Actiste

A system for measurement of glucose and for insulin injections manufactured by Brighter AB

Av evaluation of the measurement of glucose

Report from the evaluation

SKUP/2021/120

organised by SKUP at the request of Brighter AB

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1. Summary

Background
The Actiste system is a combined in vitro diagnostic device for capillary blood sampling and quantitative measurement of glucose, and medical device for insulin injections. The product is intended for monitoring of disease in persons with insulin-dependent diabetes. The sample material is fresh capillary whole blood. The system is produced by Brighter AB and was launched into the Scandinavian market May 2020. The SKUP evaluation was carried out February 2020 to February 2021 at the request of Brighter AB in Sweden.

The aim of the evaluation
The aim of the evaluation was to assess the analytical quality and user-friendliness of glucose measurements with Actiste, both when used under optimal conditions by experienced laboratory personnel and under real-life conditions by intended users (persons with diabetes). The medical device for insulin injections was not evaluated.

Materials and methods
The study design is based on the model of the Norwegian Health Economics Administration (HELFO) for test strip reimbursement in Norway. A total of 97 persons with diabetes signed up for the evaluation and 86 of them completed. All 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 the central hospital in Växjö, Sweden or at Noklus in Bergen, Norway. Fresh capillary whole blood samples from each participant were analysed on Actiste 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 8000 c 701) in the laboratory for clinical chemistry and transfusion medicine at the central hospital in Växjö, Sweden. The trueness of the comparison method was demonstrated with the standard reference material (SRM) 965b from the National Institute of Standards & Technology (NIST). Haematocrit was analysed in venous samples. The analytical results and user-friendliness were assessed according to pre-set quality goals. The quality goal for precision was a repeatability (CV) ≤5,0 %. The quality goal for accuracy follows to the International Organization for Standardization (ISO) 15197:2013 which 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 user-friendliness was assessed using a questionnaire with three given ratings; satisfactory, intermediate and unsatisfactory, and with the quality goal of a total rating of "satisfactory".

Results
The CV achieved under optimal conditions was between 3,6 and 5,8 % depending on the glucose concentration. The intended users achieved a CV between 5,3 and 7,2 %. The bias between Actiste and the comparison method was between 0,6 and 0,9 mmol/L under optimal conditions and between 0,8 and 1,5 mmol/L for the intended users. Under optimal conditions 81 – 86 % of the results, depending on lot number, were within the allowable deviation limits for accuracy and when handled by intended users, 58 % of the results were within the limits. Glucose measurements on Actiste were not affected by haematocrit in the tested range 36 – 54 %. The user-friendliness of the operation facilities was rated as unsatisfactory and the manual as intermediate, while the other topics were rated as satisfactory.

Conclusion
The quality goal for repeatability was not fulfilled neither under optimal conditions nor by intended users. The quality goal for accuracy was not fulfilled neither under optimal conditions nor by intended users. The quality goal for user-friendliness was not fulfilled.

Comments from Brighter AB
A letter with comments from Brighter AB is attached to the report.

This summary is also published in Danish, Norwegian and Swedish at www.skup.org.

2. Abbreviations and Acronyms

ADA	American Diabetes Association
BLS	Biomedical Laboratory Scientist
C-NPU	Committee on Nomenclature, Properties and Units
CI	Confidence Interval
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
HELFO	Norwegian Health Economics Administration
ISO	International Organization for Standardization
NIST	National Institute of Standards & Technology
Noklus	Norwegian Organization for Quality Improvement of Laboratory Examinations
SI	International System of Units
SKUP	Scandinavian evaluation of laboratory equipment for point of care testing
SRM	Standard Reference Material
Swedac	Swedish board for accreditation and conformity assessment

3. Introduction

The purpose of Scandinavian evaluation of laboratory equipment for point of care testing (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 in point of care settings.

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 and user-friendliness are assessed according to pre-set quality goals. To fully demonstrate the quality of a product, the end-users should be involved in the evaluation. 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

The Actiste system is an in vitro diagnostic device for capillary blood sampling, quantitative measurement of glucose and for insulin injections. The product is intended for self-testing. The sample material is fresh capillary whole blood. The system is produced by Brighter AB and was launched into the Scandinavian market May 2020. The SKUP evaluation was carried out February 2020 to February 2021 at the request of Brighter AB in Sweden.

3.3. The aim of the evaluation

The aim of the evaluation was to assess the analytical quality and user-friendliness of glucose measurements with Actiste, both when used under optimal conditions by experienced laboratory personnel and when used under real-life conditions by intended users (persons with diabetes). The Actiste system includes functions for insulin treatment; both compartments for ampoules of insulin and injection needles as well as logging of injection (e.g. time, doses). This part of the system was not tested in the evaluation.

3.4. The model for the evaluation of Actiste

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.

[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.

The evaluation included:

- Examination of the analytical quality (precision and accuracy) under optimal conditions
- Examination of the analytical quality (precision and accuracy) in the hands of intended users
- Evaluation of the user-friendliness of Actiste and its manual by the intended users
- Examination of haematocrit effect on the glucose measurements

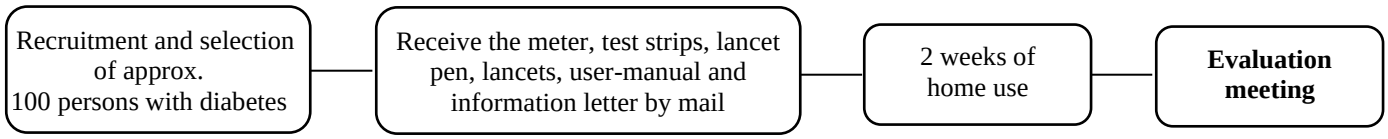

Figure 1. The evaluation process ended with the evaluation meeting. Three lot numbers of test strips called lot a, b and c, were distributed evenly among the participants by random distribution.

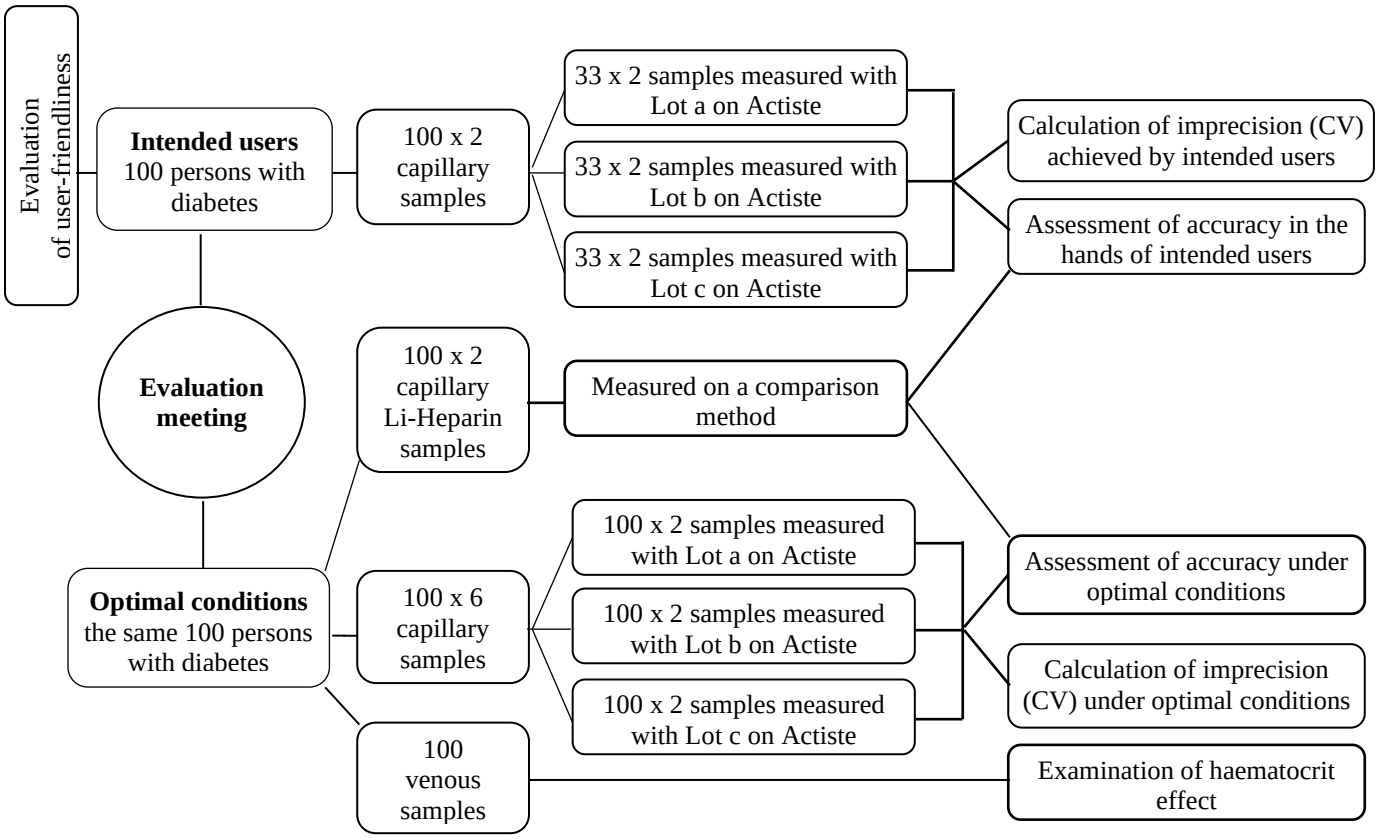

Figure 2. Flowchart illustrating the model for the evaluation of the Actiste system.

4. Quality goals

4.1. Analytical quality

The Actiste 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 [5,6].

The International Organization for Standardization (ISO) 15197:2013 standard [7] 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 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].

In Norway, the standard protocol of HELFO [2] follows the quality goal in ISO 15197:2013 [7].

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 [8]. This stricter quality goal for accuracy applies to measurements performed under optimal conditions in hospital laboratories and laboratories in primary health care centres.

4.2. User-friendliness

The evaluation of user-friendliness was carried out by asking the participants (intended users) to fill in a questionnaire, see section 6.5. The tested equipment much reach a total rating of "satisfactory" to fulfil the quality goal.

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 were 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 (one-tailed test). The distinction between the ratings, and the assessment of precision according to the quality goal, are shown in table 1. Based on the results from each glucose concentration level, an overall conclusion is drawn in the summary of the report.

Table 1. The rating of precision.

Distinction between the ratings	Assessment according to the quality goal
CV is equal or lower than the quality goal (statistically significant)	The quality goal is fulfilled
CV is equal or 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 is calculated from the results achieved under optimal conditions. The bias is also 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

The user-friendliness is assessed according to the answers and comments given in the questionnaire (see section 6.5). For each question, the participant can choose between three given ratings; satisfactory, intermediate and unsatisfactory. A written guidance with examples is available. 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 evaluating persons 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 Actiste are assessed against the following quality goals:

Repeatability (CV) ..... ≤5,0 %

Allowable deviation of the individual result from the comparison method result*
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 and <±10 % at glucose concentration ≥4,2 mmol/L) is 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 in this evaluation is plasma from capillary blood. The results are traceable to the International System of Units (SI) and are expressed in the unit mmol/L. The Committee on Nomenclature, Properties and Units (C-NPU) systematically describes clinical laboratory measurands in a database [9]. 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 Actiste

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

Figure 3. The Actiste meter.

Actiste is intended for blood glucose monitoring and insulin injections by persons with insulin-dependent diabetes. The system consists of a blood glucose meter (figure 3), test strips (manufactured by ForaCare Suisse AG), and compartments for test strips (10 pack), lancets, insulin ampoule and insulin injection needles. Sample material is fresh capillary whole blood from a finger prick. The measurement principle is electrochemical; as the glucose in the blood reacts with the reagents, including glucose dehydrogenase, on the test strip an electrical current is generated. It is measured by Actiste and the strength of the current is translated into glucose concentration. Actiste reports plasma glucose values. The measuring interval is 1,1 – 33,3 mmol/L, measurements below are marked as Low <1,1 mmol/L and above High >33,3 mmol/L. The glucose values and insulin doses are saved automatically, and the user can also add notes into the system. The person with diabetes can, in consultation with their diabetes care team, enter their personal target range in the Actiste meter. Measurements above or below this range will show the glucose concentration in red colour on the screen.

The Actiste system is provided as a cloud-based subscription service with lancets, glucose test strips and injection needles for the insulin automatically provided by mail from the supplier before the last ones are used by the person with diabetes. Analytical quality controls, two levels, are not included but can be purchased separately.

For technical details about the Actiste system, see table 2. For more information about the Actiste 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 Actiste	
Sample material	Fresh capillary whole blood
Sample volume	0,5 µL
Measuring time	5 seconds
Measuring interval	1,1 – 33,3 mmol/L
Tolerated haematocrit range	10 – 70 %
Storage capacity	3 months
Electrical power supply	Rechargeable batteries, charger with electrical cord

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 was a glucose hexokinase method implemented on Roche Cobas 8000 c 701 in the laboratory for clinical chemistry and transfusion medicine at the central hospital in Växjö, Sweden. The method uses reagents from Roche Diagnostics. The method is accredited according to ISO 15189 (2012) by the Swedish board for accreditation and conformity assessment (Swedac). The method is hereafter called "the comparison method".

In addition, samples for haematocrit were measured with Sysmex XN-10 in the laboratory at the central hospital in Växjö or with Advia 2120i or Cell-Dyn Sapphire in the laboratory of haematology at Haraldsplass university hospital, Norway.

Internal analytical quality control

Internal analytical quality control samples, two levels (Liquichek 1 and 2, BioRad), were measured each evaluation day on the comparison method.

External analytical quality control

The hospital laboratory participates in Equalis (external quality assessment in laboratory medicine in Sweden) external quality assessment (EQA) scheme for glucose (Scheme code 106/107, General clinical chemistry) with one level in ten rounds per year. The material is fresh frozen pooled human serum, some of them modified to reach pathological levels. The assigned values for glucose are based on the consensus value of 94 – 98 participants (Q1, 2021).

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 [10]. 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 were adjusted according to the NIST-targets using inverse regression. In addition, human serum controls produced by Equalis, 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 Wales [11]. The target value is given with an expanded uncertainty of <2 % (k=2).

5.4. The evaluation

5.4.1. Planning of the evaluation

Inquiry about an evaluation
Brighter AB via Thor Sundsvik, Global Product Manager – Diabetes, applied to SKUP in May 2019 for an evaluation of Actiste.

Protocol, arrangements and contract
In November 2019, the protocol for the evaluation was approved, and Brighter AB and SKUP signed a contract for the evaluation. The central hospital in Växjö, Sweden agreed to do the practical work with Actiste in the evaluation under optimal conditions. Due to low recruitment rate caused by the Covid-19 pandemic, part of the evaluation was allocated to Noklus (Norwegian Organization for Quality Improvement of Laboratory Examinations) in Bergen, Norway. All the samples for the comparison method were analysed in the laboratory in Växjö.

Training
Brighter AB was responsible for necessary training in use of the Actiste system under optimal conditions. All the participants (persons with diabetes) received the device and instructions by mail and no training was given. Brighter AB was not allowed to contact or supervise the evaluators during the evaluation period.

5.4.2. Evaluation sites and persons involved

The practical work, including sampling and measurements on Actiste, was carried out at the laboratory at the central hospital in Växjö for four months, ending in June 2020. One biomedical laboratory scientist (BLS) and one assistant nurse were involved in the practical work. The same BLS was responsible for analysing the samples on the comparison method. At Noklus the practical work was carried out by three BLSs in February 2021.

5.4.3. Recruitment and selection of participants

Recruitment
In Sweden participants were recruited in cooperation with primary health care centres in the region and through advertisements in the daily press. In Norway participants were recruited by mail inquiry sent to members of the Norwegian diabetes association (Diabetesforbundet) as well as through the medicinal clinic at Haraldsplass university hospital and by calling persons with diabetes that previously consented to be contacted for participation in evaluations of glucose meters. Participation was voluntary and written informed consent was obtained.

Selection
The participants were adults (≥18 years) and all had diabetes. The preference was insulin-dependent diabetes, but to fill up to quote of 100 participants also persons that did not use insulin were included as long as they measured glucose regularly.

5.4.4. The evaluation procedure

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

Use of Actiste at home
The participants used Actiste at home for approximately two weeks. They used Actiste 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 participant 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 Actiste 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[1]. The participants brought their assigned Actiste to the meeting. For the evaluation performed under optimal conditions, the BLSs/assistant nurse used three Actiste 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 participant) at the evaluation meeting. The same three lot numbers of test strips as distributed to the participants were used. On meter A, lot WG19E814T-ADF (called lot a) was used, on meter B, lot WG19E914T-ACE (called lot b) was used, and on meter C, lot WG19E314T-AEE (called lot c) was used for all the measurements. The measurements under optimal conditions were performed with meters and test strips stored according to the manufacture's instructions. For the evaluation performed under real-life conditions the participants made duplicate measurements on their assigned meter and test strips.

[1]Due to the pandemic of Covid-19 some of the senior participants (≥70 years) as well as participants having any symptoms of a cold could not attend their evaluation meetings in Växjö as planned. Their meetings were cancelled (≥70 years) or postponed. Participants with postponed meetings were instructed to follow the practice protocol, but also to do a few more measurements before their rescheduled evaluation meeting, so that they had the handling of Actiste fresh in memory.

Internal analytical quality control
Internal analytical quality control samples for Actiste, two levels (Actiste control solutions, ForaCare Suisse AG), were measured each evaluation day on the Actiste systems used under optimal conditions. To document correct functioning of the Actiste meters used by the participants, the BLS/assistant nurse checked these meters with level 2 (normal) 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 Actiste.

The participants washed and dried their hands before sampling. All samples for Actiste, as well as the glucose samples for the comparison method, were capillary samples collected from a finger prick. Blood samples for duplicate measurements on Actiste under optimal conditions were, for all participants but three, collected from the same finger prick. The BLS/assistant nurse 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/assistant nurse collected a first sample for the comparison method
2. The BLS/assistant nurse collected samples for meter/test strip lot A/a, B/b, C/c, A/a, B/b and C/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/assistant nurse collected a second sample for the comparison method using blood from a new finger prick
5. The BLS/assistant nurse collected a venous sample for haematocrit

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

In total, 62 % of the participants used the Actiste integrated lancing device for the blood sampling at the evaluation meeting.

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 [10]) until analysis took place. The samples were analysed during two days in February and March 2021. 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 first measurement 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 criterium with a change ≤10,0 % between the first and second comparative result is regarded as reasonable. Changes >10,0 % are regarded as unacceptable and these results were excluded.

Measurement of haematocrit
Haematocrit may influence blood glucose measurements. The venous sample for haematocrit collected from each participant (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 and study population characteristics

A total of 97 persons with diabetes signed up for the evaluation and 86 of them completed. In addition, three that had practiced at home but missed, or dropped out before, the evaluation meeting participated in the evaluation of user-friendliness. Eleven participants either could not attend the evaluation meeting due to national Covid-19 restrictions or withdrew from the evaluation for other reasons. The BLSs/assistant nurse performed 516 glucose measurements (6 measurements x 86 participants) on Actiste under optimal conditions. In addition, the BLSs/assistant nurse collected 172 capillary Li-heparin samples (2 samples x 86 participants) for glucose measurement on the comparison method. A venous sample for measurement of haematocrit was collected from 80 of the 86 participants. The intended users (persons with diabetes) performed 168 glucose measurements (2 measurements x 84 participants (see missing results)) on Actiste.

The concentration range for the glucose samples was 3,3 – 25,4 mmol/L (results from the comparison method). The concentration range for the haematocrit samples was 36 – 54 %.

The Actiste glucose meter was tested in use by 54 men and 35 women with diabetes. Average age of the participants was 55 years (range 19 – 78 years). A total of 39 participants had Type 1 diabetes and 50 had Type 2 diabetes. Of the participants, 61 self-reported as insulin dependent, 16 as not insulin dependent and 12 participants did not disclose this information. 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. In addition, the group included users of regular glucose meters as well as users of continuous glucose meters.

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

Missing results

- ID 78 and ID 97 did not practice at home and were therefore not allowed to do self-measurements at the evaluation meeting, but they were included in the evaluation performed under optimal conditions.
- ID 6, ID 44, ID 78, ID 79, ID 82 and ID 93 did not provide venous samples for measurement of haematocrit.

Omitted results

- The second measurement of the second sample analysed on the comparison method for all SKUP IDs was false too high due to evaporation (see 6.2.2), thus these results were omitted from all calculations.
- ID 22, ID 44, ID 55, ID 91 and ID 97; the deviation between the first and the second sample for the comparison method was >10,0 %, which means that the participants had unstable glucose concentrations 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.

- ID 11; the internal analytical quality control results on this ID's Actiste seemed to be of level 3 instead of level 2. The results were within approved interval for level 3. These results were removed from the calculation of the control reproducibility. The participant's results were included in all calculations.
- ID 27 and ID 53 did not practice at home. They did self-measurements on the evaluation meeting, but these results were omitted from calculations.

Excluded results (statistical outliers)

Statistical outliers in SKUP evaluations are detected by the criterion promoted by Burnett [12].

- On one date the internal quality controls (levels 2 and 3) analysed on lot c (optimal conditions) were outliers and therefore excluded from the calculation of control reproducibility. However, they both were within the allowable range and thus participant data from this date is included in all calculations.
- ID 22 was an outlier in the calculation of repeatability for lot c (optimal conditions), thus the results were excluded from this calculation as well as from the calculation of bias and assessment of accuracy (see omitted results).
- ID 38 was an outlier in the calculation of repeatability for self-measurement (intended users), thus the results were excluded from this calculation as well as from the calculation of bias. The result was included in the assessment of accuracy (the first of the duplicate measurements performed by the intended user).
- ID 30 and ID 60 were outliers in the calculation of bias for self-measurement (intended users), thus the results were excluded from this calculation. The result was included in the assessment of accuracy (the first of the duplicate measurements performed by the intended user).

Comments

- ID 36, ID 77, ID 84 and ID 86, the results from the internal analytical quality control were slightly high. The control results were included in the calculation of control reproducibility and the results from these participants were included in all calculations.
- ID 25 and ID 40 did not bring any test strips to the evaluation meeting, so they used ones from optimal conditions. The results were included in the calculations.
- ID 55; the meter did not work at the evaluation meeting, the participant borrowed one from optimal conditions.

Recorded error codes, technical errors and failed measurements

There were in total 21 errors reported during the evaluation meetings. Nine of these were deemed as preanalytical or handling errors. Of the 12 deemed as technical errors, six concerned that the meter did not detect the applied blood, three concerned mal- or non-functioning chargers, one concerned the meter turning itself off before the result was shown, on one occasion the result was not shown after analysis, and on several occasions, but only one properly registered, there were error messages (triangle symbol, no explanation to meaning was found). This adds up to 1,8 % registered technical errors (12 out of 516+168 measurements). 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 (Liquichek 1 and 2, BioRad), two levels, were within the allowable control limits (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 significant systematic difference pointed out between the paired measurements for all levels (data not shown). The second measurement in each pair of duplicates was systematically higher than the first measurement. The reason for this is most likely evaporation from the sample before the rerun as the open sample tube, with a small amount of plasma, was kept in a warm instrument both during and between runs.

The laboratory report that they normally have an imprecision (CV) of 0,8 % at level 4,9 mmol/L and 0,7 % at level 16,6 mmol/L. Raw data from this evaluation is attached for the requesting company only, see attachment 6.

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 analyses were performed on two occasions since the standards and controls (table 3 and 4) were analysed in batch with the samples from the participants, which was time consuming. The agreement between the comparison method and the NIST-standards is shown in table 3.

Table 3. 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	2021-02-15	**1,836**	5	1,93	+5,2
	2021-03-22	(1,809 – 1,863)	5	1,93	+5,0
	Total		**10**	**1,93**	**+5,1**
Level 2	2021-02-15	**4,194**	5	4,41	+5,2
	2021-03-22	(4,135 – 4,253)	5	4,39	+4,6
	Total		**10**	**4,40**	**+4,9**
Level 3	2021-02-15	**6,575**	5	6,85	+4,2
	2021-03-22	(6,481 – 6,669)	5	6,77	+3,0
	Total		**10**	**6,81**	**+3,6**
Level 4	2021-02-15	**16,35**	5	16,94	+3,6
	2021-03-22	(16,15 – 16,55)	5	16,84	+3,0
	Total		**10**	**16,89**	**+3,3**

Comments

Table 3 shows that the glucose results for the NIST-standards were above 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 [13,

14] by the following regression equations: **y = 0,9684x − 0,0558** (samples analysed February 15th) **and y=0,9738x – 0,0472** (samples analysed March 22nd).
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 Equalis, were analysed. The agreement between the comparison method and the target values from the Reference laboratory in Wales is shown in table 4.

Table 4. Trueness of the comparison method.

Control	Date	Target value glucose, (expanded uncertainty) mmol/L	n	Mean value glucose, mmol/L	Deviation from target value, %
Equalis 1	2021-02-15	**3,51**	5	3,48	–0,9
	2021-03-22	(3,45 – 3,57)	5	3,49	–0,7
	Total		**10**	**3,48**	**–0,8**
Equalis 2	2021-02-15	**15,1**	5	14,95	–0,3
	2021-03-22	(14,8 – 15,4)	5	14,89	–0,8
	Total		**10**	**14,92**	**–0,5**

Discussion
When adjusted, the comparison method gave glucose values in agreement with the glucose values from the Reference laboratory in Wales. The trueness of the comparison method was confirmed.

6.3. Analytical quality of Actiste under optimal conditions

The results below reflect the analytical quality of Actiste 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 (Actiste control solutions), two levels, were within the allowable control limits (data not shown). The reproducibility (CV) achieved with the internal analytical quality control samples were 2,45 % for level 2 (n=101) and 2,15 % for level 3 (n=101), one statistical outlier at each level was excluded from the calculation. Raw data is attached for the requesting company only, see attachment 7.

6.3.2. The precision of Actiste

Two capillary samples were collected from each participant 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 5. The results were sorted and divided into three concentration levels according to the mean of the results of Actiste. Raw data is attached for the requesting company only, see attachment 8.

Table 5. Repeatability (CV) of Actiste for glucose measured in capillary samples. Results achieved under optimal conditions.

Actiste (lot number of test strips)	Glucose level, mmol/L	n*	Excluded results (statistical outliers)	Mean value glucose, mmol/L	CV (90% CI), %
Lot a	<7	22	0	6,0	5,4 (4,3 – 7,3)
Lot b	<7	23	0	6,0	5,8 (4,6 – 7,7)
Lot c	<7	23	1**	6,0	3,9 (3,1 – 5,3)
Lot a	7 – 10	26	0	8,6	4,4 (3,5 – 5,7)
Lot b	7 – 10	24	0	8,7	3,9 (3,2 – 5,2)
Lot c	7 – 10	23	0	8,7	4,1 (3,3 – 5,5)
Lot a	>10	38	0	13,5	3,6 (3,1 – 4,5)
Lot b	>10	39	0	13,3	4,4 (3,8 – 5,5)
Lot c	>10	40	0	13,3	5,4 (4,5 – 6,6)

*The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers. An account of the number of samples is given in section 6.1.
**ID 22 was a statistical outlier according to Burnett's model [12] in the calculation of repeatability and therefore excluded.

Discussion

The CV achieved under optimal conditions was between 3,6 and 5,8 % depending on the test strip lot and concentration level. At level <7 mmol/L the CV was above but not statistically significant above the quality goal for lot a and b and below but not statistically significant below for lot c. At level 7 – 10 mmol/L the CV was below but not statistically significant below the quality goal for all three lots. At level >10 mmol/L the CV was below the quality goal for lot a,

below but not statistically significant below for lot b and above but not statistically significant above for lot c.

Conclusion
Under optimal conditions the quality goal for repeatability (CV ≤5,0 %) was most likely fulfilled at levels 7 – 10 and >10 mmol/L, but most likely not fulfilled at level <7 mmol/L. In all, the quality goal for repeatability was not fulfilled under optimal conditions.

6.3.3. The bias of Actiste

The mean deviation (bias) of Actiste results from the comparison method was calculated. The bias of Actiste with three lots of test strips is presented with a 95 % CI in table 6. 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 6. Bias of Actiste for glucose measured in capillary samples. Results achieved under optimal conditions.

Actiste (lot number of test strips)	Glucose level Comparison method, mmol/L	n*	Excluded results (statistical outliers)	Mean value Comparison method, glucose mmol/L	Mean value Actiste, glucose mmol/L	Bias (95 % CI), mmol/L	Bias, %
Lot a	<7	25	0	5,6	6,3	0,67 (0,55 — 0,78)	11,9
Lot b	<7	25	0	5,6	6,2	0,62 (0,47 — 0,76)	11,0
Lot c	<7	25	0	5,6	6,2	0,65 (0,50 — 0,79)	11,5
Lot a	7 – 10	22	0	8,4	9,2	0,78 (0,54 — 1,03)	9,3
Lot b	7 – 10	22	0	8,4	9,2	0,78 (0,59 — 0,97)	9,2
Lot c	7 – 10	22	0	8,4	9,3	0,87 (0,66 — 1,08)	10,3
Lot a	>10	34	0	12,9	13,8	0,92 (0,76 — 1,09)	7,2
Lot b	>10	34	0	12,9	13,7	0,79 (0,57 — 1,00)	6,1
Lot c	>10	34	0	12,9	13,8	0,92 (0,75 — 1,09)	7,1

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

Discussion
There was a statistically significant bias between the methods. Actiste gave systematically higher results than the comparison method.

6.3.4. The accuracy of Actiste

To evaluate the accuracy of glucose results on Actiste, the agreement between Actiste and the comparison method is illustrated in a difference plot (figure 4). The limits for the allowable deviation according to the quality goal (same as in ISO 15197:2013), are shown with stippled lines. All the first measurements from Actiste are included in the plot. The plot illustrates both random and systematic errors, reflecting the total measuring error in the Actiste results. The accuracy is summarised in table 7. Raw data is attached for the requesting company only, see attachment 6 and 8.

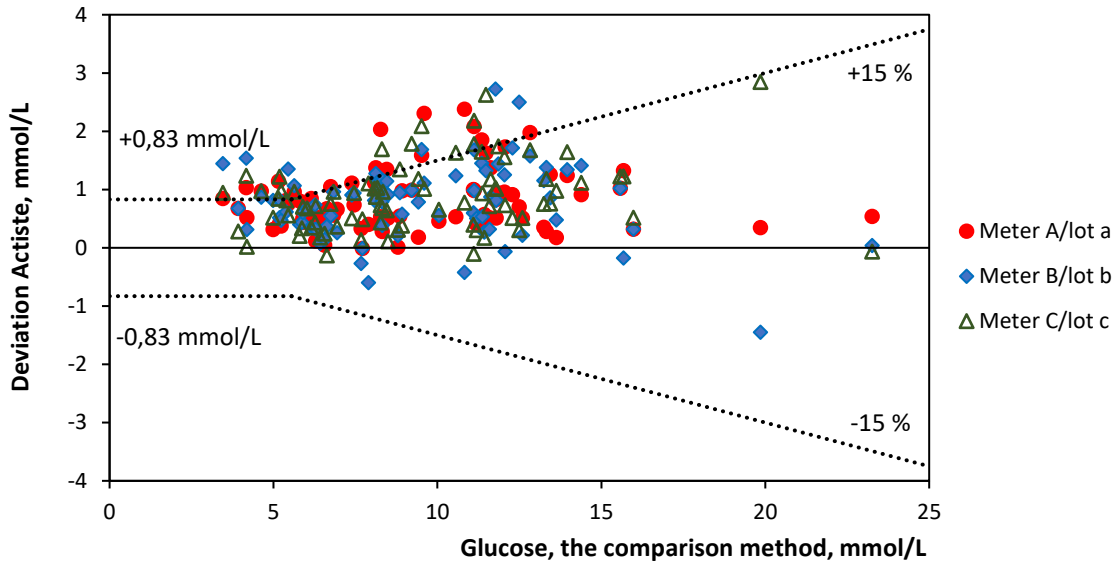

Figure 4. Accuracy of glucose results on Actiste under optimal conditions. The x-axis represents the mean glucose result of the comparison method. The y-axis represents the glucose deviation in mmol/L of the first capillary measurement on Actiste from the mean result of the corresponding sample of the comparison method. The different lots of test strips are illustrated with the symbols ● (lot a), ♦ (lot b) and △ (lot c). Stippled lines represent the allowable deviation limits; 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) = 81 per lot number. An account of the number of samples is given in section 6.1.

Table 7. Accuracy of Actiste for glucose measured in capillary samples. Results achieved under optimal conditions.

Lot	n*	Percentage of results within given limits, % (n)	
		Limits used in ISO 15197:2013**	Stricter Swedish quality goal***
a	81	81 (66)	60 (49)
b	81	86 (70)	53 (43)
c	81	81 (66)	53 (43)

*An account of the number of samples is given in section 6.1.
**<±0,83 mmol/L at conc. <5,55 mmol/L and <±15 % at conc. ≥5,55 mmol/L.
***<±0,42 mmol/L at conc. <4,2 mmol/L and <±10 % at conc. ≥4,2 mmol/L.

Discussion

As shown in figure 4, the glucose results from Actiste tend to be higher than the results from the comparison method for all three lot numbers, which is consistent with the calculated bias.

Out of 81 results, 66, 70 and 66 (lot a, b and c, respectively) were inside the limits for allowable deviation of ±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, corresponding to 81, 86 and 81 %, respectively within the limits. Table 7 also shows the number of results within the stricter Swedish quality goal (see section 4.1). These results are for information only.

Conclusion

Under optimal conditions the quality goal for accuracy was not fulfilled.

6.3.5. Effect of haematocrit

According to the technical specifications for Actiste, the glucose measurements are not affected by haematocrit values from 10 to 70 %. To measure the effect of haematocrit on Actiste, a venous sample for haematocrit was collected from the participants at the evaluation meeting. Investigation of the effect was based on the measurements on Actiste 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.

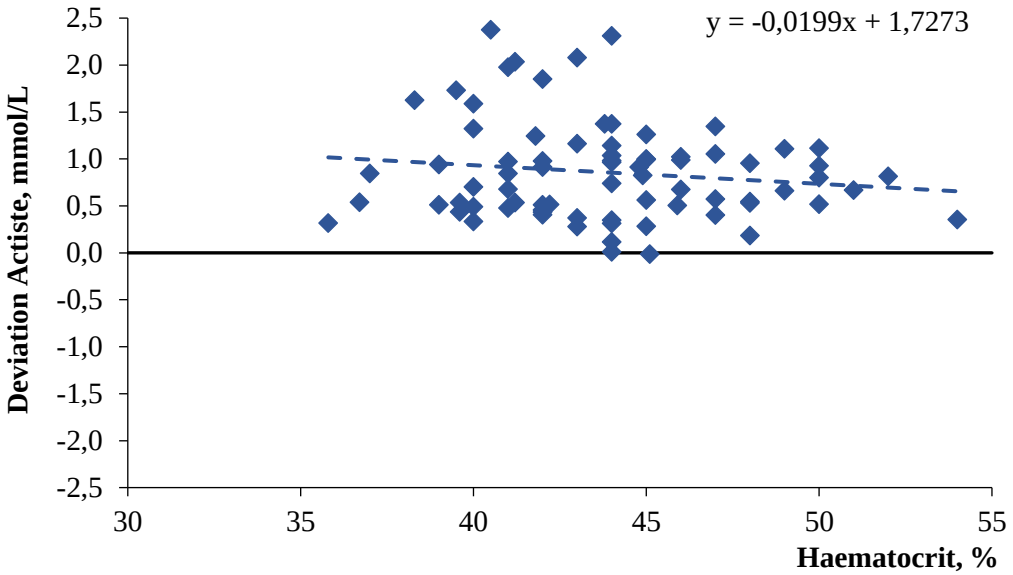

Figure 5. The effect of haematocrit on glucose measurements on Actiste meter A (with lot a) measured under optimal conditions. The x-axis shows the haematocrit value in percent. The y-axis shows the difference in glucose concentration between the first measurement on Actiste and the mean result of the corresponding sample of the comparison method in mmol/L. Number of results (n) = 76.

Discussion

The slope of the trend-line in figure 5 is (–0,02), with a 95 % CI from (–0,052) to (+0,013). The slope is not statistically significant different from zero. Glucose measurements on Actiste were not affected by haematocrit within the range tested (36 – 54 %).

6.4. Analytical quality of Actiste achieved by intended users

The results below reflect the analytical quality of Actiste 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 Actiste meters used by the intended users were checked with the internal analytical quality control (Actiste control solutions, level 2 (normal)), by the BLS/assistant nurse at the evaluation meeting. All results but four were within allowable control limits (data not shown), the data from these four participant meters are still included in all calculations. The reproducibility (CV) achieved with the internal analytical quality control was 4,8 % (n=110 (n >86 due to duplicate measurements at the Swedish site)). Raw data is attached for the requesting company only, attachment 10.

6.4.2. The precision of Actiste

The participants collected two capillary samples for measurements on their assigned Actiste 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 8. The results were sorted and divided into three concentration levels according to the mean of the results of Actiste. Raw data is attached for the requesting company only, attachment 11.

Table 8. Repeatability (CV) of Actiste for glucose measured in capillary samples. Results achieved by intended users.

Glucose level, mmol/L	n*	Excluded results (statistical outliers)	Mean value glucose, mmol/L	CV (90 % CI), %
<7	17	0	6,0	6,8 (5,3 – 9,6)
7 – 10	24	0	8,6	5,3 (4,3 – 7,0)
>10	41	1**	13,7	7,2 (6,1 – 8,9)

* The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers. An account of the number of samples is given in section 6.1.
**ID 38 was a statistical outlier according to Burnett's model [12] in the calculation of repeatability and therefore excluded.

Discussion

The CV achieved by intended users was between 5,3 and 7,2 % depending on the concentration level. At level 7 – 10 mmol/L the CV was above, but not statistically significant above, the quality goal. At levels <7 and >10 mmol/L the CV was above the quality goal.

Conclusion

When measurements were performed by the intended users the quality goal for repeatability (CV ≤5,0 %) was not fulfilled.

6.4.3. The bias of Actiste

The mean deviation (bias) of Actiste results from the comparison method was calculated. The bias of Actiste is presented with a 95 % CI in table 9. 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 11.

Table 9. Bias of Actiste for glucose measured in capillary samples. Results achieved by intended users.

Glucose level Comparison method, mmol/L	n*	Excluded results (statistical outliers)	Mean value Comparison method, glucose mmol/L	Mean value Actiste, glucose mmol/L	Bias (95 % CI), mmol/L	Bias, %
<7	23	0	5,7	6,5	0,83 (0,58 — 1,07)	14,6
7 – 10	21	0	8,4	9,5	1,14 (0,80 — 1,48)	13,6
>10	34	2**	12,6	14,1	1,52 (1,25 — 1,79)	12,0

* The given number of results (n) were counted before the exclusion of statistical outliers. Mean and CV were calculated after the exclusion of statistical outliers. An account of the number of samples is given in section 6.1.
**ID 30 and 60 were statistical outliers according to Burnett's model [12] in the calculation of bias and therefore excluded.

Discussion

There was a statistically significant bias between the methods. Actiste gave systematically higher results than the comparison method, which is consistent with the results under optimal conditions.

6.4.4. The accuracy of Actiste

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

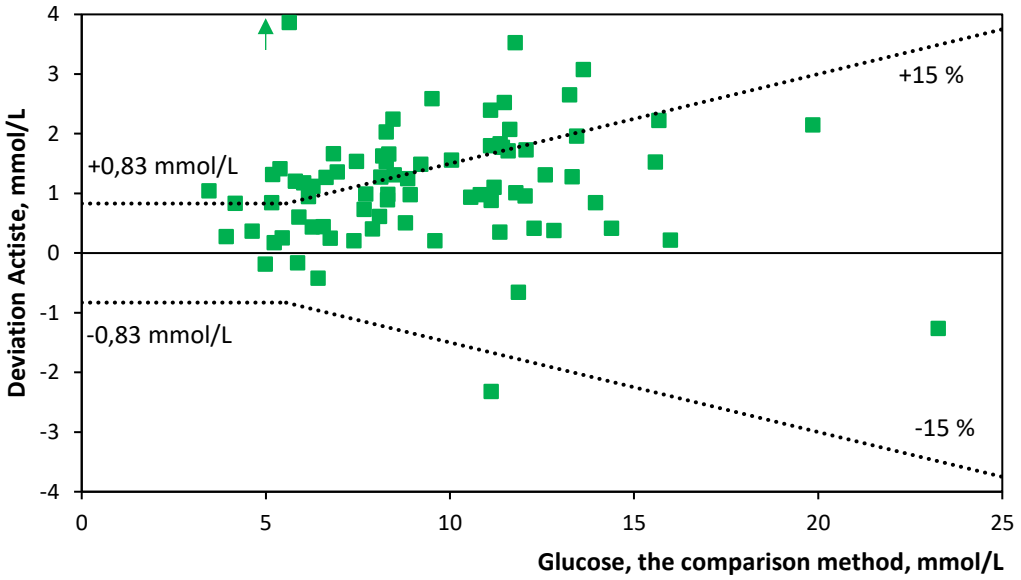

Figure 6. Accuracy of glucose results on Actiste achieved by intended users (three lots of test strips). The x-axis represents the mean glucose result of the comparison method. The y-axis represents the glucose deviation in mmol/L of the first capillary measurement on Actiste from the mean result of the corresponding sample of the comparison method. Stippled lines represent allowable deviation limits; 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. The arrow marks one result outside the plot; ID 38. Number of results (n) = 78. An account of the number of samples is given in section 6.1.

Discussion

As shown in figure 6, the glucose results from Actiste tend to be higher than the results from the comparison method, which is consistent with the results under optimal conditions. Out of 78 results 44 were inside the limits for allowable deviation of ±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, corresponding to 56 % within the limits.

Conclusion

When measurements were performed by the intended users the quality goal for accuracy was not 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.

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

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. SKUP suggests that 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. The questionnaire is adapted for blood glucose meters. No adjustment to Actiste, being a device with several applications, is done.

Comment
In this evaluation, the user-friendliness was assessed by 89 persons with diabetes.

Table A. Rating of operation facilities

Topic (n)	Rating % (n)	Rating % (n)	Rating % (n)	No opinion % (n)
To measure a sample (79)	Satisfactory 53 (42)	Intermediate 32 (25)	Unsatisfactory 14 (11)	No opinion 1 (1)
To insert the test strip (81)	Satisfactory 72 (58)	Intermediate 25 (20)	Unsatisfactory 2 (2)	No opinion 1 (1)
To apply blood (81)	Satisfactory 88 (71)	Intermediate 9 (7)	Unsatisfactory 2 (2)	No opinion 1 (1)
Reading of the test result (82)	Satisfactory 95 (78)	Intermediate 2 (2)	Unsatisfactory 1 (1)	No opinion 1 (1)
Specimen volume (78)	Satisfactory 80 (62)	Intermediate 12 (9)	Unsatisfactory 5 (4)	No opinion 4 (3)
Design instrument (79)	Satisfactory 19 (15)	Intermediate 47 (37)	Unsatisfactory 33 (26)	No opinion 1 (1)
Design test strip (80)	Satisfactory 45 (36)	Intermediate 35 (28)	Unsatisfactory 18 (14)	No opinion 2 (2)
Sources of errors (79)	Satisfactory 53 (42)	Intermediate 8 (6)	Unsatisfactory 6 (5)	No opinion 33 (26)
Cleaning / Maintenance (80)	Satisfactory 58 (46)	Intermediate 15 (12)	Unsatisfactory 0 (0)	No opinion 28 (22)
Hygiene, when using the test (81)	Satisfactory 63 (51)	Intermediate 28 (23)	Unsatisfactory 4 (3)	No opinion 5 (4)
Size and weight of instrument and package (80)	Satisfactory 19 (15)	Intermediate 49 (39)	Unsatisfactory 32 (26)	No opinion 0 (0)
In total; how easy did you find the usage of the instrument? (78)	Satisfactory 33 (26)	Intermediate 49 (38)	Unsatisfactory 17 (13)	No opinion 1 (1)
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 or disposable***	+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			**Unsatisfactory**	

*According to the package insert of the test strips, the test strips can be stored between 2 and 30°C.

Positive comments

A total of 49 participants had one or more positive comments regarding the operation facilities of Actiste. The most often reported positive comments were regarding:

1. All-in-one system (21)

2. The use of the meter (12); the meter is easy to use, needs a small amount of blood, fast results
3. The display (10); clear display
4. Functions (5); useful that the device displays average values and curves of glucose history
5. Size (4); although the system is quite large, it is okay since it is all-in-one
6. Test strips (3); good absorption
7. Charger (3); functional with charger and long battery time

Negative comments

A total of 69 participants had one or more negative comments regarding the operation facilities of Actiste. The most often reported negative comments were regarding:

1. The test strips (45); difficult to get the strip out of the package, difficult to insert them into the strip compartment and to get them out of there (common to spill test strips when trying to get one out), because the strip goes far into the meter it is difficult to remove the strip without getting blood on your fingers, too much waste from the package
2. Size (43); big (not discreet to use, not suitable for a pocket/small handbag), heavy
3. Lancet pen/lancets (31); difficult to handle the pen, difficult and time consuming to insert and remove lancet, not enough depth
4. Learning (24); difficult to learn and to use, many procedure steps
5. Hatches (22); many hatches, difficult to open them and some fell off
6. Error messages (8); many error messages or not receiving results
7. Material (8); felt cheap/plastic
8. Charger (6); three faulty chargers (could not charge at all or had to keep the meter attached to charger to be able to analyse) and comments on the magnetism working poorly.

A total of 76 participants had used the manual, insert or quick guide.

Table B. Rating of the information in the manual/insert/quick guide

Topic (n)	**Rating** % (n)	**Rating** % (n)	**Rating** % (n)	**Option** % (n)
Table of contents/Index (75)	Satisfactory 64 (48)	Intermediate 19 (14)	Unsatisfactory 3 (2)	No opinion 15 (11)
Specimen collection; description and illustrations (74)	Satisfactory 69 (51)	Intermediate 26 (19)	Unsatisfactory 5 (4)	No opinion 0 (0)
Description of how to insert a test strip (74)	Satisfactory 76 (56)	Intermediate 19 (14)	Unsatisfactory 5 (4)	No opinion 0 (0)
Description of measurement procedure (76)	Satisfactory 82 (62)	Intermediate 14 (11)	Unsatisfactory 4 (3)	No opinion 0 (0)
Description of how to read the result (76)	Satisfactory 87 (66)	Intermediate 7 (5)	Unsatisfactory 4 (3)	No opinion 3 (2)
Description of the sources of error (76)	Satisfactory 40 (30)	Intermediate 12 (9)	Unsatisfactory 3 (2)	No opinion 46 (35)*
Help for troubleshooting (76)	Satisfactory 34 (26)	Intermediate 14 (11)	Unsatisfactory 5 (3)	No opinion 46 (35)*
Readability / Clarity of presentation (76)	Satisfactory 72 (55)	Intermediate 22 (17)	Unsatisfactory 5 (4)	No opinion 0 (0)
General impression (75)	Satisfactory 63 (47)	Intermediate 28 (21)	Unsatisfactory 8 (6)	No opinion 1 (1)
Measurement principle	**Satisfactory**	Intermediate	Unsatisfactory	
Available insert in Danish, Norwegian, Swedish	**Satisfactory****	Intermediate	Unsatisfactory	
Total rating by SKUP		**Intermediate**		

*Presumably, persons that had no, or few error messages did not read sources of errors and troubleshooting, hence many "no opinion" answers.
**Available in Swedish and Norwegian.

Positive comments
A total of 16 participants had one or more positive comments regarding the manual/quick guide. The most often reported positive comments were regarding:

1. The manual is good and easily understood (11)
2. The explanations/illustrations are good (6)
3. The quick guide is very good (2)

Negative comments
A total of 40 participants had one or more negative comments regarding the manual/quick guide. The most often reported negative comments were regarding:

1. The format (big, folded paper) (5), they want a booklet instead

2. Size of the text is too small (5)
3. Descriptions; some are hard to understand; mainly how to use the lancet pen (5), and how to insert/remove test strip (5)
4. Too little information of error messages and troubleshooting (4)
5. General impression; too comprehensive, complicated both to read and to use for learning the Actiste system

Table C. Rating of time factors (filled in 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 day or disposable	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**		

*The test strips are packed in pouches of 10. Once opened the test strips are stable for 7 days if stored with desiccant. Since the meter is intended for persons with insulin-dependent diabetes, 10 test strips are used quickly, hence 7 days' stability is satisfactory.

Table D. Rating of analytical quality control (filled in 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 unsatisfactory. The many negative comments regarding the design of the meter including problems with hatches as well as handling of test strips, lancet pen and lancets, and the difficulties in learning and using the system, are deemed to impair the user-friendliness gravely, which explains the total assessment of unsatisfactory.

Assessment of the information in the manual/quick guide (table B)
The manual/quick guide was assessed as intermediate. The rating is based on the negative comments regarding the readability of the manual/quick guide and poor descriptions of several of the procedure steps, which impairs the user-friendliness.

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 was lower than the repeatability of the patient samples.

Conclusion
In all, the user-friendliness of the operation facilities was rated as unsatisfactory, the manual/quick guide was rated as intermediate, and the time factors and quality control possibilities were rated as satisfactory. The quality goal for user-friendliness was not fulfilled.

7. References

1. Christensen NG., Monsen G. & Sandberg S. Utprøving av analyseinstrumenter, 1997. Alma Mater Forlag.
2. Helfo. www.helfo.no
3. Stöckl D. *et al.* Desirable routine analytical goals for quantities assayed in serum. *Eur J Clin Biochem* 1995; **33** (3): 157 – 169.
4. American Diabetes Association. Self-monitoring of blood glucose. *Diabetes Care* 1996; **19** (suppl 1): 62 – 66.
5. Skeie S., Thue G. & Sandberg S. Patient-derived quality specifications for instruments used in self-monitoring of blood glucose. *Clin Chem* 2001; **47** (1): 67 – 73.
6. Kvalitetssikring og kvalitetskrav til laboratoriemedicinske aktiviteter i almen praksis. Udarbejdet af Regionernes Lønnings- og Takstnævn (RTLN) og Praktiserende Lægers Organisation (PLO). 2010. https://www.laeger.dk/sites/default/files/kvalitetssikring_og_kvalitetskrav_til_laboratoriemedicinske_aktiviteter_i_almen_praksis_2010.pdf (accessed 2021-05-07).
7. In vitro diagnostic test systems - Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus, ed. ISO 15197:2013.
8. Equalis. https://www.equalis.se/sv/produkter-tjanster/kunskapsstod/projekt-for-nationell-harmonisering/nationella-kvalitetsmal/ (accessed 2021-03-16).
9. The IFCC – IUPAC terminology for properties and units. http://www.ifcc.org/ifcc-scientific-division/sd-committees/c-npu/npusearch/(accessed 2021-03-16).
10. National Institute of Standards and Technology, Certificate of Analysis, Standard Reference Material®965b, Glucose in Frozen Human Serum.
11. Weqas. http://www.weqas.com/services/referencelab/gcms-glucose/
12. Burnett RW. Accurate estimation of standard deviations for quantitative methods used in clinical chemistry. *Clin Chem* 1975; **21** (13): 1935 – 1938.
13. Krutchkoff RG. Classical and inverse regression methods of calibration. *Technometrics* 1967; **9** (3): 425 – 439.
14. Tellinghuisen J. Inverse vs. classical calibration for small data sets. *Fresenius J. Anal. Chem.* 2000; **368** (6): 585 – 588.

Attachments

1. The organisation of SKUP
2. Facts about Actiste
3. Information about manufacturer, retailers and marketing
4. Product specifications for this evaluation, Actiste
5. Statistical expressions and calculations
6. Raw data glucose, results from the comparison method
7. Raw data glucose, internal analytical quality control results, Actiste, optimal conditions
8. Raw data glucose, Actiste results, optimal conditions
9. Raw data haematocrit
10. Raw data, internal analytical quality control results, Actiste, on intended users' meters
11. Raw data glucose, Actiste results, intended users
12. Comments from Brighter AB

Attachments with raw data are included only in the copy to Brighter AB.

The organisation of SKUP

Scandinavian evaluation of laboratory equipment for point of care testing, 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 laboratory equipment for point of care testing. 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.org.

[1] Noklus (Norwegian Organization for 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 Regioner” (Swedish Association of Local Authorities and Regions), “Svenska Läkaresällskapet” (Swedish Society of Medicine) and IBL (Swedish Institute of Biomedical Laboratory Science).

Facts about Actiste

This form is filled in by Brighter AB.

Table 1. Basic facts

Name of the measurement system	Actiste
Dimensions and weight	163,7 x 52,8 x 23,2 mm, 127 g
Components of the measurement system	BG meter, test strips, injection needles and lancing consumables
Measurand	Plasma glucose
Sample material	Human whole blood, capillary or venous
Sample volume	0,5 µL
Measuring principle	Electro-chemistry
Traceability	ISO 15197:2013
Calibration	Plasma Calibration
Measuring range	1,1 – 33,3 mmol/l
Haematocrit range	10 – 70 %
Measurement time	5 Seconds
Operating conditions	• Blood glucose test: +8 to +40°C • Injecting insulin: According to specification for the specific insulin used with the device Ambient temperature limits storage: • With test strips inside and insulin cartridge installed: According to specification for the specific insulin used with the device but not below +2°C and not above +30°C • With insulin installed, but no test strips inside: According to specification for the specific insulin used with the device. • With test strips inside, but no insulin cartridge installed: +2°C to +30°C • Without either insulin or test strips: -10°C to +45°C • It takes approximately 10 to 15 minutes to warm Actiste up from –10°C to +8°C if brought into room temperature.
Electrical power supply	AC Adapter that is used to charge the rechargeable battery
Recommended regular maintenance	None within lifetime of device
Package contents	Actiste is delivered together with a Medical AC Adapter that is used to charge the battery and IFU

Necessary equipment not included in the package	N/A. The Actiste service provides lancets, needles and test strip consumables out of consumption, except desired insulin cartridges. No reorder is necessary in normal operation as it will be shipped automatically.

Table 2. Post analytical traceability

Is input of patient identification possible?	Only if user subscribes and get approval from Brighter
Is input of operator identification possible?	Only if user subscribes and get approval from Brighter
Can the instrument be connected to a bar-code reader?	No, but every device has a unique QR-code for identification
Can the instrument be connected to a printer?	Only when the patient signs up for the service
What can be printed?	Depends of role
Can the instrument be connected to a PC?	Yes, but it requires specific key and encoder by Brighter
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?	Ex. < 1500 BG values inside instrument (min 10 year of data in cloud system)
Is it possible to trace/search for measurement results?	Yes and NO (define role of investigator)

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

Name of the test strips	Test strip for blood glucose measurement. For self-test by ForaCare
Stability in unopened sealed vial	18 months from manufacturing
Stability in opened vial	7 days in Actiste compartment
Package contents	10 teststrips (blister bag)

Table 4. Quality control

Electronic self check	Yes
Recommended control materials and volume	Actiste control solutions by ForaCare. Level 2, 4 mL/vial (enough for 100 measurements). Level 3 available upon request.
Stability in unopened sealed vial	12 months
Stability in opened vial	3 months
Package contents	1 vial, 4 mL/vial

Information about manufacturer, suppliers and marketing

This form is filled in by Brighter AB.

Table 1. Marketing information

Manufacturer	Brighter AB
Retailers in Scandinavia	Denmark: None Norway: None Sweden: Brighter AB
In which countries is the system marketed	Globally ☒ will be Scandinavia ☐ Europe ☐
Date for start of marketing the system in Scandinavia	20 May 2020
Date for CE-marking	September 3rd 2019
In which Scandinavian languages is the manual available	Swedish

Product specifications for this evaluation, Actiste

A total of 100 Actiste blood glucose meters were used in this evaluation. Three meters, meter A, B and C, were used under optimal conditions. On meter A test strip lot a was used, on meter B lot b was used, and on meter C lot c was used.

Actiste serial numbers

Meter	Serial number
A	ACT00000040641
B	ACT00000039541
C	ACT00000038941

Actiste internal analytical quality control solutions

Control	Lot no	Expiry date	Used by
Level 2	WAA19B01	2021-02-14	Sweden
Level 3	BAA19A01	2021-01-18	Sweden
Level 2	WAA19E01	2021-05-06	Norway
Level 3	BAA19E01	2021-05-08	Norway

The target values are specified per test strip lot number, see table below.

Actiste test strips

Lot number	Alias	Expiry date	Target value control level 2, mmol/L	Target value control level 3, mmol/L
WG19E314T-ADF	Lot a	2021-02-28	6,4 – 8,7	15,9 – 21,6
WG19E314T-ACE	Lot b	2021-02-28	6,4 – 8,7	15,9 – 21,6
WG19E314T-AEE	Lot c	2021-02-28	6,4 – 8,8	15,9 – 21,4

Other equipment

Equipment	Penetrating depth (mm) / Volume (µL)	Lot number	Expiry date	Supplier	Article number	Used by
Medlance lancet, high flow Red	2,0 mm			OneMed	221016	Optimal conditions Sweden
ACCU-CHEK Safe-T-Pro Plus	2,3 mm	41818050	2022-04	Roche	41818050	Optimal conditions Norway
Droplet lancet 28G	Adjustable depth	X13N3	2022-11-01	Included in Actiste system		Participants*
Microvette 300 LH	300 µL	9072511	2022-06-30	Sarstedt AB	20.1309	Sweden
Microvette CB 300 LH	300 µL	9072011	2022-05-31	Sarstedt AS	16.443.100	Norway

*Participants could also use they own lancing device with accompanying lancets.

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.

Raw data glucose, results from the comparison method

Shown to the requesting company only.

Raw data glucose, internal analytical quality control results, Actiste, optimal conditions

Shown to the requesting company only.

Raw data glucose, Actiste results, optimal conditions

Shown to the requesting company only.

Raw data haematocrit

Shown to the requesting company only.

Raw data, internal analytical quality control results, Actiste, on intended users' meters

Shown to the requesting company only.

Raw data glucose, Actiste results, intended users

Shown to the requesting company only.

Comments from Brighter AB

BRIGHTER EXECUTIVE SUMMARY

Internal investigation in relation to evaluation of Actiste performed by SKUP (coordinated by Equalis AB) during the period of time from May 2020 to March 2021

1. Brighter performed a qualifying type approval according to ISO 15197:2013 at the external institute of IDT Germany in 2018/May (N-002685-R1.0 / IDT-1820(2)-A-BK, and N-002700-R1.0 / IDT-1820(1)-A-BK). It is important to realize differences between the SKUP test protocol and ISO. The ISO testing in respect to accuracy showed a total of 98%, as it says in the Actiste data sheet.

2. Using Cobas control instruments with NIST SRM 965b as control for trueness explains part of the bias that pushes the total result of accuracy away from the target. In the type approval (IDT) the bias was concluded to be from -4.2% to -3.7% (a negative bias).

3. The fact that the SKUP trial was delayed due to Corona/Covid-19 pandemic pushed the BG-test strip due date to the very end of life (10-17 month from production). It must be understood that better precision and accuracy would be expected in the normal first 3-6 month, that would be the typical/normal test period with SKUP.

4. SKUP has indicated that a few of the participants did not handle the test strips according to the IFU / short guide. Any misuse of test strip (storage outside of blister pack or sealed Actiste compartment) will risk the accuracy and validity of BG results, this goes with any BG meter based on glucose dehydrogenase technology and patients are always reminded to be aware.

5. We note a big spread in the usability feedback from patients in the SKUP test. From the answers we see the importance that users must be interested and understand the benefit of a combined (3in1) and connected device including technology for transmission of biometrics data. In a normal real life application the patient and/or the prescriber would be aware of the differences from an ordinary non connected minimalistic BG meter for personal use.

Conclusion:

Brighter is grateful for results of SKUP tests for a valuable input to the continuous improvement of Actiste. It has become clear that Actiste should be aimed for users that will understand the benefits of a 3 in 1 device that will store and share biodata for short and long-term understanding and continuous learning about his/her diabetes.