Accu-Chek Instant

A system for measurement of glucose
manufactured by Roche Diabetes Care GmbH

Report from the evaluation

SKUP/2017/113

organised by SKUP at the request of Roche Diagnostics Scandinavia AB

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The report was written by SKUP, Autumn 2017. Main author was Marianne Risa, SKUP in Norway. In order to use the SKUP name in marketing, it has to be referred to www.skup.nu and the report code in question; SKUP/2017/113. For this purpose, the company can use a logotype containing the report code available for the requesting company together with the final report. A correct format of referral in scientific publications will be "SKUP. Report from the evaluation SKUP/2017/113. Accu-Chek Instant (Roche Diabetes Care GmbH), a system for measurement of glucose, www.skup.nu (*accessed date*)." The organisation of SKUP is described in attachment 1.

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Attachments with raw data are included only in the copy to Roche Diagnostics Scandinavia AB.

1. Summary

Background
The Accu-Chek Instant system is an in vitro diagnostic device for quantitative measurement of glucose. The product is intended for professional use and self-testing. The sample material is fresh capillary whole blood. The system is produced by Roche Diabetes Care GmbH and is not launched into the Scandinavian market to date. The SKUP evaluation was carried out in May - June 2017 at the request of Roche Diagnostics Scandinavia AB.

The aim of the evaluation
The aim of the evaluation was to assess analytical quality and user-friendliness of Accu-Chek Instant, both when used under optimal conditions by experienced laboratory personnel and under real-life conditions by intended users (persons with diabetes). The analytical results were assessed according to pre-set quality goals.

Materials and methods
A total of 90 persons with diabetes signed up for the evaluation and 88 of them completed. All the participants received the device and instructions by mail and no training was given. They used the device for approximately two weeks at home, before they attended an evaluation meeting at SKUP. Fresh capillary whole blood samples from each participant were analysed on Accu-Chek Instant under optimal conditions as well as by the participants. Three lots of test strips were used. Capillary samples from the same individuals were analysed on a comparison method (a glucose hexokinase method for measurement of glucose in plasma, implemented on Roche Cobas 6000). The quality goal for precision was a repeatability (CV) ≤5,0 %. The quality goal for accuracy was set according to the International Organization for Standardization (ISO) ISO 15197:2013. This quality goal states that at least 95 % of the individual glucose results shall be <±0,83 mmol/L of the average measured values of the reference measurement procedure at glucose concentration <5,55 mmol/L or <±15 % at glucose concentration ≥5,55 mmol/L. The quality goal for user-friendliness was a total rating of "satisfactory".

Results
The CV achieved under optimal conditions was between 1,6 and 2,9 % depending on the concentration level. The intended users achieved a CV between 2,1 and 5,7 %. The high imprecision at 5,7 % refers to results with glucose concentration <7 mmol/L. There was a bias between Accu-Chek Instant and the comparison method. The bias was between -0,08 and -0,65 mmol/L. Under optimal conditions, 100 % of the results were within the allowable deviation limits for accuracy and when handled by intended users, 99 % of the results were within the limits. Glucose measurements on Accu-Chek Instant were not affected by haematocrit (tested haematocrit range 29 - 50 %). The user-friendliness was rated as satisfactory. The fraction of tests wasted due to technical errors was 0,4 %.

Conclusion
The quality goal for repeatability was fulfilled under optimal conditions, but not fulfilled by intended users due to the higher imprecision for glucose concentration <7 mmol/L. The quality goal for accuracy was fulfilled both under optimal conditions and by intended users. The quality goal for user-friendliness was fulfilled.

Comments from Roche Diagnostics Scandinavia AB
Roche Diagnostics Scandinavia AB has accepted the report without further comments.

2. Abbreviations and Acronyms

ADA	American Diabetes Association
BLS	Biomedical Laboratory Scientist
CI	Confidence Interval
C-NPU	Committee on Nomenclature, Properties and Units
CV	Coefficient of Variation
DEKS	Danish Institute of External Quality Assurance for Laboratories in Health Care
EQA	External Quality Assessment
Equalis	External quality assessment in laboratory medicine in Sweden
FAD	Flavin Adenine Dinucleotide
HDH	Haraldsplass Deaconess Hospital
HELFO	Norwegian Health Economics Administration
ISO	International Organization for Standardization
LADA	Latent Autoimmune Diabetes of Adults
NFKK	Nordic Federation of Clinical Chemistry
NIST	National Institute of Standards & Technology
Noklus	Norwegian Quality Improvement of Laboratory Examinations
NS-EN ISO	Norsk Standard_Europeisk Norm International Organization for Standardization
SI	International System of Units
SKUP	Scandinavian evaluation of laboratory equipment for primary health care
SRM	Standard Reference Material

3. Introduction

The purpose of SKUP is to improve the quality of near-patient testing in Scandinavia by providing objective information about analytical quality and user-friendliness of laboratory equipment. This information is generated by organising SKUP evaluations.

3.1. The concept of SKUP evaluations

SKUP evaluations follow common guidelines and the results from various evaluations are comparable[1]. The evaluation set-up and details are described in an evaluation protocol and agreed upon in advance. The analytical results are assessed according to pre-set quality goals. To fully demonstrate the quality of a product, the end-users should be involved in the evaluations. If possible, SKUP evaluations are carried out using three lot numbers of test strips from separate and time-spread productions. Some evaluation codes are followed by an asterisk (*), indicating an evaluation with a more specific objective. The asterisk is explained on the front page of these protocols and reports.

3.2. Background for the evaluation

Accu-Chek Instant system is an in vitro diagnostic device for quantitative measurement of glucose. The product is intended for professional use, self-testing and self-management. The sample material is fresh capillary whole blood. The system is produced by Roche Diabetes Care GmbH and is not launched into the Scandinavian market to date. The SKUP evaluation was carried out in May - June 2017 at the request of Roche Diagnostics Scandinavia AB.

3.3. The aim of the evaluation

The aim of the evaluation was to assess analytical quality and user-friendliness of Accu-Chek Instant, both when used under optimal conditions by experienced laboratory personnel and when used under real-life conditions by intended users (persons with diabetes).

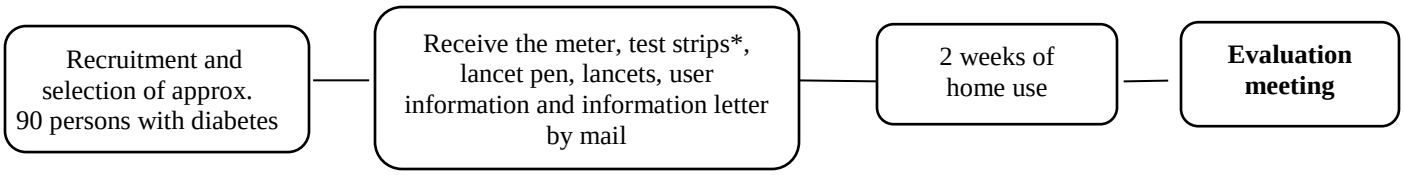
3.4. The model for the evaluation of Accu-Chek Instant

SKUP evaluations for quantitative methods are based upon the fundamental guidelines in a book concerning evaluations of laboratory equipment in primary health care [1]. SKUP's model for glucose user-evaluations is based on a standard model used by Norwegian Health Economics Administration (HELFO) for test strip reimbursement in Norway [2].
This evaluation consisted of two parts (figure 1 and 2). One part of the evaluation was carried out under optimal conditions by experienced laboratory personnel. This part documents the quality of the system under conditions as favourable as possible for achieving good analytical quality. The other part of the evaluation was carried out by intended users. This part documents the quality of the system under real-life conditions.

The evaluation included:

- Examination of analytical quality (precision and accuracy) under optimal conditions
- Examination of analytical quality (precision and accuracy) in the hands of intended users
- Evaluation of user-friendliness of Accu-Chek Instant and it's manual
- Examination of haematocrit effect on the glucose measurements

[1]SKUP evaluations are under continuous development. In some cases, it may be difficult to compare earlier protocols, results and reports with more recent ones.



* Three lots of test strips were distributed evenly between the participants (random distribution).

Figure 1. The evaluation process ending with the Evaluation meeting

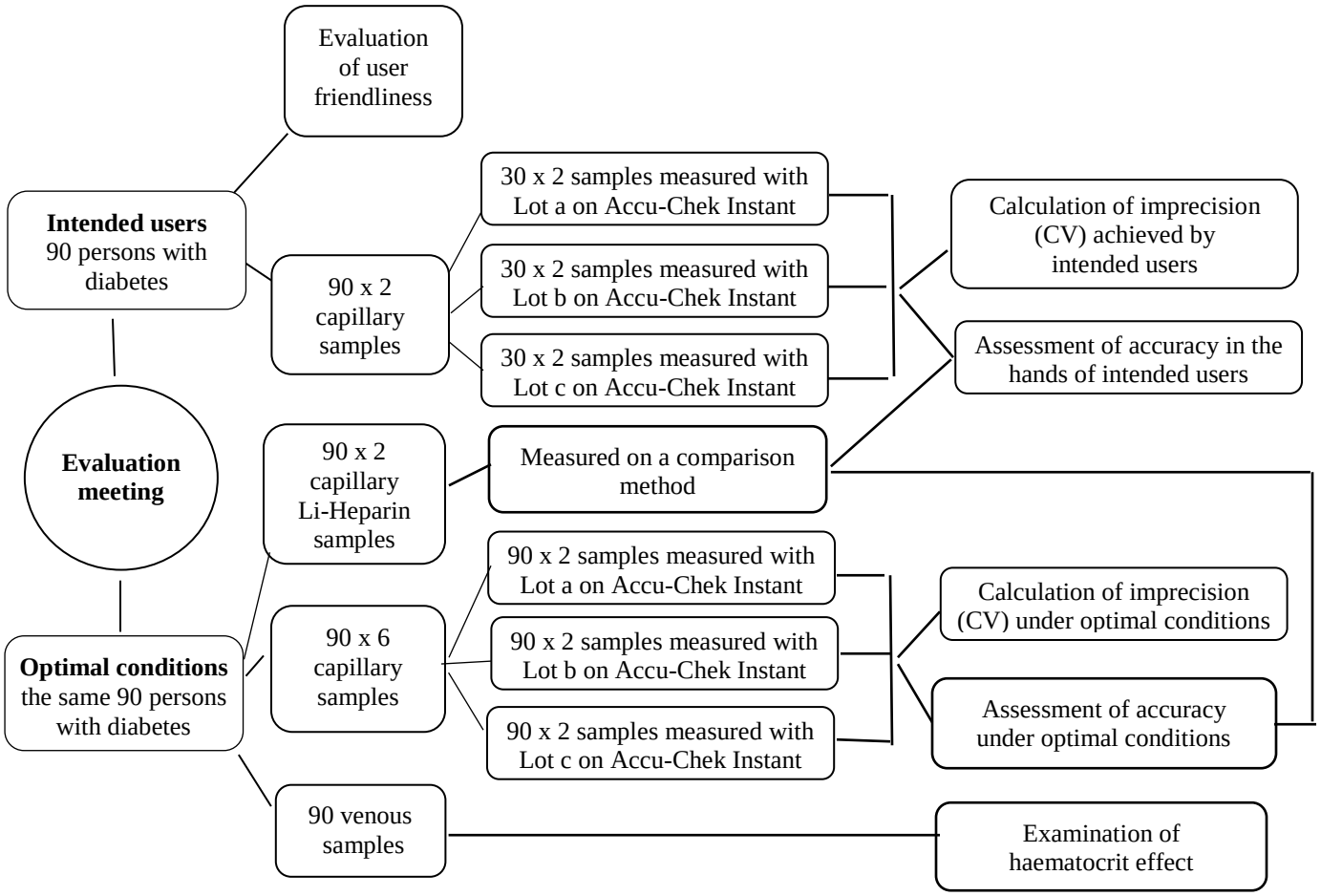


Figure 2. Flowchart illustrating the model for the evaluation of Accu-Chek Instant

4. Quality goals

4.1. Analytical quality

The Accu-Chek Instant system is designed for monitoring blood glucose, and the quality goals are set according to this.

For blood glucose meters intended for monitoring, good precision of the method is important [3]. According to the American Diabetes Association (ADA), the imprecision of new glucose devices must be less than 5 % [4]. Other authors also recommend an imprecision of 5 % or less [5-7].

The International Organization for Standardization (ISO) 15197:2013 standard [8] is an international protocol for evaluating meters designed for glucose monitoring, and gives the following minimum acceptable accuracy requirement for measurements made by trained laboratory staff as well as measurements performed by persons with diabetes:
At least 95 % of the individual glucose results shall fall within ±0,83 mmol/L of the average measured values of the reference measurement procedure at glucose concentrations <5,55 mmol/L, or within ±15 % at glucose concentrations ≥5,55 mmol/L.

In Norway, the standard protocol of HELFO [2] follows the quality goal in ISO 15197:2013 [8].

In Sweden, national quality goals for glucose measurements follow the requirements in ISO 15197:2013. Glucose meters used for monitoring some groups of patients, for example those using continuous glucose monitoring, where the glucose meter is used as a calibrator unit, and women with gestational diabetes, should fulfil stricter quality goals for accuracy. At least 95 % of the individual glucose results shall fall within ±0,42 mmol/L of the results of the comparison method at glucose concentrations <4,2 mmol/L, or within ±10 % at glucose concentrations ≥4,2 mmol/L [9]. This stricter quality goal for accuracy applies to measurements performed under optimal conditions in hospital laboratories and laboratories in primary health care centres.

In Denmark, the analytical quality goals for point-of-care glucose measurement systems (capillary whole blood measurements) are a coefficient of variation (CV) <4 % and a bias <3 % [6, 7].

4.2. User-friendliness

The evaluation of user-friendliness is carried out by asking the participants (intended users) to fill in a questionnaire, see section 6.5.

Technical errors
SKUP recommends that the fraction of tests wasted due to technical errors should not exceed 2 %.

4.3. Principles for the assessments

To qualify for an overall good assessment in a SKUP evaluation, the measuring system must show satisfactory analytical quality as well as satisfactory user-friendliness.

4.3.1. Assessment of analytical quality

The analytical results are assessed according to pre-set quality goals.

Precision

The decision whether the achieved CV fulfils the quality goal or not, is made on a 5 % significance level. The distinction between the ratings, and the assessment of precision according to the quality goal, are shown in table 1.

Table 1. The rating of precision

Distinction between the ratings	Assessment according to the quality goal
CV is lower than the quality goal (statistically significant)	The quality goal is fulfilled
CV is lower than the quality goal (not statistically significant)	Most likely the quality goal is fulfilled
CV is higher than the quality goal (not statistically significant)	Most likely the quality goal is not fulfilled
CV is higher than the quality goal (statistically significant)	The quality goal is not fulfilled

Bias

SKUP does not set separate quality goals for bias. The confidence interval (CI) of the measured bias is used for deciding if a difference between the evaluated method and the comparison method is statistically significant (two-tailed test, 5 % significance level). The bias of all three lots of test strips will be calculated from the results achieved under optimal conditions. The bias will also be discussed in connection with the accuracy.

Accuracy

The accuracy is illustrated in difference plots with limits for allowable deviation according to the quality goal. The fraction of results within the limits is counted. The accuracy is assessed as either fulfilling the quality goal or not fulfilling the quality goal.

Effect of haematocrit

The effect of haematocrit is shown with a trend-line and a regression equation in a difference plot.

4.3.2. Assessment of user-friendliness

User-friendliness is assessed according to answers and comments given in the questionnaire (see section 6.5). For each question, the participant can choose between three given ratings. The responses from the participants are reviewed and summed up. To achieve the overall rating "satisfactory", the tested equipment must reach a total rating of "satisfactory" in all four subareas of characteristics described in section 6.5.

Technical errors

The biomedical laboratory scientists (BLSs) performing the measurements under optimal conditions register error codes, technical errors and failed measurements during the evaluation. The fraction of tests wasted due to technical errors is calculated and taken into account in connection with the assessment of user-friendliness.

4.4. SKUP's quality goals in this evaluation

As agreed upon when the protocol was drawn up, the results from the evaluation of Accu-Chek Instant are assessed against the following quality goals:

Repeatability (CV) ..... ≤5,0 %

Allowable deviation of the individual result from the comparison method result (according to ISO 15197:2013) *
for glucose concentrations <5,55 mmol/L ..... ≤±0,83 mmol/L
and for glucose concentrations ≥5,55 mmol/L ..... ≤±15 %

Required percentage of individual results
within the allowable deviation limits……..... ≥95 %

User-friendliness, overall rating..... Satisfactory

* The number of results within a stricter Swedish quality goal (allowable deviation in the individual result from the comparison method result <±0,42 mmol/L at glucose concentration <4,2 mmol/L or <±10 % at glucose concentration ≥4,2 mmol/L) will be reported, but not assessed in the report.

5. Materials and methods

5.1. Definition of the measurand

The measurement system intends to measure the substance concentration of glucose in blood plasma. For the evaluated system the sample material is capillary blood and for the comparison method the sample material is capillary blood in this evaluation. The results are traceable to the International System of Units (SI) and are expressed with the unit mmol/L. The Committee on Nomenclature, Properties and Units (C-NPU) systematically describes clinical laboratory measurands in a database [10]. The NPU code related to the measurand in this evaluation is NPU22089 (for random sample). In this report, the term "glucose" will be used for the measurand.

5.1.1. Other variables measured

Another variable measured in the evaluation is haematocrit, expressed in %.

5.2. The evaluated measurement system Accu-Chek Instant

The information in this section derives from the company's information material.

The Accu-Chek Instant system is designed for blood glucose testing performed by persons with diabetes or by health care professionals. The system consists of a blood glucose meter and dry reagent test strips (figure 3). The Accu-Chek Instant test strips can be used with two different meters; Accu-Chek Instant and Accu-Chek Instant S. In this evaluation, Accu-Chek Instant is used. The glucose measurement is based on biosensor technology. Glucose dehydrogenase converts glucose in the blood sample to gluconolactone. The enzyme in the reaction is a flavin adenine dinucleotide (FAD) dependent glucose dehydrogenase. The system is automatically switched on and calibrated when a test strip is inserted. Coding of the meter is not necessary. The sample material is fresh capillary whole blood, preferably from a finger prick, but it is also possible to use blood samples from alternative sites. Accu-Chek Instant reports plasma glucose values. The meter has a target range color indicator, which indicates whether the blood glucose result falls above, within, or below a pre-set range of values. Analytical quality controls are not included in the starting set, but can be purchased separately.

Figure 3. The Accu-Chek Instant system

For technical details about the Accu-Chek Instant system, see table 2. For more information about the Accu-Chek Instant system, and name of the manufacturer and the suppliers in the Scandinavian countries, see attachment 2 and 3. For product specifications in this evaluation, see attachment 4.

Table 2. Technical details from the manufacturer

Technical details for Accu-Chek Instant	
Sample material	Fresh capillary whole blood
Sample volume	0,6 µL
Measuring time	<4 seconds
Measuring range	0,6 – 33,3 mmol/L
Tolerated haematocrit range	10 to 65 %
Storage capacity	At least 720 blood glucose results and 30 control results in memory, but only the last blood glucose result and the current control result, can be viewed on the meter*
Electrical power supply	Two 3 volt lithium batteries (coin cell type CR2032)

* To view other stored results, the results must be transferred to a compatible software application.

5.3. The selected comparison method

A selected comparison method is a fully specified method which, in the absence of a Reference method, serves as a common basis for the comparison of the evaluated method.

5.3.1. The selected comparison method in this evaluation

The selected comparison method in this evaluation is a glucose hexokinase method implemented on Roche Cobas 6000 in the clinical chemistry laboratory at Haraldsplass Deaconess Hospital (HDH) in Bergen, Norway. The method uses reagents from Roche Diabetes Care. The method is accredited according to NS-EN ISO 15189 (2012) (Norsk Standard_Europeisk Norm International Organization for Standardization). The method is hereafter called "the comparison method".

The samples for haematocrit were measured with Advia 2120i or Cell-Dyn Sapphire at the laboratory at HDH.

Internal analytical quality control

Internal analytical quality control samples, two levels (Autonorm Human Liquid Control Solution, Sero AS), were measured each evaluation day on the comparison method.

External analytical quality control

The hospital laboratory participates in a Labquality external quality assessment (EQA) scheme for glucose (Scheme code 2050, Serum B and C, Labquality Oy) with two levels four rounds per year. The assigned values for glucose are based on transferred values from the reference material "Serum X" of Nordic Federation of Clinical Chemistry (NFKK) [11].

5.3.2. Verification of the analytical quality of the comparison method

Precision

Repeatability (CV) of the comparison method was calculated from duplicate measurements of capillary Li-heparin patient samples collected under optimal conditions.

Trueness

To document the trueness of the comparison method, the standard reference material (SRM) 965b from National Institute of Standards & Technology (NIST) was used [12]. SRM 965b consists of ampoules with human serum with certified concentrations of glucose at four levels with given uncertainties. If necessary, the comparison method's results will be adjusted according to the NIST-targets. In addition, human serum controls, produced by Norwegian Quality Improvement of Laboratory Examinations (Noklus), with glucose concentrations at two levels were analysed. These controls have target values determined with an isotope-dilution gas chromatography/mass spectrometry method in a Reference laboratory in Belgium [13]. The target value is given with an expanded uncertainty of 1,5 – 2 % (k=2).

5.4. The evaluation

5.4.1. Planning of the evaluation

Inquiry about an evaluation

Roche Diagnostics Scandinavia AB via Senior Product Manager Jenny Hemingway applied to SKUP in September 2016 for an evaluation of Accu-Chek Instant. The new meter was expected to be ready for use early in 2017. Roche and SKUP agreed that the practical work in the evaluation should start in spring 2017.

Contract, protocol and arrangements

In March 2017, Roche Diagnostics Scandinavia AB and SKUP signed a contract for the evaluation. In May 2017, the protocol for the evaluation was approved. The laboratory at HDH agreed to analyse the samples for the comparison method.

Training

Roche Diagnostics Scandinavia AB was responsible for necessary training in use of the Accu-Chek Instant system under optimal conditions. The Accu-Chek Instant system was not launched in Scandinavia before start-up of the evaluation and the representatives from Roche were not trained themselves. The BLSs responsible for the practical work were well familiar with blood glucose measurement systems. In agreement with Roche, it was therefore decided that no further training from Roche was given. All the participants (persons with diabetes) received the device and instructions by mail and no training was given.

5.4.2. Evaluation sites and persons involved

The practical work, including sampling and measurements on Accu-Chek Instant, was carried out at Noklus during four weeks in May - June 2017. Three BLSs were involved in the practical work. At the laboratory at HDH, one BLS was responsible for analysing the samples on the comparison method.

5.4.3. Recruitment and selection of participants

Recruitment

Participants were recruited by mail inquiry sent to members of the local branch of The Norwegian Diabetes Association.

Selection

Participants were selected at random, but with the criterion to get variety in the group according to gender, diabetes type, age and how often the participants normally performed blood glucose measurements.

5.4.4. The evaluation procedure

The participants received the Accu-Chek Instant meter by mail, along with test strips, lancet pen, lancets, user information and an information letter with explanations regarding what to do with the Accu-Chek Instant device during the period at home. Three lots of test strips were distributed evenly between the participants (random distribution). The participants could choose whether to use the distributed lancing device, or the lancet device they usually use.

Use of Accu-Chek Instant at home
The participants used Accu-Chek Instant at home for approximately two weeks. They used Accu-Chek Instant in addition to their own glucose meter, and they continued to carry out self-measurements with their own meter as usual. During the first week, the participants got familiarised with the new device. Each diabetes patient had approximately 25 test strips to their disposal for this. If preferred, they could perform the measurements at the same time as performing measurements with their own meter. During the second week, the participants performed duplicate measurements on Accu-Chek Instant on five different days. The results were recorded in a provided form for documentation of the training efforts.

Evaluation meeting
After the two-weeks' practice period at home, the participants met, one by one, for an evaluation meeting with the BLS. The participants brought their assigned Accu-Chek Instant to the meeting. For the evaluation performed under optimal conditions, the BLSs used three Accu-Chek Instant blood glucose meters (called meter A, B and C). For all the participants, two measurements were performed with each of the three meters (totally six measurements for each diabetes patient) at the evaluation meeting. The same three lot numbers of test strips as distributed to the participants were used. On meter A, lot 907277 (called lot a) was used, on meter B, lot 907599 (called lot b) was used, and on meter C, lot 907604 (called lot c) was used for all the measurements.

Internal analytical quality control
Meter A, B and C were checked with the manufacturer's control solutions, Accu-Chek Aviva Control 1 (range 1,7 - 3,3 mmol/L) and Control 2 (range 14,0 - 19,0 mmol/L), each evaluating day. To document correct functioning of the Accu-Chek Instant meters used by the participants, the BLS checked these meters with Control 2 at the evaluation meeting. Reproducibility (CV) as achieved with the quality control material was calculated.

Handling of samples and measurements
Before samples were collected, the participants' assigned devices were equilibrated to room temperature, while the participants filled in the questionnaire regarding user-friendliness of Accu-Chek Instant.

The participants washed and dried their hands before sampling. All samples for Accu-Chek Instant, as well as the glucose samples for the comparison method, were capillary samples collected from a finger prick. Blood samples for duplicate measurements on Accu-Chek Instant under optimal conditions were mainly collected from the same finger prick. The BLS wiped off the first drop of blood before the first measurement and between the sets of duplicates (meter A, B and C). The sampling sequence was carried out as quickly as possible in order to reduce possible changes in glucose concentration during sampling.

Blood sampling and analysis for each participant were carried out in the following order:
1. The BLS collected a first sample for the comparison method
2. The BLS collected samples for meter A, B, C, A, B and C (the order of the measurements on meter A, B and C was changed between each participant)
3. The participant pricked himself/herself and collected duplicate samples for measurements on his/her assigned meter
4. The BLS collected a second sample for the comparison method in a new finger prick
5. The BLS collected a venous sample for haematocrit

In case of error codes, the test was repeated if possible until a result was obtained.

Most of the participants used the distributed Accu-Chek FastClix lancing device for the blood sampling. The participants' measurements were performed with the test strips delivered to them for the evaluation.

Samples for the comparison method were collected into Microvette Li-heparin tubes (300 µL) from Sarstedt. The samples were centrifuged immediately for three minutes at 10 000 g, and plasma was separated. The plasma samples were frozen directly and stored at minus 80°C (according to storing procedure for the SRM from NIST [12]) until analysis took place. The samples were analysed during two days in June 2017. All first samples for the comparison method were analysed once; all second samples were analysed in duplicate (see section 5.3.2). The mean of the comparison method was calculated as the mean value of the first sample result and the average result of the second sample. This mean is an estimate of the true glucose value and is referred to as the mean result of the comparison method.

Stability of glucose concentration during sampling time
The stability of glucose concentration during sampling was supervised by means of the capillary samples for the comparison method taken at the start and in the end of each sampling sequence. Based on experience from several previous glucose meter user-evaluations, a stability criteria with a change <10 % between the first and second comparative result is regarded as reasonable. Changes >10 % are regarded as unacceptable and these results will be excluded.

Measurement of haematocrit
Haematocrit may influence blood glucose measurements. The venous sample for haematocrit collected from each diabetes patient (voluntarily) was measured within six hours.

6. Results and discussion

Statistical expressions and calculations used by SKUP are shown in attachment 5.

6.1. Number of samples

A total of 90 persons with diabetes signed up for the evaluation and 88 of them completed. Two participants withdrew from the evaluation for various reasons. The BLSs performed 528 glucose measurements (6 measurements x 88 patients) on Accu-Chek Instant under optimal conditions. In addition, the BLSs collected 176 capillary Li-heparin samples (2 samples x 88 patients) for glucose measurement on the comparison method. A venous sample for measurement of haematocrit was collected from 85 of the 88 participants. The intended users (persons with diabetes) performed 176 glucose measurements (2 measurements x 88 patients) on Accu-Chek Instant.

The concentration range for the glucose samples was 3,4 – 17,7 mmol/L (results from the comparison method).

The concentration range for the haematocrit samples was 29 – 50 %.

The Accu-Chek Instant glucose meter was tested in use by 41 men and 47 women with diabetes. Average age of the participants was 57 years (range 22 – 82 years). A total of 35 participants had Type 1 diabetes, three had Latent Autoimmune Diabetes of Adults (LADA), 48 had Type 2 diabetes, two participants did not know/specified their type of diabetes. The group included persons from a range of self-monitoring frequencies, i.e. persons who perform self-monitoring often and those who perform self-monitoring less frequently.

An account of the number of samples not included in the calculations is given below.

Missing results
For three of the participants (ID 24, ID 103 and ID 124), no sample for haematocrit was collected. Control result is missing for three of the participants' meters and for one of the control measurements performed under optimal conditions.

Omitted results
For ID 29, ID 45 and ID 117, the deviation between the first and the second sample for the comparison method was >10 %, which means that these participants had an unstable glucose concentration during the sampling sequence time. Sample results from these participants were removed before calculation of bias and the assessment of accuracy, and also before the assessment of haematocrit effect.

Excluded results
Statistical outliers in SKUP evaluations are detected by the criterion promoted by Burnett [14]. The difference between the two results for ID 32 was detected as an outlier in the calculation of repeatability for meter C (optimal condition), thus the results were excluded from this calculation and did neither enter into the calculation of bias. The difference between the two results for ID 80 was detected as an outlier in the calculation of repeatability achieved by the intended users, thus the results were excluded from this calculation.

Comment
ID 66 had forgotten his test strips at home, and performed the measurements at the evaluation meeting with test strips made available there. The results were included in the calculations.

Recorded error codes, technical errors and failed measurements
The BLSs got no error codes on their measurements, whereas the intended users got error codes on seven of their measurements during the evaluation. Four of these error codes were due to user errors (E-4 errors "not enough blood"), and the remaining three were technical errors/tests wasted (E-3 errors "A meter or test strip error has occurred").

The percentage of tests wasted in this evaluation was:
(3 errors / (528 measurements + 176 measurements)) x 100 = 0,4 %.

The SKUP recommendation of a fraction of ≤2 % tests wasted due to technical errors was achieved.

6.2. Analytical quality of the selected comparison method

6.2.1. Internal analytical quality control

All results from the internal analytical quality control (Autonorm Human Liquid Control Solutions, Sero AS), two levels, were within the limits set by the laboratory for the controls (data not shown).

6.2.2. The precision of the comparison method

Duplicate measurements of the second capillary blood patient samples were performed on the comparison method. The results were checked to meet the imposed condition for using formula 1 in attachment 5. There was a systematic difference pointed out between the paired measurements for all levels (data not shown). The difference was small, but statistically significant. When using highly precise methods, even negligible differences are easily pointed out as statistically significant. The systematic differences pointed out lead to a minor overestimation of CVs of the comparison method.

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 3. The results were sorted and divided into three glucose concentration levels according to the first measurement of the comparison method. Raw data is attached for the requesting company only, see attachment 6.

Table 3. Repeatability, glucose, capillary blood samples, comparison method

Glucose level, Comparison method, mmol/L	n	Excluded results	Mean value glucose, mmol/L	CV (90 % CI), %
<7	23	0	5,6	1,4 (1,1 – 1,8)
7 – 10	34	0	8,3	1,0 (0,8 – 1,3)
>10	31	0	12,7	1,0 (0,9 – 1,3)

An account of the number of samples is given in section 6.1.

Discussion

The CV for the comparison method was between 1,0 and 1,4 %.

6.2.3. The trueness of the comparison method

In order to demonstrate the trueness of the comparison method, SRM 965b standards from NIST were analysed. The agreement between the comparison method and the NIST-standards is shown in table 4.

Table 4. SRM 965b measured on the comparison method

SRM 965b	Date	Certified glucose concentration, (uncertainty) mmol/L	n	Mean value glucose, mmol/L	Deviation from target value, %
Level 1	26.06.17	**1,836** (1,809 – 1,863)	5	1,88	+2,6
	27.06.17		5	1,88	+2,4
	Total		**10**	**1,88**	**+2,5**
Level 2	26.06.17	**4,194** (4,135 – 4,253)	5	4,39	+4,6
	27.06.17		5	4,29	+2,3
	Total		**10**	**4,34**	**+3,4**
Level 3	26.06.17	**6,575** (6,481 – 6,669)	5	6,71	+2,1
	27.06.17		5	6,66	+1,3
	Total		**10**	**6,69**	**+1,7**
Level 4	26.06.17	**16,35** (16,15 – 16,55)	5	16,75	+2,5
	27.06.17		5	16,41	+0,4
	Total		**10**	**16,58**	**+1,4**

Comments

Table 4 shows that the glucose results for the NIST-standards were just above the upper uncertainty limit or close to the upper uncertainty limit for all levels. All results from the comparison method were therefore adjusted according to the certified NIST-targets. The adjustment was carried out by means of inverse calibration [15, 16] by the following regression equations: **y = 0,978x − 0,0314** (for samples analysed the 26th of June) and **y = 1,0001x – 0,0733** (for samples analysed the 27th of June).

Further on in the report, whenever a result from the comparison method is presented, the result has already been adjusted according to this.

To verify the trueness of the adjusted comparison method results, human serum controls produced by Noklus, were analysed. The agreement between the comparison method and target values from the Reference laboratory in Belgium is shown in table 5.

Table 5. Trueness of the comparison method

Control	Date	Target value glucose, (expanded uncertainty) mmol/L	n	Mean value glucose, mmol/L	Deviation from target value, %
Noklus 1	26.06.17	**5,71** (5,62 – 5,80)	5	5,81	1,7
	27.06.17		5	5,76	0,9
	Total		**10**	**5,79**	**1,3**
Noklus 2	26.06.17	**11,94** (11,70 – 12,18)	5	12,18	2,0
	27.06.17		5	12,07	1,1
	Total		**10**	**12,12**	**1,5**

Discussion

The comparison method gave glucose values in agreement with the glucose values from the Reference laboratory in Belgium. The trueness of the comparison method was confirmed.

6.3. Analytical quality of Accu-Chek Instant under optimal conditions

The results below reflect the analytical quality of Accu-Chek Instant under optimal conditions. The results document the quality of the system under conditions as favourable as possible for achieving good analytical quality.

6.3.1. Internal analytical quality control

All results from the internal analytical quality control (Accu-Chek Aviva), two levels, were within allowable control limits (data not shown). Still one of the measurements of Control level 2 on meter A was detected as a statistical outlier and therefore excluded. The reproducibility (CV) achieved with the internal analytical quality control samples were 4,1 % for level 1 (n=53) and 2,4 % for level 2 (n=52). Raw data is attached for the requesting company only, see attachment 7.

6.3.2. The precision of Accu-Chek Instant

Two capillary samples were collected from each diabetes patient for measurements with lot a, lot b and lot c at the evaluation meeting. The results were checked to meet the imposed condition for using formula 1 in attachment 5. There were no systematic differences pointed out between the paired measurements (data not shown).

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 6. The results were sorted and divided into three concentration levels according to the first measurement on Accu-Chek Instant. Raw data is attached for the requesting company only, see attachment 8.

Table 6. Repeatability, glucose, capillary samples, Accu-Chek Instant. Results achieved under optimal conditions.

Accu-Chek Instant (lot number of test strips)	Glucose level, mmol/L	n	Excluded results	Mean value glucose, mmol/L	CV (90% CI), %
Lot a	<7	24	0	5,5	1,8 (1,5 – 2,4)
Lot b	<7	28	0	5,6	2,9 (2,3 – 3,8)
Lot c	<7	27	0	5,6	2,1 (1,6 – 2,7)
Lot a	7 – 10	41	0	8,4	2,2 (1,9 – 2,7)
Lot b	7 – 10	37	0	8,4	2,8 (2,4 – 3,4)
Lot c	7 – 10	36	1*	8,4	1,8 (1,6 – 2,3)
Lot a	>10	23	0	12,7	1,6 (1,3 – 2,2)
Lot b	>10	23	0	12,5	1,8 (1,4 – 2,4)
Lot c	>10	25	0	12,4	1,8 (1,5 – 2,3)

*The given numbers of results (n) are counted before exclusion of results. Mean and CV are calculated after exclusion of results. ID 32 is a statistical outlier according to Burnett's model [14] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion

The CV achieved under optimal conditions was between 1,6 and 2,9 %. As the upper CI values for all levels are ≤5,0 %, the CVs are statistically significant below the quality goal.

Conclusion

Under optimal conditions, the quality goal for repeatability (CV≤5,0 %) was fulfilled.

6.3.3. The bias of Accu-Chek Instant

The mean deviation (bias) of Accu-Chek Instant results from the comparison method was calculated. The bias of Accu-Chek Instant with three lots of test strips is presented with a 95 % CI in table 7. The results were sorted and divided into three concentration levels according to the mean results of the comparison method. Raw data is attached for the requesting company only, see attachment 6 and 8.

Table 7. Bias, glucose, capillary samples, Accu-Chek Instant. Results achieved under optimal conditions.

Accu-Chek Instant (lot number of test strips)	Glucose level Comparison method, mmol/L	n	Excluded results	Mean value Comparison method, glucose mmol/L	Mean value Accu-Chek Instant, glucose mmol/L	Bias (95 % CI), mmol/L	Bias, %
Lot a	<7	23	0	5,8	5,8	0,00 ((–0,08) – (+0,07))	0,0
Lot b	<7	23	0	5,8	5,7	–0,13 ((–0,21) – (–0,04))	–2,2
Lot c	<7	23	0	5,8	5,7	–0,08 ((–0,14) – (–0,02))	–1,4
Lot a	7 – 10	32	0	8,3	8,1	–0,18 ((–0,26) – (–0,11))	–2,2
Lot b	7 – 10	32	0	8,3	8,0	−0,32 ((−0,39) – (−0,24))	–3,8
Lot c	7 – 10	31	0	8,3	8,1	–0,23 ((–0,30) – (–0,16))	–2,8
Lot a	>10	30	0	12,5	12,0	–0,46 ((–0,61) – (–0,32))	–3,7
Lot b	>10	30	0	12,5	11,9	–0,65 ((–0,80) – (–0,50))	–5,2
Lot c	>10	30	0	12,5	12,0	–0,56 ((–0,71) – (–0,41))	–4,5

An account of the number of samples is given in section 6.1.

Discussion

The glucose measurements on Accu-Chek Instant showed systematic lower glucose results than the comparison method for all glucose levels with all three lot numbers of test strips except for glucose level <7 mmol/L with lot a. For lot b and c at this level, the bias from the comparison method was –0,13 and –0,08 mmol/L, respectively. For glucose level 7 – 10 mmol/L, the bias from the comparison method was between –0,18 and –0,32 mmol/L, and for glucose level >10 mmol/L, the bias was between –0,46 and –0,65 mmol/L.

6.3.4. The accuracy of Accu-Chek Instant

To evaluate the accuracy of glucose results on Accu-Chek Instant, the agreement between Accu-Chek Instant and the comparison method is illustrated in a difference plot (figure 4). The limits for allowable deviation, according to the quality goal (ISO 15197:2013), are shown with stippled lines. All first measurements from Accu-Chek Instant are included in the plot. The plot illustrates both random and systematic errors, reflecting the total measuring error in the Accu-Chek Instant results. The accuracy is summarised in table 8. Raw data is attached for the requesting company only, see attachment 6 and 8.

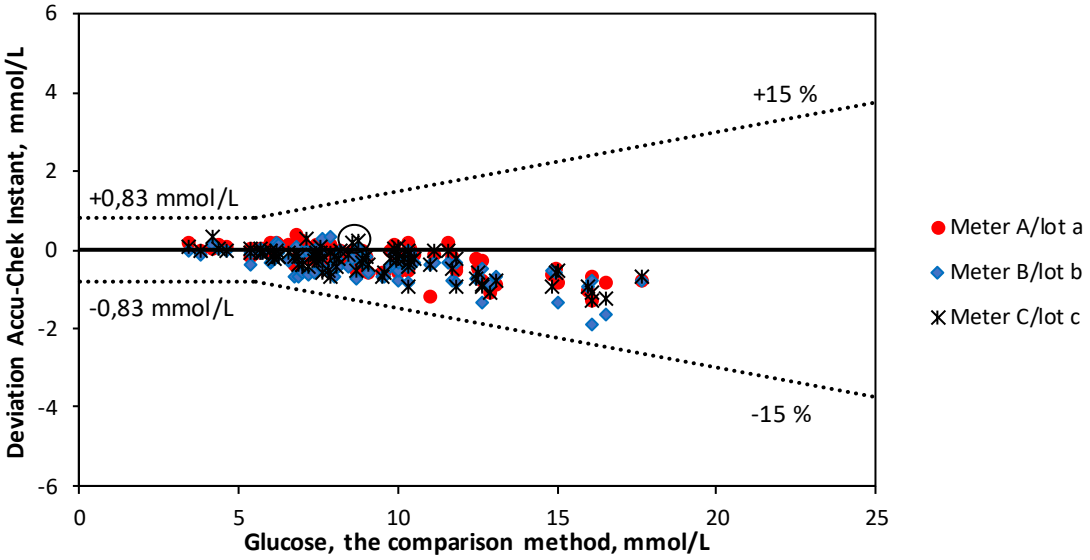


Figure 4. Accuracy of glucose results on Accu-Chek Instant under optimal conditions. The x-axis represents the mean glucose result of the comparison method. The y-axis represents the glucose deviation in mmol/L of the first capillary measurement on Accu-Chek Instant from the mean result of the corresponding sample of the comparison method. The different lots of test strips are illustrated as lot a (●), lot b (♦) and lot c (x). Stippled lines represent allowable deviation limits set in ISO 15197:2013 (within ±0,83 mmol/L of the results of the comparison method for glucose concentrations <5,55 mmol/L and within ±15 % for glucose concentrations ≥5,55 mmol/L). Number of results (n) = 85. ID 32, statistical outlier from the calculations of repeatability (lot c), is illustrated with a circle around the symbol. An account of the number of samples is given in section 6.1.

Table 8. Accuracy, glucose, capillary samples, Accu-Chek Instant. Results achieved under optimal conditions.

Lot	n	Percentage of results within given limits, %	
		ISO 15197:2013[1]	**Stricter Swedish quality goal[2]**
a	85	100	99
b	85	100	98
c	85	100	100

[1] ISO 15197:2013: <±0,83 mmol/L at conc. <5,55 mmol/L or <±15 % at conc. ≥5,55 mmol/L
[2] Stricter Swedish quality goal: <±0,42 mmol/L at conc. <4,2 mmol/L or <±10 % at conc. ≥4,2 mmol/L
An account of the number of samples is given in section 6.1.

Discussion
Figure 4 shows that the Accu-Chek Instant glucose results were slightly lower than the results from the comparison method, which correspond to the calculated bias in section 6.3.3. The summing up in table 8 shows that all the results obtained under optimal conditions were within allowable deviation limits specified in ISO 15197:2013. Table 8 also shows the number of results within the stricter Swedish quality goal (see section 4.1). These results are for information only. No distinct differences between the three lots of test strips were observed.

Conclusion
Under optimal conditions, the quality goal for accuracy was fulfilled.

6.3.5. Effect of haematocrit

According to the technical specifications for Accu-Chek Instant, the glucose measurements are not effected by haematocrit values from 10 to 65 %. To measure the effect of haematocrit on Accu-Chek Instant, a venous sample for haematocrit was collected from the participants at the evaluation meeting. Investigation of the effect was based on the measurements on Accu-Chek Instant meter A (with lot a) under optimal conditions. The effect of haematocrit is shown with a trend-line and a regression equation in figure 5. Raw data is attached for the requesting company only, attachment 6, 8 and 9.

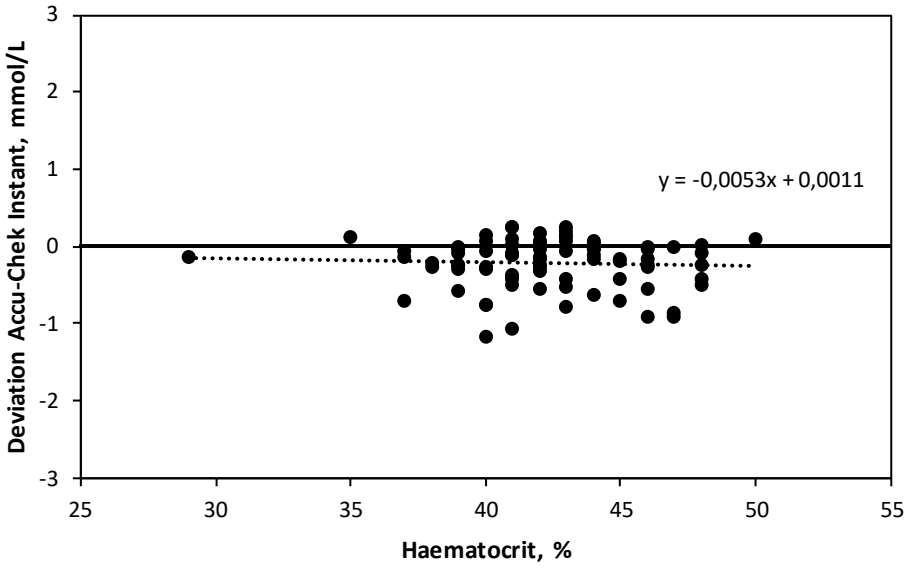


Figure 5. The effect of haematocrit on glucose measurements on Accu-Chek Instant meter A (with lot a) measured under optimal conditions. The x-axis shows the haematocrit value in percent. The y-axis shows the difference in glucose concentration between Accu-Chek Instant and the mean result of the corresponding sample of the comparison method in mmol/L. Number of results (n) = 82.

Discussion

The slope of the trend-line in figure 5 is (–0,005), with a 95 % CI from (–0,026) to (+0,016). The slope is not statistically significant different from zero. Glucose measurements on Accu-Chek Instant were not affected by haematocrit within the range tested (29 – 50 %).

6.4. Analytical quality of Accu-Chek Instant achieved by intended users

The results below reflect the analytical quality of Accu-Chek Instant under real-life conditions in the hands of intended users (persons with diabetes). The results may deviate from the results achieved under optimal conditions.

6.4.1. Internal analytical quality control

The Accu-Chek Instant meters used by the intended users were checked with the internal analytical quality control (Accu-Chek Aviva Control 2), by the BLS at the evaluation meeting. All results were within allowable control limits (data not shown). Still the control measurements performed on two of the intended users assigned meters (ID 24 and ID 86) were detected as statistical outliers and therefore excluded. The reproducibility (CV) achieved with the internal analytical quality control was 1,9 % (n=83). Raw data is attached for the requesting company only, attachment 10.

6.4.2. The precision of Accu-Chek Instant

The participants collected two capillary samples for measurements on their assigned Accu-Chek Instant at the evaluation meeting. The results were checked to meet the imposed condition for using formula 1 in attachment 5. A systematic difference was pointed out between the paired measurements for concentration level < 7 mmol/L and for concentration level 7 – 10 mmol/L (data not shown). The differences were small, but statistically significant. The result of the second sample was in average 0,2 mmol/L higher than the first sample result for concentration level <7 mmol/L and in average 0,1 mmol/L higher for concentration level 7 – 10 mmol/L. No explanation for these systematic differences has been found. The sampling procedure, as well as the measurement procedure, were identical for all samples and measurements throughout the evaluation. For concentration level > 10 mmol/L, no systematic differences were pointed out (data not shown).

The precision is presented as repeatability (CV). The CV with a 90 % CI is shown in table 9. The results were sorted and divided into three concentration levels according to the first measurement on Accu-Chek Instant. Raw data is attached for the requesting company only, attachment 11.

Table 9. Repeatability, glucose, capillary samples, Accu-Chek Instant. Results achieved by intended users.

Glucose level Accu-Chek Instant, mmol/L	n	Excluded results	Mean value glucose, mmol/L	CV (90 % CI), %
<7	32	0	5,8	5,7* (4,8 – 7,2)
7 – 10	33	0	8,7	2,1 (1,7 – 2,7)
>10	23	1**	12,4	3,5 (2,8 – 4,7)

* In a simulated set of data, the average systematic difference described above, was removed for this concentration level, and the CV was recalculated. The CV for concentration level <7 mmol/L was still not below 5,0 %. As a consequence, the repeatability is calculated without taking this systematic difference into consideration.
** The given numbers of results (n) are counted before exclusion of results. Mean and CV are calculated after exclusion of results. ID 80 is statistical outlier according to Burnett's model [14] and therefore excluded. An account of the number of samples is given in section 6.1.

Discussion
The CV achieved by intended users was between 2,1 and 5,7 % depending on the concentration level. The CV for the concentration level <7 mmol/L was 5,7 %, which is higher than the quality goal, but not statistically significant higher. The CV achieved for this concentration level is also different from the CVs achieved for the two other concentration levels and the CVs achieved under optimal conditions, mainly due to four duplicate measurements with a difference between the results of approximately 1,0 mmol/L. There are no error codes or other comments to these measurements; therefore these results have been included in the calculation. For concentration level 7 – 10 mmol/L and concentration level >10 mmol/L, the upper CI values are ≤5,0 %, and the CVs for these two levels are statistically significant below the quality goal.

Conclusion
When measurements were performed by the intended users the quality goal for repeatability (CV≤5,0 %) was most likely not fulfilled for concentration level <7 mmol/L. However, the quality goal was fulfilled for concentration level 7 – 10 mmol/L and concentration level >10 mmol/L.

6.4.3. The accuracy of Accu-Chek Instant

To evaluate the accuracy of glucose results on Accu-Chek Instant, the agreement between Accu-Chek Instant and the comparison method is illustrated in a difference plot (figure 6). The limits for allowable deviation, according to the quality goal (ISO 15197:2013), are shown with stippled lines. All first measurements from Accu-Chek Instant are included in the plot. The plot illustrates both random and systematic errors, reflecting the total measuring error in the Accu-Chek Instant results. The accuracy is summarised in table 10. Raw data is attached for the requesting company only, attachment 6 and 11.

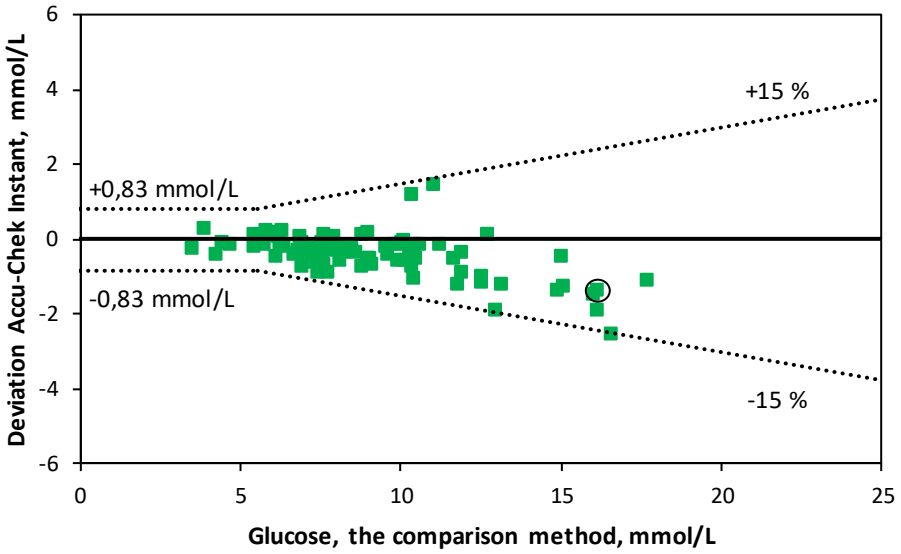


Figure 6. Accuracy of glucose results on Accu-Chek Instant achieved by intended users (three lots of test strips). The x-axis represents the mean glucose result of the comparison method. The y-axis represents the glucose deviation in mmol/L of the first capillary measurement on Accu-Chek Instant from the mean result of the corresponding sample of the comparison method. Stippled lines represent allowable deviation limits set in ISO 15197:2013 (within ±0,83 mmol/L of the results of the comparison method for glucose concentrations <5,55 mmol/L and within ±15 % for glucose concentrations ≥5,55 mmol/L). Number of results (n) = 85. ID 80, statistical outlier from the calculations of repeatability, is illustrated with a circle around the symbol. An account of the number of samples is given in section 6.1.

Table 10. Accuracy, glucose, capillary samples, Accu-Chek Instant. Results achieved by intended users (three lots of test strips).

n	Percentage of results within ISO 15197:2013[1], %
85	99

[1] ISO 15197:2013: <±0,83 mmol/L at conc. <5,55 mmol/L or <±15 % at conc. ≥5,55 mmol/L
An account of the number of samples is given in section 6.1.

Discussion
Figure 6 shows that the Accu-Chek Instant glucose results were slightly lower than the results from the comparison method. This corresponds to the results found under optimal conditions. The summing up in table 10 shows that 99 % of the results obtained by the intended users were within the allowable deviation limits specified in ISO 15197:2013.

Conclusion
When measurements were performed by the intended users the quality goal for accuracy was fulfilled.

6.5. Evaluation of user-friendliness

6.5.1. Questionnaire to the evaluators

The most important response regarding user-friendliness comes from the intended users themselves. The end-users often emphasise other aspects than those pointed out by more extensively trained laboratory personnel.

At the evaluation meeting each participant filled in a questionnaire about the user-friendliness of the measurement system. Since the manual is not available in Norwegian, SKUP assessed the manual in this evaluation.

The questionnaire is divided into four subareas:

Table A) Rating of operation facilities. Is the system easy to handle?
Table B) Rating of the information in the manual / insert / quick guide
Table C) Rating of time factors for the preparation and the measurement
Table D) Rating of performing internal and external analytical quality control

The participants filled in table A. SKUP filled in table B, C and D and in addition, topics marked with grey colour in table A.

In the tables, the first column shows what is up for consideration. The rest of the columns show the rating options. The total rating is an overall assessment by SKUP of the described property, and not necessarily the arithmetic mean of the rating in the rows. Consequently, a single poor rating can justify an overall poor rating, if this property seriously influences on the user-friendliness of the system.

The intermediate category covers neutral ratings assessed as neither good nor bad.

An assessment of the user-friendliness is subjective, and the topics in the questionnaire may be emphasised differently by different users. The assessment can therefore vary between different persons. However, the feedback from approximately 90 persons with diabetes will give a clear indication whether there is anything in particular to remark about the blood glucose measurement system.

Comment
In this evaluation, the user-friendliness was assessed by 88 persons with diabetes.

Table A. Rating of operation facilities

Topic (n)	**Rating** % (n)	**Rating** % (n)	**Rating** % (n)	**Option** % (n)
To measure a sample (88)	Satisfactory 91 (80)	Intermediate 7 (6)	Unsatisfactory 2 (2)	No opinion 0 (0)
To insert the test strip (88)	Satisfactory 85 (75)	Intermediate 13 (11)	Unsatisfactory 2 (2)	No opinion 0 (0)
To apply blood (88)	Satisfactory 89 (78)	Intermediate 8 (7)	Unsatisfactory 3 (3)	No opinion 0 (0)
Reading of the test result (88)	Satisfactory 99 (87)	Intermediate 1 (1)	Unsatisfactory 0 (0)	No opinion 0 (0)
Specimen volume (87)	Satisfactory 83 (72)	Intermediate 15 (13)	Unsatisfactory 1 (1)	No opinion 1 (1)
Instrument / test strip design (86)	Satisfactory 79 (68)	Intermediate 17 (15)	Unsatisfactory 3 (3)	No opinion 0 (0)
Sources of errors (86)	Satisfactory 64 (55)	Intermediate 10 (9)	Unsatisfactory 6 (5)	No opinion 20 (17)
Cleaning / Maintenance (86)	Satisfactory 77 (66)	Intermediate 5 (4)	Unsatisfactory 1 (1)	No opinion 17 (15)
Hygiene, when using the test (87)	Satisfactory 90 (78)	Intermediate 7 (6)	Unsatisfactory 2 (2)	No opinion 1 (1)
Size and weight of package (88)	Satisfactory 91 (80)	Intermediate 8 (7)	Unsatisfactory 1 (1)	No opinion 0 (0)
In total; how easy did you find the usage of the instrument? (88)	Satisfactory 86 (76)	Intermediate 11 (10)	Unsatisfactory 2 (2)	No opinion 0 (0)
Storage conditions for tests, unopened package	+15 to +30°C	+2 to +8°C	–20°C	
Storage conditions for tests, opened package	+15 to +30°C	+2 to +8°C	–20°C	
Environmental aspects: waste handling	No precautions	Sorted waste	Special precautions	
Intended users	Health care personnel or patients	Laboratory experience	Biomedical laboratory scientists	
Total rating by SKUP	**Satisfactory**			

Positive comments
A total of 47 participants had one or more positive comments regarding the operation facilities of Accu-Chek Instant. The most often reported positive comments were:

1. Comments regarding the use of the meter (30); the meter is easy to use, has short measuring time, needs a small amount of blood
2. The meter has a convenient size, small, lightweight (16)
3. Comments regarding the display (7); easy to read the result, clear numbers, illuminated numbers, large numbers

Negative comments
A total of 46 participants had one or more negative comments regarding the operation facilities of Accu-Chek Instant. The most often reported negative comments were:

1. Comments regarding the test strips (20); difficult to get the strip out of the box, small test strips, difficult to insert the strip into the meter, single test strips, because the strip goes far into the meter it is difficult to remove the strip without getting blood on your fingers, the strip must be pulled out after measurement
2. Comments regarding the software of the meter (8); not possible to see previous measurements, see the date or specify details regarding a measurement (comment from SKUP: Roche has a compatible software application available for Accu-Chek Instant. To view other stored results, the results must be transferred to the application)
3. Error codes (6)

Table B. Rating of the information in the manual (rated by SKUP in this evaluation)

Topic	Rating	Rating	Rating
Table of contents / Index	**Satisfactory**	Intermediate	Unsatisfactory
Preparations / Pre-analytic procedure	**Satisfactory**	Intermediate	Unsatisfactory
Specimen collection	**Satisfactory**	Intermediate	Unsatisfactory
Measurement procedure	**Satisfactory**	Intermediate	Unsatisfactory
Reading of result	**Satisfactory**	Intermediate	Unsatisfactory
Description of the sources of error	**Satisfactory**	Intermediate	Unsatisfactory
Help for troubleshooting	**Satisfactory**	Intermediate	Unsatisfactory
Readability/Clarity of presentation	**Satisfactory**	Intermediate	Unsatisfactory
General impression	**Satisfactory**	Intermediate	Unsatisfactory
Measurement principle[1]	**Satisfactory**	Intermediate	Unsatisfactory
Available insert in Danish, Norwegian, Swedish[2]	**Satisfactory**	Intermediate	Unsatisfactory
Total rating by SKUP	**Satisfactory**		

[1] The measuring principle is not mentioned in the manual but can be found in the package insert for the test strips.
[2] The insert will be available in the local language in the countries where the system will be launched.

Table C. Rating of time factors (rated by SKUP)

Topic	Rating	Rating	Rating
Required training time	**<2 hours**	2 to 8 hours	>8 hours
Durations of preparations / Pre-analytical time	**<6 min.**	6 to 10 min.	>10 min.
Duration of analysis	**<10 sec.**	10 to 30 sec.	>30 sec.
Stability of test, unopened package	**>5 months**	3 to 5 months	<3 months
Stability of test, opened package	**>30 days**	14 to 30 days	<14 days
Stability of quality control material, unopened	**>5 months**	3 to 5 months	<3 months
Stability of quality control material, opened	**>6 days or disposable**	2 to 6 days	≤1 day
Total rating by SKUP	**Satisfactory**		

Table D. Rating of analytical quality control (rated by SKUP)

Topic	Rating	Rating	Rating
Reading of the internal quality control	**Satisfactory**	Intermediate	Unsatisfactory
Usefulness of the internal quality control	**Satisfactory**	Intermediate	Unsatisfactory
External quality control	**Satisfactory**	Intermediate	Unsatisfactory
Total rating by SKUP	**Satisfactory**		

6.5.2. Assessment of the user-friendliness

Assessment of the operation facilities (table A)
The operation facilities were in total assessed as satisfactory. The users had both positive and negative comments regarding the operation facilities.

Assessment of the information in the manual (table B)
The manual was assessed as satisfactory.

Assessment of time factors (table C)
The time factors were assessed as satisfactory.

Assessment of analytical quality control possibilities (table D)
The analytical quality control possibilities were assessed as satisfactory. The imprecision achieved with the internal analytical quality control material (Accu-Chek Aviva Control 1 and Control 2), equals the imprecision of the patient samples.

Conclusion
In all, the user-friendliness of Accu-Chek Instant and its manual was rated as satisfactory. The quality goal for user-friendliness was fulfilled.

7. References

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Attachments

1. The organisation of SKUP
2. Facts about Accu-Chek Instant
3. Information about manufacturer, retailers and marketing
4. Product specifications for this evaluation, Accu-Chek Instant
5. Statistical expressions and calculations
6. Raw data glucose, results from the comparison method
7. Raw data glucose, internal analytical quality control results, Accu-Chek Instant, optimal conditions
8. Raw data glucose, Accu-Chek Instant results, optimal conditions
9. Raw data haematocrit
10. Raw data glucose, internal analytical quality control results, Accu-Chek Instant, intended users
11. Raw data glucose, Accu-Chek Instant results, intended users
12. List of previous SKUP evaluations

Attachments with raw data are included only in the copy to Roche Diagnostics Scandinavia AB.

The organisation of SKUP

Scandinavian evaluation of laboratory equipment for primary health care, *SKUP*, is a co-operative commitment of Noklus[1] in Norway, DEKS[2] in Denmark, and Equalis[3] in Sweden. SKUP was established in 1997 at the initiative of laboratory medicine professionals in the three countries. SKUP is led by a Scandinavian *steering committee* and the secretariat is located at Noklus in Bergen, Norway.

The purpose of SKUP is to improve the quality of near patient testing in Scandinavia by providing objective and supplier-independent information about analytical quality and user-friendliness of laboratory equipment. This information is generated by organising SKUP *evaluations*.

SKUP offers manufacturers and suppliers evaluations of equipment for primary health care and also of devices for self-monitoring. Provided the equipment is not launched onto the Scandinavian market, it is possible to have a confidential pre-marketing evaluation. The company requesting the evaluation pays the actual testing costs and receives in return an impartial evaluation.

There are *general guidelines* for all SKUP evaluations and for each evaluation a specific *SKUP protocol* is worked out in co-operation with the manufacturer or their representatives. SKUP signs *contracts* with the requesting company and the evaluating laboratories. The analytical results are assessed according to *pre-set quality goals*. To fully demonstrate the quality of a product, the *end-users* should be involved in the evaluations.

Each evaluation is presented in a *SKUP report* to which a unique *report code* is assigned. The code is composed of the acronym SKUP, the year the report was completed and a serial number. A report code, followed by an asterisk (*), indicates an evaluation with a more specific objective. The asterisk is explained on the front page of these protocols and reports.

SKUP reports are published at www.skup.nu.

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[1] Noklus (Norwegian Quality Improvement of Laboratory Examinations) is a national not for profit organisation offering activities for quality improvement to all medical laboratory services in Norway. Noklus was established in 1992 and is governed by a management committee consisting of representatives from the Norwegian Government, the Norwegian Medical Association and the Norwegian Society of Medical Biochemistry, with the Norwegian Association of Local and Regional Authorities (KS) as observer.

[2] DEKS (Danish Institute for External Quality Assurance for Laboratories in Health Care) is a non-profit organisation owned by the Capital Region of Denmark on behalf of all other Regions in Denmark.

[3] Equalis AB (External quality assessment in laboratory medicine in Sweden) is a limited company in Uppsala, Sweden, owned by “Sveriges Kommuner och Landsting” (Swedish Association of Local Authorities and Regions), “Svenska Läkaresällskapet” (Swedish Society of Medicine) and IBL (Swedish Institute of Biomedical Laboratory Science).

Facts about Accu-Chek Instant

This form is filled in by Roche Diagnostics Scandinavia AB

Table 1. Basic facts

Name of the measurement system:	Accu-Chek Instant Blood Glucose Monitoring System
Dimensions and weight:	Width: 48.6 mm Depth: 15.3mm Height: 77.1mm Weight: 40 grams
Components of the measurement system:	1 Accu-Chek Instant meter with batteries 1 Carry Case 1 Accu-Chek FastClix lancing device 1 Accu-Chek FastClix lancets Carry Case Instructions for Use
Measurand:	Glucose
Sample material:	Capillary whole blood
Sample volume:	0.6µL
Measuring principle:	The enzyme on the test strip, a FAD-dependent glucose dehydrogenase (GDH) expressed in A. Oryzae, converts the glucose in the blood sample to gluconolactone. This reaction creates a harmless DC electrical current that the meter interprets for the blood glucose result. The sample and environmental conditions are evaluated using AC and DC signals.
Traceability:	The ID-GCMS method as the method of highest metrological quality (order) is traceable to a primary NIST standard. Using this traceability chain, the results obtained with these test strips for control solutions can also be traced back to the NIST standard.
Calibration:	The system (meter and test strips) is calibrated with venous blood containing various glucose concentrations as a calibrator. The reference values are obtained using the hexokinase method which is calibrated using the ID-GCMS method.
Measuring range:	0.6–33.3 mmol/L
Linearity:	Each linearity test kit consists of 6 levels of linearity solutions manufactured to produce a linear relationship within the set. Record the following values as the target values on the x-axis of the linearity log. LINEARITY L1 L2 L3 L4 L5 L6 mmol/L 1.5 2.5 6.4 16.5 27.6 30.2
Measurement time:	< 4 seconds
Operating conditions:	Use the test strips at temperatures between 4 and 45 °C.
Electrical power supply:	Two 3 volt lithium batteries (coin cell type CR2032)

Recommended regular maintenance:	Gently wipe the meter's surface with a soft cloth slightly dampened (wring out any excess liquid) with one of these cleaning solutions: • 70 % isopropyl alcohol • Mild dishwashing liquid mixed with water • 10 % household bleach solution (1 part bleach plus 9 parts water) made the same day
Package contents:	1 Accu-Chek Instant meter with batteries 1 Carry Case 1 Accu-Chek FastClix lancing device 1 Accu-Chek FastClix lancets Instructions for Use
Necessary equipment not included in the package:	Accu-Chek Instant test strips and Accu-Chek Instant controls

Table 2. Post analytical traceability

Is input of patient identification possible?	Yes: the software user can manually enter patient identification information related to the data that has be transferred from the device.
Is input of operator identification possible?	Yes: the software user/operator can manually enter any information, including operator identification, as a note.
Can the instrument be connected to a bar-code reader?	No
Can the instrument be connected to a printer?	With Accu-Chek SmartPix PC software
What can be printed?	Data from the device and any other data that the user manually enters into the PC software
Can the instrument be connected to a PC?	Yes with USB cable
Can the instrument communicate with LIS (Laboratory Information System)? If yes, is the communication bidirectional?	Yes: the device can communicate to a LIS if it complies with the Continua USB standard interface. The Smart Pix PC software is bi-directional in that the software user can update the date/time and blood glucose target range settings in the device.
What is the storage capacity of the instrument and what is stored in the instrument?	720 blood glucose results and 32 control results with time and date
Is it possible to trace/search for measurement results?	The software allows the user to search for blood glucose results after the data has been transferred from the device.

Table 3. Facts about the reagent/test strips/test cassettes

Name of the reagent/test strips/test cassettes:	Accu-Chek Instant test strips
Stability in unopened sealed vial:	18 months from manufacture date
Stability in opened vial:	18 months from manufacture date
Package contents:	Pack containing test strips and package inserts

Table 4. Quality control

Electronic self check:	Yes
Recommended control materials and volume:	Accu-Chek Instant controls (2 × 2.5 mL control solutions)
Stability in unopened sealed vial:	24 months from manufacture date
Stability in opened vial:	3 months
Package contents:	Pack containing 2 × 2.5 mL control solution and package inserts

Information about manufacturer, suppliers and marketing

This form is filled in by Roche Diagnostics Scandinavia AB

Table 1. Marketing information

Manufacturer:	Roche Diabetes Care GmbH Sandhofer Strasse 116 68305 Mannheim, Germany
Suppliers in Scandinavia:	Denmark: Roche Diagnostics A/S Industriholmen 59 2650 Hvidovre-Copenhagen www.roche.dk Norway: Roche Diabetes Care Norge AS Brynsengfaret 6B PB 6610 Etterstad 0607 Oslo www.roche.no Sweden: Roche Diagnostics Scandinavia AB Karlsbodavägen 30 Box 147 SE-161 26 Bromma www.roche.se
In which countries is the system marketed:	Globally X Scandinavia ☐ Europe ☐
Date for start of marketing the system in Scandinavia:	October, 2017
Date for CE-marking:	November, 2016
In which Scandinavian languages is the manual available:	Swedish

Product specifications for this evaluation, Accu-Chek Instant

Accu-Chek Instant serial numbers
A total of 91 Accu-Chek Instant blood glucose meters were used in this evaluation.
Three meters (serial no. 95900018487 (meter A), 95900018286 (meter B) and 95900017760 (meter C)) were used by the BLSs under optimal conditions.

Accu-Chek Instant test strips

Lot 907277	Expiry date 2018-05-05
Lot 907599	Expiry date 2018-05-11
Lot 907604	Expiry date 2018-05-24

Accu-Chek Aviva Control Solutions (Control 1 and Control 2)

Lot 60100651	Expiry date 2018-03-31
Target value Control 1	1,7 – 3,3 mmol/L
Target value Control 2	14,0 – 19,0 mmol/L

Blood sampling device used by the BLSs (single use only)
Sterilised lancing equipment intended for professional use with puncture depth 1,1 – 2,3 mm, was used by the BLSs

Blood sampling device used by the diabetes patients
The diabetes patients could choose whether to use the distributed Accu-Chek FastClix lancing device with Accu-Chek FastClix lancets, or the lancet device and lancets they usually use.

Accu-Chek FastClix lancing device

Lot GRD 063	Expiry date 2020-02-28
Lot GRC 363	Expiry date 2019-08-31

Accu-Chek FastClix lancets

Lot GRD 386	Expiry date 2020-09-30
Lot GRD 406	Expiry date 2020-09-30
Lot WPE 070 B	Expiry date 2020-10-31

Tubes used for sampling for the designated comparison method
Microvette CB 300 LH (lithium-heparin) manufactured by Sarstedt AS

Lot 6071111	Expiry date 2019-04-30

Statistical expressions and calculations

This chapter with standardised text deals with the statistical expressions and calculations used by SKUP. The statistical calculations will change according to the type of evaluation. The descriptions in this document are valid for evaluations of quantitative methods with results on the ratio scale.

Statistical terms and expressions

The definitions in this section come from the International Vocabulary of Metrology - Basic and general concepts and associated terms; VIM [a].

Precision

Definition: Precision is the closeness of agreement between measured quantity values obtained by replicate measurements on the same or similar objects under stated specified conditions.

Precision is measured as *imprecision*. Precision is descriptive in general terms (good, poor e.g.), whereas the imprecision is expressed by means of the standard deviation (SD) or coefficient of variation (CV). SD is reported in the same unit as the analytical result. CV is usually reported in percent.

To be able to interpret an assessment of precision, the precision conditions must be defined.
Repeatability is the precision of consecutive measurements of the same component carried out under identical measuring conditions (within the measuring series).
Reproducibility is the precision of discontinuous measurements of the same component carried out under changing measuring conditions over time.

Trueness

Definition: Trueness is the closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value.

Trueness is inversely related to systematic measurement error. Trueness is measured as *bias*. Trueness is descriptive in general terms (good, poor e.g.), whereas the bias is reported in the same unit as the analytical result or in percent.

Accuracy

Definition: Accuracy is the closeness of agreement between a measured quantity value and the true quantity value of a measurand.

Accuracy is not a quantity and cannot be expressed numerically. Accuracy is descriptive in general terms (good, poor e.g.). A measurement is said to be more accurate when it offers a smaller measurement error. Accuracy can be illustrated in a difference plot.

a. International vocabulary of metrology – Basic and general concepts and associated terms, VIM, 3rd edition, JCGM 200;2012. www.bipm.org

Statistical calculations

Statistical outliers

The criterion promoted by Burnett [b] is used for the detection of outliers. The model takes into consideration the number of observations together with the statistical significance level for the test. The significance level is set to 5 %. The segregation of outliers is made with repeated truncations, and all results are checked. Where the results are classified according to different concentration levels, the outlier-testing is carried out at each level separately. Statistical outliers are excluded from the calculations.

Calculation of imprecision

The precision of the evaluated method is assessed by use of paired measurements of genuine patient sample material. The results are usually divided into three concentration levels, and the estimate of imprecision is calculated for each level separately, using the following formula [c,d,e]:

$$SD = \sqrt{\frac{\sum d^2}{2n}}$$

d = difference between two paired measurements (formula 1)
n = number of differences

This formula is used when the standard deviation can be assumed reasonable constant across the concentration interval. If the coefficient of variation is more constant across the concentration interval, the following formula is preferred:

$$CV = \sqrt{\frac{\sum (d/m)^2}{2n}}$$

m = mean of paired measurements (formula 2)

The two formulas are based on the differences between paired measurements. The calculated standard deviation or CV is still a measure of the imprecision of single values. The imposed condition for using the formulas is that there is no systematic difference between the 1st and the 2nd measurement of the pairs. The CV is given with a 90 % confidence interval.

Calculation of bias

The mean deviation (bias) at different concentration levels is calculated. A paired t-test is used with the mean values of the duplicate results on the comparison method and the mean values of the duplicate results on the evaluated method. The mean difference is shown with a 95 % confidence interval.

Assessment of accuracy

The agreement between the evaluated method and the comparison method is illustrated in a difference plot. The x-axis represents the mean value of the duplicate results on the comparison method. The y-axis shows the difference between the first measurement on the evaluated method and the mean value of the duplicate results on the comparison method. The number of results within the quality goal limits is counted and assessed.

b. Burnett RW. Accurate estimation of standard deviations for quantitative methods used in clinical chemistry. *Clin Chem* 1975; **21** (13): 1935 – 1938.
c. Dahlberg G. Statistical methods for medical and biological students, 1940. Chapter 12, Errors of estimation. George Allen & Unwin Ltd.
d. Saunders E. Tietz textbook of clinical chemistry and molecular diagnostics, 2006. Chapter 14, Linnet K., Boyd J. Selection and analytical evaluation of methods – with statistical techniques. Elsevier Saunders ISBN 0-7216-0189-8.
e. Fraser C.G. Biological variation: From principles to practice, 2006. Chapter 1, The Nature of Biological Variation. AACC Press ISBN 1-890883-49-2.

List of previous SKUP evaluations

The 30 latest SKUP evaluations

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2017/113	Glucose[1]	Accu-Chek Instant	Roche Diabetes Care GmbH
SKUP/2017/111	Glucose[1]	*Confidential*	
SKUP/2017/112	Glucose[1]	Accu-Chek Guide	Roche Diabetes Care GmbH
SKUP/2016/110	PT (INR)	Xprecia Stride Coagulation system	Siemens Healthcare Diagnostics INC
SKUP/2015/107	Strep A	QuickVue Dipstick Strep A Test	Quidel Corporation
SKUP/2015/109	PT (INR)	microINR portable coagulometer	iLine Microsystems S.L.
SKUP/2015/108	HbA1c	*Confidential*	
SKUP/2015/102	HbA1c	*Confidential*	
SKUP/2015/106*	Strep A	QuikRead go	Orion Diagnostica Oy
SKUP/2014/101	HbA1c	InnovaStar analyzer	DiaSys Diagnostic Systems GmbH
SKUP/2014/104	PT (INR)	ProTime InRythm	ITC International Technidyne Corporation
SKUP/2014/105	Glucose[1]	Accu-Chek Aviva	Roche Diagnostics
SKUP/2014/103	PT (INR)	*Confidential*	
SKUP/2013/87	Glucose[1]	Wella Calla Light	Med Trust Handelsges.m.b.H.
SKUP/2013/100	Glucose[1]	Mylife Unio	Bionime Corporation
SKUP/2013/97	NT-proBNP	Cobas h 232 POC system	Roche Diagnostics GmbH
SKUP/2013/92	CRP	Eurolyser smart 700/340	Eurolyser Diagnostica GmbH
SKUP/2013/99*	Glucose	Accu-Chek Mobile	Roche Diagnostics
SKUP/2013/98*	Glucose	Accu-Chek Aviva	Roche Diagnostics
SKUP/2013/85	Glucose, β-Ketone	Nova StatStrip	Nova Biomedical Corporation, USA
SKUP/2013/96	Hemoglobin	DiaSpect Hemoglobin T	DiaSpect Medical GmbH
SKUP/2013/68	Allergens	ImmunoCap Rapid	Phadia AB Marknadsbolag Sverige
SKUP/2012/95	Glucose[1]	Mendor Discreet	Mendor Oy
SKUP/2012/94	Glucose[1]	Contour XT	Bayer Healthcare
SKUP/2012/91	HbA1c	Quo-Test A1c	Quoient Diagnostics Ltd
SKUP/2011/93*	Glucose	Accu-Chek Performa	Roche Diagnostics
SKUP/2011/90	CRP	*i*-Chroma	BodiTech Med. Inc.
SKUP/2011/84*	PT (INR)	Simple Simon PT and MixxoCap	Zafena AB
SKUP/2011/86	Glucose[1]	OneTouch Verio	LifeScan, Johnson & Johnson
SKUP/2011/77	CRP	*Confidential*	

*Some evaluation codes are followed by an asterisk (*), indicating an evaluation with a more specific objective. The asterisk is explained on the front page of these protocols and reports.

[1] Including a user-evaluation among diabetes patients