico			X		X	
Netherlands	X			X		
Austria	X	X		X		
Portugal	X			X		
Spain		X				X
Czech Republic	X					X
Turkey	X					X
UK	X					X
South Africa		X		X		
Sweden	X				X	
Switzerland	X	X		X		X

VIII Organisations and Persons Involved

Country	Organisation	Person
EQA Organisers		
AT	ÖQUASTA	Christoph Buchta, Mathias M. Mueller
BE	Sciensano	Yolande Lenga
CH	CSCQ	Pierre-Alan Morandi, Dagmar Kesseler
CZ	SEKK	Marek Budina, Josef Kratochvila, Bedrich Friedecky
DE	INSTAND	Patricia Kaiser
DE	Reference Institute for Bioanalytics	Anja Kessler
ES	SEQC^{ML}	Montserrat Ventura Alemany, Carmen Perich Alsina, Carmen González Gómez
FR	Biologie Prospective	Jean-Pascal Siest
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IE	IEQAS	Hazel Graham, Anne Kane, Thomas P. Smith, Ned Barrett
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Mono S Laboratory		
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NL	Data Processing	Irene de Graaf
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