Accu-Chek Aviva

Meter and test strips
designed for glucose self-measurement
and measurements by health care professionals
Manufactured by Roche Diagnostics GmbH

Report from the evaluation SKUP/2013/98*

organised by SKUP at the request of Roche Diagnostics Scandinavia AB

* This evaluation is a follow-up of a previous evaluation

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The report was written by SKUP, April - May 2013.
For more details about SKUP, see attachment 1.
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Attachment 6 and 8 are included only in the copy to Roche Diagnostics Scandinavia AB.

1. Summary

Background for the evaluation
Accu-Chek Aviva is a blood glucose monitoring system designed for blood testing performed by health care professionals as well as by persons with diabetes. The system is produced by Roche Diagnostics GmbH and is already launched in Scandinavia. The Accu-Chek Aviva system was evaluated by SKUP in 2005. Later Roche has modified the test strip chemistry to prevent maltose interference. Roche Scandinavia ordered this new evaluation to get documentation required in the Swedish tender system. Because of the earlier evaluation, there was no need to involve the end-users or to evaluate the user-friendliness in the present SKUP evaluation.

The aim of the evaluation
The aim of the evaluation of Accu-Chek Aviva was to
- assess the analytical quality under standardised and optimal conditions, achieved by a biomedical laboratory scientist in an outpatient clinic and in two hospital wards
- examine the variation between three lots of test strips

Materials and methods
Capillary samples from 81 persons with diabetes and 9 persons without diabetes were collected. The sampling was carried out at Haraldsplass Diaconal Hospital. For each person two measurements on Accu-Chek Aviva were carried out, and a capillary sample was directly prepared for measurement with a selected comparison method. Three test strip lots were used.

Results
- For glucose level <7 mmol/L the repeatability CV was 2,8%, and the recommended quality goal (CV ≤5%) was fulfilled. For glucose level 7—10 mmol/L and glucose level >10 mmol/L the repeatability CV was 4,2% and 4,5%, respectively. The upper CI value is >5%, and the two data sets are inconclusive on fulfilling the quality goal. Most likely the quality goal is fulfilled.
- The glucose measurements on Accu-Chek Aviva showed systematic lower glucose results than the comparison method. The bias was between −0,2 and −0,7 mmol/L. The deviation was small, but statistically significant. All results except one were within the accuracy quality limits. The quality goal for accuracy specified in ISO 15197:2003 was fulfilled.
- The three lots of Accu-Chek Aviva test strips showed results in agreement.
- The percentage of technical errors was 1,4%.

Conclusion
The repeatability CV was between 2,8 and 4,5%. The recommended quality goal (CV≤5%) was fulfilled for glucose level <7 mmol/L. For glucose level >7 mmol/L the quality goal is most likely fulfilled. The glucose measurements on Accu-Chek Aviva showed systematic lower glucose results than the comparison method. The deviation was between −0,2 and −0,7 mmol/L. The results fulfilled the quality goal for accuracy specified in ISO 15197:2003. The three lots of Accu-Chek Aviva test strips showed agreeing results. The percentage of technical errors fulfilled the goal (≤2%).

Comments from Roche
Roche gratefully accepted the report and had no additional comments.

2. Abbreviations

ADA	American Diabetes Association
BLS	Biomedical Laboratory Scientist
CI	Confidence Interval
C-NPU	Committee on Nomenclature, Properties and Units
CV	Coefficient of Variation
DAK-E	Danish Quality Unit of General Practice
EQA	External Quality Assessment
Equalis	External quality assurance in laboratory medicine in Sweden
GDH	Glucose Dehydrogenase
HDH	Haraldsplass Diaconal Hospital
HELFO	the Norwegian Health Economics Administration
IFCC	the International Federation of Clinical Chemistry and Laboratory Medicine
ISO	International Organization for Standardization
IUPAC	the International Union of Pure and Applied Chemistry
NIST	National Institute of Standards & Technology
Noklus	Norwegian Quality Improvement of Primary Care Laboratories
SKUP	Scandinavian evaluation of laboratory equipment for primary health care
SRM	Standard Reference Material

3. Quality goals

3.1 Analytical quality

There are different criteria for setting quality specifications for analytical methods. Ideally the quality goals should be set according to the medical demands the method has to meet. For glucose it is natural that the quality specification is set according to whether the analysis is used for diagnostic purpose or for monitoring diabetes. Accu-Chek Aviva is designed for monitoring blood glucose. The quality goals are set according to this.

Precision
According to the American Diabetes Association (ADA) the imprecision (CV) of new glucose devices must be less than 5% [1]. Other authors also recommend an imprecision of 5% or less [2-4].

Accuracy
The International Organization for Standardization (ISO)-standard 15197:2003 [5] is an international protocol for evaluating meters designed for glucose monitoring, and gives the following minimum acceptable accuracy requirement:
Ninety-five percent (95%) of the individual glucose results shall fall within ±0,83 mmol/L of the results of the comparison method at glucose concentrations <4,2 mmol/L and within ±20% at glucose concentrations ≥4,2 mmol/L.

Quality goals in Denmark
Analytical quality goals for point of care glucose measurement systems: CV <4% and bias <±3% [3,4].

Other analytical quality limits
The number of results within fixed limits of ±15% and ±10% will be reported, but not further assessed in this report.

Variation between lots
The agreement between three lots of test strips will be assessed. No specific quality goal for lot variation is set.

Technical errors
SKUP recommends that the percentage of "tests wasted" caused by technical errors should not exceed 2%. The evaluating person registers the number of error codes and technical errors during the evaluation.

3.2 Principles for the assessments

3.2.1 Assessment of the analytical quality

The analytical results are assessed according to the quality goals set for the evaluation.

Precision

The decision whether the achieved coefficient of variation (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**
The CV is lower than the quality goal	The quality goal is fulfilled
The CV is lower than the quality goal (not statistically significant)	Data is inconclusive on fulfilling the quality goal. Most likely the quality goal is fulfilled
The CV is higher than the quality goal (not statistically significant)	Data is inconclusive on fulfilling the quality goal. Most likely the quality goal is not fulfilled
The CV is higher than the quality goal	The quality goal is not fulfilled

Accuracy

The accuracy is illustrated in a difference-plot with limits for the allowable deviation according to the quality goal. The percentage of results within the limits is calculated.
The accuracy is judged as either fulfilling the quality goal or not fulfilling the quality goal.

3.3 SKUP´s quality goals in this evaluation

The results from the evaluation of Accu-Chek Aviva were assessed against the following quality goals as agreed in the protocol:

Repeatability CV …… ≤5%
Allowable deviation in the individual result from the comparison method result (according to ISO 15197:2003)
for glucose concentration <4,2 mmol/L ……≤0,83 mmol/L
for glucose concentration ≥4,2 mmol/L …… ≤±20%
Required percentage of individual results within the allowable deviation …… ≥95%
Percentage of technical errors …… ≤2%

4. Materials and methods

4.1 Definition of the measurand

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and International Union of Pure and Applied Chemistry (IUPAC) work in a joint Committee on Nomenclature, Properties and Units (C-NPU). The descriptions of clinical laboratory tests are listed in the ”NPU database” [6]. In the database the full name is given for the measurand together with which unit the result should be reported in. In this report the term “glucose” will be used for the measurand. Glucose concentrations will be given in mmol/L.

4.2 The evaluated measurement system, Accu-Chek Aviva

Accu-Chek Aviva is a blood glucose monitoring system based on electrochemical technology. The system consists of the Accu-Chek Aviva meter (figure 1) and dry reagent test strips. The system is designed for blood glucose testing performed by persons with diabetes or by health care professionals. Fresh, whole blood (capillary, venous, arterial or neonatal blood) is required to perform a blood glucose test. Accu-Chek Aviva reports plasma glucose values. The system is calibrated with a black snap-in code chip already placed in the device. The black code chip works for all Accu-Chek Aviva test strips and shall be left in place even when the user receives code chips with other colours and numbers in new packages of test strips. The test strips are packed in a plastic bottle with flip-top closure and desiccant. The system requires a blood volume of 0,6 µL. The blood is automatically drawn into the test strip. The result is shown in 5 seconds. According to the manufacturer, it is possible to use blood samples from alternative sites as the forearm, upper arm, thigh or lower leg on Accu-Chek Aviva. The meter has the capacity of storing 500 test results in the memory.

Figure 1. Accu-Chek Aviva meter

Test principle of Accu-Chek Aviva (according to Roche)
Glucose dehydrogenase converts glucose to gluconolactone. The enzyme in the reaction is a modified glucose dehydrogenase enzyme (Mut. Q-GDH). The enzyme is modified to prevent maltose interference.

$$\text{Glucose} + \text{Mediator}_{\text{Oxidized}} \xrightarrow{\text{Mut. Q-GDH}} \text{Gluconolactone} + \text{Mediator}_{\text{Reduced}}$$

A summary of technical data for Accu-Chek Aviva is shown in table 2. For more details, see attachment 2. For name of the manufacturer and suppliers in the Scandinavian countries, see attachment 3. For product information, see attachment 4.

Table 2. Technical data from the manufacturer

Technical data for Accu-Chek Aviva	
Sample material	Fresh whole blood (capillary, venous, arterial or neonatal whole blood)
Sample volume	0,6 µL
Measuring time	5 seconds
Measuring range	0,6 – 33,3 mmol/L
Tolerated haematocrit range	10 – 65%
Memory capacity	500 results
Electrical power supply	One 3-volt lithium battery

4.3 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 a field method.

4.3.1 The selected comparison method in this evaluation

The selected comparison method in this evaluation is the routine method for quantitative determination of glucose in human serum and plasma in the laboratory at Haraldsplass Diaconal Hospital (HDH) in Bergen. The method is a photometric glucose hexokinase method. The method is implemented on Cobas 6000 System from Roche Diagnostics. The laboratory can document good analytical quality of the method through participation in an external analytical quality assessment program.

4.3.2 Verification of the analytical quality of the comparison method

Precision

The repeatability of the comparison method was estimated from duplicate measurements of capillary patient samples.

Trueness

To document the trueness of the comparison method, the standard reference material (SRM 965b) from National Institute of Standards & Technology, NIST, was used [7]. The SRM 965b consists of ampoules with human serum with certified concentrations of glucose at four levels, with given uncertainties.

Internal quality control

Autonorm Human Liquid Control Solutions at two levels from SERO AS were included in the measuring series in this evaluation.

External quality control

Human serum controls, produced by Norwegian Quality Improvement of Primary Care Laboratories (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 [8]. The controls are used in Noklus's External Quality Assessment (EQA) program.

4.4 The evaluation

4.4.1 Planning of the evaluation

Background for the evaluation
Accu-Chek Aviva is a blood glucose monitoring system designed for blood testing performed by health care professionals as well as by persons with diabetes. The Accu-Chek Aviva system is produced by Roche Diagnostics GmbH and supplied in Scandinavia by Roche Diagnostics Scandinavia. Accu-Chek Aviva is already launched in Scandinavia. The Accu-Chek Aviva system was evaluated by SKUP in a user-evaluation in 2005 (SKUP/2005/44) [9]. Later Roche has modified the test strip chemistry to prevent maltose interference. This change does not affect the handling of the instrument, thus there was no need to involve the end-users or to evaluate the user-friendliness in the present SKUP evaluation. Roche Diagnostics Scandinavia ordered this new evaluation to get objective documentation of the optimal analytical quality of the test strip in combination with the Accu-Chek Aviva meter, as part of documentation required in the Swedish tender system.

Inquiry about an evaluation
Malin Lundgren, Roche Diagnostics Scandinavia, applied to SKUP in April 2012 for an evaluation of Accu-Chek Aviva glucose meter with Accu-Chek Aviva test strips.

Protocol, contract and agreement
The protocol for the evaluation was approved in January 2013. Roche Diagnostics Scandinavia and SKUP signed a contract about the evaluation in January 2013. The laboratory at HDH agreed to analyse the samples for the comparison method.

Preparations, training program and practical work
SKUP started the preparations for the evaluation in December 2012. Marianne Risa, biomedical laboratory scientist (BLS), was familiar with the Accu-Chek system, and further training from Roche was not necessary. The meters and test strips for the evaluation were received in January and February 2013. The practical work with the evaluation was carried out during six weeks in the period February - April 2013.

4.4.2 Evaluation sites and persons involved

Persons responsible for the evaluation are shown in table 3.

Table 3. Persons responsible for various parts of the evaluation

Name	Title	Place	Responsibility
Malin Lundgren	Jr Product Manager	Roche Diagnostics Scandinavia	Ordered the evaluation/ Contact person
Grete Monsen	Organisation Secretary	SKUP/Noklus	Responsible for the evaluation
Marianne Risa	BLS	SKUP/Noklus	Preparations for the evaluation Practical work with the evaluation Statistical calculations Author of the report
Grethe Kalleklev and Henriette Mohn Soldal	BLS	Laboratory at HDH	Practical work with the comparison method

4.4.3 The evaluation model

The SKUP evaluation
SKUP evaluations are based upon the fundamental guidelines in the book "*Utprøving av analyseinstrumenter*" [10]. SKUP's model for glucose user-evaluation is based on a standard model used by The Norwegian Health Economics Administration (HELFO) for test strip reimbursement in Norway [11].

The evaluation of Accu-Chek Aviva
The evaluation of Accu-Chek Aviva comprises the following studies:

- An examination of the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in an outpatient clinic and in two hospital wards
    - Precision
    - Accuracy according to the quality goal given in ISO 15197:2003
- An examination of the variation between three lots of test strips

4.4.4 Evaluation procedure

Internal analytical quality control
The Accu-Chek Aviva meter was checked by means of the manufacturer's control solutions every day it was used.

Blood sampling
Capillary samples from 81 persons with diabetes and 9 persons without diabetes were collected. The sampling of the persons with diabetes was carried out in an outpatient clinic and in two hospital wards at HDH. Two measurements on Accu-Chek Aviva were carried out for all the 90 persons, and a capillary sample was directly prepared for the comparison method. The two blood samples for the measurements on Accu-Chek Aviva were collected from the same finger prick. The first drop of blood was wiped off before the first measurement. Blood was also wiped off between the measurements. If necessary a new finger prick was made for the sample for the comparison method. Three different lots of test strips were used.

Handling of the samples for the comparison method
The samples for the comparison method were taken from a finger capillary using Microvette Li-heparin tubes (300 µL) from Sarstedt. The samples were centrifuged immediately for three minutes at 10 000 g, and plasma was separated into suitable sample vials. The plasma samples were frozen directly and stored at minus 80°C at Noklus until the analysis took place (according to the storing procedure for the standard reference material from NIST [7]).
The samples were analysed during three days in April 2013.

Recording of results
All results were registered in a form provided by SKUP and signed by the evaluator. If the meter showed an error code while analysing a sample, a new measurement was made. Error codes were recorded.

5. Results and discussions

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

5.1 Number of samples

Capillary samples from 90 individuals were included in the evaluation.
The total number of samples was:
90 capillary samples x 2 (duplicate measurements on Accu-Chek Aviva)
90 capillary samples x 1 (for the comparison method), analysed in duplicate

5.1.1 Excluded results

The following result is excluded:

- ID 33 was excluded as an outlier according to Burnett's model [12] in the calculation of repeatability on Accu-Chek Aviva and was removed before calculation of trueness and lot variation

5.1.2 Failed measurements

A total of 214 measurements (180 patient samples and 34 control measurements) were performed on Accu-Chek Aviva. Three of these measurements failed; error code E-4.
Percentage of technical errors was: (3/214) x 100 = 1,4%

Comments
Error code description from the owner's booklet:
E-4 Not enough blood or control solution was drawn into the test strip for measurement or was applied after the test had started.

Discussion
The percentage of technical errors was 1,4% and the goal (≤2%) was fulfilled.

5.2 Analytical quality of the selected comparison method

5.2.1 Internal quality control

In the daily operation of the comparison method, the analytical quality of the method is monitored with internal quality control solutions at two levels of glucose concentrations. All control results from the evaluation period (three days) were inside the limits of the target values for the controls. The results are not shown.

5.2.2 The precision of the comparison method

Repeatability

The samples for the comparison method were analysed in duplicate, and the imprecision was calculated by means of these duplicate results. The formula used for the calculation of repeatability (formula 1) is shown in attachment 5. The results have been checked to meet the imposed condition for using the formula (data not shown). The repeatability of the comparison method with 90% confidence interval (CI) is shown in table 4. The raw data is shown in attachment 6 (only available for the producer).

Table 4. Repeatability of the comparison method with capillary blood samples in the hospital laboratory

Glucose interval, mmol/L	n	Excluded results	Mean value glucose, mmol/L	CV (90% CI), %
<7	23	0	5,70	0,8 (0,7 — 1,1)
7 – 10	26	0	8,67	1,4 (1,2 — 1,8)
>10	41	0	14,49	1,2 (1,0 — 1,5)

Discussion

The precision of the comparison method was good. The repeatability CV was approximately 1%.

5.2.3 The trueness of the comparison method

In order to demonstrate the trueness of the comparison method, the SRM 965b standards purchased from NIST, were analysed. The agreement between the comparison method and the NIST-standards is shown in table 5.

Table 5. Standard Reference Material (SRM 965b) measured on the comparison method

SRM 965b	Date	Certified glucose concentration mmol/L (uncertainty)	n	Mean value glucose, mmol/L	Deviation from target value, %
Level 1	09.04.13	**1,836** (1,809 — 1,863)	5	1,83	−0,1
	11.04.13		5	1,85	0,8
	Total		**10**	**1,84**	**0,3**
Level 2	09.04.13	**4,194** (4,135 — 4,253)	5	4,24	1,0
	11.04.13		5	4,18	−0,4
	Total		**10**	**4,21**	**0,3**
Level 3	09.04.13	**6,575** (6,481 — 6,669)	5	6,55	−0,4
	11.04.13		5	6,55	−0,3
	Total		**10**	**6,55**	**−0,4**
Level 4	09.04.13	**16,35** (16,15 — 16,55)	5	16,34	0,0
	11.04.13		5	16,20	−0,9
	Total		**10**	**16,27**	**−0,5**

To verify the trueness of the 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 6.

Table 6. Trueness of the comparison method

Control	Date	Target value glucose, mmol/L	n	Mean value glucose, mmol/L	Deviation from target value, %
Noklus 1	09.04.13	5,71	5	5,70	−0,2
	11.04.13		5	5,75	0,7
	Total		**10**	**5,73**	**0,3**
Noklus 2	09.04.13	11,94	5	11,97	0,2
	11.04.13		5	12,01	0,6
	Total		**10**	**11,99**	**0,4**

Discussion

The trueness of the comparison method was good.

5.3 Analytical quality of Accu-Chek Aviva

5.3.1 Internal quality control

The Accu-Chek Aviva meter was checked with the manufacturer's control solutions every day the meter was in use. The reproducibility CV was 2,4% and 2,2% for control 1 and control 2, respectively (n=17). All results were within the control range printed on the test strip boxes. Raw data is shown in attachment 7.

5.3.2 Comparison of the 1st and 2nd measurements

Two capillary samples were collected of each person for measurements on Accu-Chek Aviva. For the calculation of imprecision, the results have been checked to meet the imposed condition for using formula 1 in attachment 5. No systematic difference was pointed out between the paired measurements on Accu-Chek Aviva (data not shown).

5.3.3 The precision of Accu-Chek Aviva

Repeatability under standardised and optimal measuring conditions
The repeatability obtained with capillary blood samples is shown in table 7. The results are sorted and divided into three glucose levels according to the first measurement on Accu-Chek Aviva. Raw data is shown in attachment 8.

Table 7. Repeatability, Accu-Chek Aviva. Results achieved with capillary blood samples

Glucose interval, mmol/L	n	Excluded results	Mean value glucose, mmol/L	CV(90% CI) %
<7	23	0	5,5	2,8 (2,2 — 3,8)
7 – 10	30	0	8,6	4,2 (3,5 — 5,3)
>10	37	1*	14,0	4,5 (3,8 — 5,7)

The given numbers of results (n) are counted before the exclusion of outliers. Mean and CV are calculated after the exclusion of outliers.
* One statistical outlier (ID 33) according to Burnett's model

Discussion, repeatability
For glucose level <7 mmol/L the repeatability CV was 2,8%, and the recommended quality goal was fulfilled. For glucose levels 7—10 mmol/L and >10 mmol/L the repeatability CV was 4,2% and 4,5%, respectively. The upper CI values are >5%. Therefore the data is inconclusive on fulfilling the quality goal of ≤5%, but most likely the quality goal is fulfilled.

5.3.4 The trueness of Accu-Chek Aviva

The mean deviation of Accu-Chek Aviva results from the comparison method results (bias) was calculated from the results achieved by the BLS. The measurements on Accu-Chek Aviva were performed with three lots of test strips. The results are sorted and divided into three glucose levels according to the mean results on the comparison method. The trueness of Accu-Chek Aviva is shown in table 8.

Table 8. Trueness of Accu-Chek Aviva

Glucose level Comparison method, mmol/L	**n**	**Excluded results**	**Comparison method mean glucose, mmol/L**	**Accu-Chek Aviva mean glucose, mmol/L**	**Bias (95% CI), mmol/L**
<7	23	0	5,7	5,5	−0,15 ((−0,23) — (−0,07))
7 — 10	26	0	8,7	8,3	−0,33 ((−0,48) — (−0,18))
>10	40	0	14,3	13,6	−0,68 ((−0,92) — (−0,44))

Discussion

The glucose measurements on Accu-Chek Aviva showed systematic lower glucose results than the comparison method. The bias from the comparison method was between −0,2 and −0,7 mmol/L. The bias was small, but statistically significant.

5.3.5 The accuracy of Accu-Chek Aviva

To evaluate the accuracy of the results on Accu-Chek Aviva, the agreement between Accu-Chek Aviva and the comparison method is illustrated in an accuracy plot. The plot shows the deviation of single measurement results on Accu-Chek Aviva from the true value, and gives a picture of both random and systematic errors, reflecting the total measuring error on Accu-Chek Aviva. The accuracy is demonstrated for the first measurements of the duplicate results, only. Three different lots of test strips were used. The accuracy of Accu-Chek Aviva, with three lots of test strips, is shown in figure 2. The accuracy is summarised in table 9.

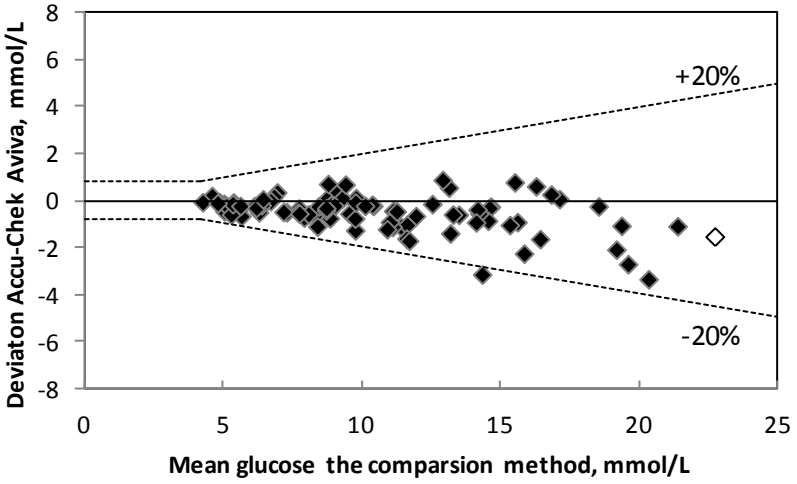

Figure 2. Accuracy. Accu-Chek Aviva with three test strip lots under standardised and optimal measuring conditions. The x-axis represents the mean value of the duplicate results on the comparison method. The y-axis shows the difference between the first measurement on Accu-Chek Aviva and the mean value of the duplicate results on the comparison method. Stippled lines represent quality goal limits set in ISO 15197:2003 (within ±0,83 mmol/L for glucose concentrations <4,2 mmol/L and within ±20% for glucose concentrations ≥4,2 mmol/L). ID 33, a statistical outlier in the calculation of repeatability on Accu-Chek Aviva, is shown with an open symbol. Number of results (n) = 90.

Table 9. Accuracy of Accu-Chek Aviva, n= 90

Percentage of results within given limits, %		
ISO 15197:2003	**Fixed limit**	
≤±0,83 mmol/L at conc. <4,2 mmol/L or ≤±20% at conc. ≥4,2 mmol/L	**±15%**	**±10%**
99	98	86

Discussion

Figure 2 shows that Accu-Chek Aviva glucose results were slightly lower than the results from the comparison method. All results except one were inside the accuracy quality limits. The quality goal in ISO 15197:2003 was fulfilled. Table 9 shows that 99% of the results were inside the accuracy quality limits specified in ISO 15197:2003. The number of results within limits of ±15% and ±10% were 98% and 86%, respectively. These results are for information only, and will not be further assessed.

5.3.6 Variation between three lots of test strips

The measurements on Accu-Chek Aviva were performed with three lots of test strips from different productions. The mean deviation from the comparison method with 95% confidence interval for each of the three lots was calculated as an indirect measure of the lot variation. To get a sufficient number of results in each group, the deviation was calculated for the entire glucose concentration range. The deviation with three lots of test strips is shown in table 10.

Table 10. Lotdeviation

Accu-Chek Aviva, lot number of test strips	**n**	**Excluded results**	**Comparison method mean, mmol/L**	**Accu-Chek Aviva mean, mmol/L**	**Deviation (95% CI), mmol/L**
491485	30	1*	9,8	9,3	−0,47 ((−0,64) — (−0,29))
491502	29	0	10,0	9,6	−0,42 ((−0,61) — (−0,22))
491517	30	0	11,1	10,8	−0,36 ((−0,60) — (−0,12))

The given numbers of results (n) are counted before the exclusion of outliers. Mean and deviation are calculated after the exclusion of outliers.
* One statistical outlier (ID 60) according to Burnett's model

Discussion

The three lots of Accu-Chek Aviva test strips showed agreeing results. All three lots showed slightly lower results than the comparison method. The deviation was small, but statistically significant. The results still fulfil the quality goal in ISO 15197:2003.

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11. www.helfo.no (menu Helsepersonell – Leverandører).
12. Burnett RW. Accurate Estimation of Standard Deviations for Quantitative Methods Used in Clinical Chemistry. *Clinical Chemistry* 1975; **21** (13): 1935 – 1938.

Attachments

1. The organisation of SKUP
2. Facts about Accu-Chek Aviva
3. Information about manufacturer, retailers and marketing
4. Product information, Accu-Chek Aviva
5. Statistical expressions and calculations
6. Raw data glucose, results from the comparison method
7. Raw data glucose, internal quality control, Accu-Chek Aviva
8. Raw data glucose, Accu-Chek Aviva results under standardised and optimal conditions
9. "SKUP-info". Summary for primary health care (in Norwegian)
10. List of previous SKUP evaluations

Attachment 6 and 8 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, DAK-E[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 on 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. A *complete evaluation* requires one part performed by experienced laboratory personnel as well as one part performed by the intended users.

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 and a serial number. A report code, followed by an asterisk (*), indicates a special evaluation, not complete according to the guidelines, e.g. the part performed by the intended users was not included in the protocol. If suppliers use the SKUP name in marketing, they have to refer to www.skup.nu and to the report code in question. For this purpose the company can use a logotype available from SKUP containing the report code.

SKUP reports are published at www.skup.nu.

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[1] Noklus (Norwegian Quality Improvement of Primary Care Laboratories) is an organisation founded by Kvalitetsforbedringsfond III (Quality Improvement Fund III), which is established by The Norwegian Medical Association and the Norwegian Government. Noklus is professionally linked to “Seksjon for Allmennmedisin” (Section for General Practice) at the University of Bergen, Norway.

[2] SKUP in Denmark is placed in Hillerød Hospital. SKUP in Denmark reports to DAK-E (Danish Quality Unit of General Practice), an organisation that is supported by KIF (Foundation for Quality and Informatics) and Faglig udvalg (Professional Committee), which both are supported by DR (The Danish Regions) and PLO (The Organisation of General Practitioners in Denmark).

[3] Equalis AB (External quality assurance 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 Aviva

Parts of this form are filled in by Roche Diagnostics Scandinavia AB.

Table 1. Basic facts

Name of the measurement system:	Accu-Chek Aviva
Dimensions and weight:	Width: 53 mm Depth: 21mm Height: 94 mm Weight: 60 grams
Components of the measurement system:	Blood glucose meter, Accu-Chek Multiclix Lancing device, Accu-Chek Aviva test strips
Measurand:	Glucose
Sample material:	Fresh whole blood (capillary, venous, arterial or neonatal whole blood)
Sample volume:	0,6 µL
Measuring principle:	Electrochemical
Traceability:	Traceable to NIST standard
Calibration:	Calibrated using venous blood with various glucose concentrations. The reference values are obtained using a validated test method. This test method is referenced to the hexokinase method and is traceable to a NIST standard.
Measuring range:	0,6 mmol/L to 33,3 mmol/L
Linearity:	0,6 mmol/L to 33,3 mmol/L
Measurement duration:	5 sec
Operating conditions:	8°C–44°C (43°F–111°F)
Electrical power supply:	3 volt Lithium batteries (type CR2032)
Recommended regular maintenance:	Weekly cleaning with soapy water or methanol
Package contents:	Meter, lancing device, 10 test strips, manual, quick reference guide
Necessary equipment not included in the package:	None

Table 2. Post analytical traceability

Is input of patient identification possible?	No
Is input of operator identification possible?	No
Can the instrument be connected to a bar-code reader?	No
Can the instrument be connected to a printer?	Yes
What can be printed?	All stored patient data and control values
Can the instrument be connected to a PC?	Yes
Can the instrument communicate with LIS (Laboratory Information System)? If yes, is the communication bidirectional?	No
What is the storage capacity of the instrument and what is stored in the instrument?	500 Test results and 20 control values
Is it possible to trace/search for measurement results?	Yes

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

Name of the reagent/test strips/test cassettes:	Accu-Chek Aviva test strips
Stability in unopened sealed vial:	18 months
Stability in opened vial:	18 months
Package contents:	50 test strips, strip insert

Table 4. Quality control

Electronic self check:	Yes
Recommended control materials and volume:	Aviva controls (2 levels per package) 2,5 ml per vial
Stability in unopened sealed vial:	24 month from date of manufacture
Stability in opened vial:	3 months
Package contents:	2 levels per package: 2,5 ml per vial

Information about manufacturer, retailers and marketing

Table 1. Marketing information

Manufacturer:	Roche Diagnostics
Retailers in Scandinavia:	Denmark: **Roche a/s, Diagnostics** Industriholmen 59, 2650 Hvidovre Phone: +45 36 39 99 54 www.accu-chek.dk Norway: **Roche Diagnostics Norge AS** Brynsengfaret 6B, PB 6610 Etterstad N-0607 Oslo, Norway Phone: +47 23 37 33 00 www.accu-chek.no Sweden: **Roche Diagnostics Sweden** Box 147, 161 26 Bromma, Sweden Phone: +46 8 40488 00 www.accu-chek.se
In which countries is the system marketed:	Globally X Scandinavia ☐ Europe ☐
Date for start of marketing the system in Scandinavia:	Already on the market since 2012
Date for CE-marking:	June 2010
In which Scandinavian languages is the manual available:	All

Product information, Accu-Chek Aviva
SKUP/2013/98*

Accu-Chek Aviva serial number
One Accu-Chek Aviva blood glucose meter (serial no. 53740335734) was used in this evaluation.

Accu-Chek Aviva test strips

Lot 491485	Expiry 2014-03-31
Lot 491502	Expiry 2014-04-30
Lot 491517	Expiry 2014-04-30

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

Lot 20100628	Expiry 2014-07
Target value Control 1:	1,7 – 3,3 mmol/L
Target value Control 2:	14,1 – 19,1 mmol/L

Blood sampling device (single use only)

Accu-Chek Softclix Pro	
Accu-Chek Softclix Pro Lancets	Lot WIT 44 H 2

Statistical expressions and calculations

This chapter with standardised text deals with the statistical expressions and calculations used by SKUP. The chapter is a short extract of the comprehensive SKUP-document "Statistics in SKUP reports", presented at www.skup.nu, under the option "The SKUP evaluation". The statistical calculations will change according to the type of evaluation. The descriptions in section 4.2 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 ISO/IEC Guide 99; International Vocabulary of Metrology, 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. A measurement is said to be more accurate when it offers a smaller measurement error. Accuracy can be illustrated in a difference-plot. Accuracy is descriptive in general terms (good, poor e.g.).

a. ISO/IEC Guide 99:2007, International vocabulary of metrology – Basic and general concepts and associated terms, VIM, 3rd edition, JCGM 200:2008

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

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

d = difference between two paired measurements
n = number of differences

(formula 1)

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 based on results achieved under optimal measuring conditions. 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 field method. The mean difference is shown with a 95% confidence interval.

Assessment of accuracy

The agreement between the field 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 field 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*". Clinical Chemistry 1975; **21** (13): 1935 – 1938
c. 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*", ISBN 0-7216-0189-8
d. Fraser, C.G, Biological variation: *From principles to practice*. 2006. Chapter 1 "*The Nature of Biological Variation*". AACC Press. ISBN 1-890883-49-2

Raw data glucose, internal quality control, Accu-Chek Aviva

Accu-Chek Aviva Control	Lot-no	Expiry	Glucose level mmol/L
Control 1	20100628	2014-07	1,7 - 3,3
Control 2			14,1 - 19,1

Accu-Chek Aviva Control Solution,
analysed on the biomedical laboratory scientist's meter

Date	Control 1 glucose, mmol/L	Control 2 glucose, mmol/L
2013.02.20	2,4	17,6
2013.02.21	2,6	16,4
2013.02.22	2,5	16,7
2013.02.28	2,6	17,1
2013.03.01	2,6	16,8
2013.03.06	2,6	17,3
2013.03.07	2,6	16,8
2013.03.12	2,5	16,9
2013.03.13	2,5	17,4
2013.03.14	2,5	16,9
2013.03.19	2,5	16,5
2013.03.20	2,5	16,8
2013.03.21	2,5	16,9
2013.04.02	2,6	17,2
2013.04.02	2,5	16,4
2013.04.02	2,5	16,7
2013.04.03	2,6	17,5

SKUP-info

Accu-Chek Aviva blodsukkerapparat fra Roche Diagnostics
Sammendrag fra en tilleggsutprøving i regi av SKUP

Konklusjon
For glukoseresultater <7 mmol/L var presisjonen på Accu-Chek Aviva god med en CV på 2,8 %. For glukoseresultater >7 mmol/L var presisjonen akseptabel med en CV mellom 4,2 og 4,5 %. Accu-Chek Aviva viste systematisk lavere glukoseresultater enn sammenligningsmetoden. Avviket var mellom − 0,2 og − 0,7 mmol/L. Internasjonale kvalitetsmål fra ISO 15197:2003, med et avvik mindre enn ± 20 % fra en anerkjent glukosemetode, ble oppnådd.

Accu-Chek Aviva er beregnet til måling av blodsukker. Systemet er produsert av Roche Diagnostics GmbH, og består av Accu-Chek Aviva blodsukkerapparat og Accu-Chek Aviva teststrimmel. Apparatet skal ikke kodes av brukeren. Apparatet leveres med en forhåndsinnsatt svart aktiveringsbrikke. Brikken skal ikke skiftes selv om man bruker teststrimler fra pakninger som inneholder en annen aktiveringsbrikke. Apparatet slås automatisk på når man setter inn en teststrimmel. Det kreves 0,6 µL blod til hver måling. Målingen tar 5 sekunder. Accu-Chek Aviva kan lagre 500 resultat.

Utprøvingen
Accu-Chek Aviva ble prøvd ut av SKUP i 2005 (SKUP/2005/44). Senere har Roche modifisert teststrimmelens kjemi for å hindre maltoseinterferens. Tilleggsutprøvingen av Accu-Chek Aviva ble utført under optimale betingelser av laboratorieutdannet personale. Glukoseresultatene fra Accu-Chek Aviva ble sammenlignet med resultatene fra en anerkjent sykehusmetode. Det ble tatt prøver av 81 personer med diabetes og av 9 personer uten diabetes.

Resultater
For glukoseresultater <7 mmol/L var presisjonen på Accu-Chek Aviva god med en CV på 2,8 %. For glukoseresultater >7 mmol/L var presisjonen akseptabel med en CV mellom 4,2 og 4,5 %. Accu-Chek Aviva viste systematisk lavere glukoseresultater enn sammenligningsmetoden. Avviket var mellom − 0,2 og − 0,7 mmol/L. Kvalitetsmålet fra ISO 15197:2003, som tillater avvik opp til ± 20 % fra en anerkjent metode for måling av glukose, ble oppnådd.

Tilleggsinformasjon
En fullstendig rapport fra utprøvingen av Accu-Chek Aviva, SKUP/2013/98*, finnes på SKUPs nettside, www.skup.nu. Opplysninger om pris fås ved å kontakte leverandør. Laboratoriekonsulentene i Noklus kan gi nyttige råd om analysering av glukose på legekontor. De kan også orientere om det som finnes av alternative metoder/utstyr.

List of previous SKUP evaluations

Summaries and complete reports from the evaluations are found at www.skup.nu. In addition, SKUP reports are published at www.skup.dk, where they are rated according to the national Danish quality demands for near patient instruments used in primary health care. SKUP summaries are translated into Italian by Centre for Metrological Traceability in Laboratory Medicine (CIRME), and published at http://users.unimi.it/cirme. SKUP as an organisation has no responsibility for publications of SKUP results on these two web-sites.

Recent SKUP evaluations

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2013/98*	Glucose	Accu-Chek Aviva	Roche Diagnostics
SKUP/2013/96	Haemoglobin	DiaSpect Hemoglobin T	DiaSpect Medical GmbH
SKUP/2012/95	Glucose[1]	Mendor Discreet	Mendor Oy
SKUP/2012/94	Glucose[1]	Contour XT	Bayer HealthCare
SKUP/2011/93*	Glucose	Accu-Chek Performa	Roche Diagnostics
SKUP/2012/91	HbA1c	Quo-Test A1c	Quoient Diagnostics Ltd
SKUP/2011/90	CRP	*i*-Chroma	BodiTech Med. Inc.
SKUP/2010/89*	Glucose	FreeStyle Lite	Abbott Laboratories
SKUP/2010/88*	HbA1c	*Confidential*	
SKUP/2011/86	Glucose[1]	OneTouch Verio	LifeScan, Johnson & Johnson
SKUP/2013/85	Glucose	StatStrip	Nova Biomedical
SKUP/2011/84*	PT-INR	Simple Simon PT and MixxoCap	Zafena AB
SKUP/2010/83*	Glucose	*Confidential*	
SKUP/2010/82*	Glucose, protein, blood, leukocytes, nitrite	Medi-Test URYXXON Stick 10 urine test strip and URYXXON Relax urine analyser	Macherey-Nagel GmBH & Co. KG
SKUP/2010/81*	Glucose	mylife PURA	Bionime Corporation
SKUP/2010/80	PT (INR)	INRatio2	Alere Inc.
SKUP/2010/79*	Glucose, protein, blood, leukocytes, nitrite	CombiScreen 5SYS Plus urine test strip and CombiScan 100 urine analyser	Analyticon Biotechnologies AG
SKUP/2010/78	HbA1c	In2it	Bio-Rad
SKUP/2011/77	CRP	*Confidential*	
SKUP/2009/76*	HbA1c	*Confidential*	
SKUP/2009/75	Glucose	Contour	Bayer HealthCare
SKUP/2009/74	Glucose[1]	Accu-Chek Mobile	Roche Diagnostics
SKUP/2010/73	Leukocytes	HemoCue WBC	HemoCue AB
SKUP/2008/72	Glucose[1]	*Confidential*	
SKUP/2009/71	Glucose[1]	GlucoMen LX	A. Menarini Diagnostics
SKUP/2011/70*	CRP	smartCRP system	Eurolyser Diagnostica GmbH
SKUP/2008/69*	Strep A	Diaquick Strep A test	Dialab GmbH
SKUP/2013/68	Allergens	ImmunoCap Rapid	Phadia AB
SKUP/2010/67	Allergens	*Confidential*	
SKUP/2008/66	Glucose[1]	DANA DiabeCare IISG	SOOIL Developement co. Ltd
SKUP/2008/65	HbA1c	Afinion HbA1c	Axis-Shield PoC AS
SKUP/2007/64	Glucose[1]	FreeStyle Lite	Abbott Laboratories
SKUP/2007/63	Glucose[1]	*Confidential*	
SKUP/2007/62*	Strep A	QuikRead	Orion Diagnostica Oy
SKUP/2008/61	CRP	i-CHROMA	BodiTech Med. Inc.
SKUP/2007/60	Glucose[1]	*Confidential*	
SKUP/2007/59	Glucose[1]	Ascensia BREEZE2	Bayer HealthCare
SKUP/2006/58	HbA1c	*Confidential*	

*A report code followed by an asterisk indicates evaluations at special request from the supplier, or evaluations that are not complete according to SKUP guidelines, e.g. the part performed by the intended users was not included in the protocol.

[1] Including a user-evaluation among diabetes patients