ONETOUCH® Ultra™

A meter designed for glucose self-measurement
manufactured by LifeScan, Johnson & Johnson

Report from an evaluation
organised by

SKUP

The evaluation was ordered by LifeScan in Denmark

SKUP/2005/39

SKUP in Norway, NOKLUS, Division of General Practice, University of Bergen, 5009 Bergen, www.SKUP.nu

Summary

Background
OneTouch Ultra is a meter designed for glucose self-measurements by diabetics. The meter is produced by LifeScan, Johnson & Johnson, and is supplied in Scandinavia by LifeScan. OneTouch Ultra was launched onto the Norwegian market in the autumn 2002.

In order to give reimbursement for the test strips, The National Social Insurance Office (*Rikstrygdeverket*) in Norway instructs the companies to carry out an evaluation that includes a user-evaluation among diabetics. The evaluation of OneTouch Ultra is done under the direction of SKUP during the spring of 2005.

The aim of the evaluation
The aim of the evaluation of OneTouch Ultra is to

- reflect the analytical quality under standardised and optimal conditions (performed by a biomedical laboratory scientist)
- reflect the analytical quality by the users (77 diabetics)
- compare the analytical quality among diabetics with and without training
- compare the analytical quality among diabetics before and after three weeks of practise
- check the variation between three lots of test strips
- examine if hematocrit interferes with the measurements
- evaluate OneTouch Ultra regarding user-friendliness
- evaluate the OneTouch Ultra user-manual

Materials and methods
77 diabetics took part in the evaluation. 39 participants had two consultations (the "training group") and 38 participants had one consultation (the "post group"). At the first consultation the diabetics at the training group were given a standardised instruction about the OneTouch Ultra before they did a finger prick and performed two measurements on the meter. The biomedical laboratory scientist also took capillary samples of the diabetics and measured twice at OneTouch Ultra. In addition, two capillary samples were taken to a designated comparison method. The post group received the OneTouch Ultra by post and no training was given. Both groups of diabetics carried out a practice period of approximately three weeks at home, before they were called for a second consultation. The blood glucose sampling and measurement procedures at the first consultation were repeated, and in addition a sample for hematocrit was taken. Three different lots of test strips were used in the evaluation. All the participants finally answered questionnaires about the user-friendliness and the user-manual of OneTouch Ultra.

Results

- OneTouch Ultra shows acceptable precision. The CV is < 5 % under standardised and optimal measuring conditions and between 2 and 6 % when the measurements are performed by diabetics.
- The agreement with a designated comparison method is good. Quality goals set in ISO 15197 are achieved under standardised and optimal measuring conditions. When handled by the diabetics, OneTouch Ultra also shows good results. 98,7 % of these results are

within the “adjusted ISO-goal” and 97,4 % are also within the quality goals set in ISO 15197.

- The three lots of test strips that were used showed significantly lower values than the comparison method. The measured differences are between -0,3 and -0,9 mmol/L. In spite of these systematic deviations, the results attain the quality goal.
- Glucose measurements at OneTouch Ultra seem to be affected by the hematocrit values of the samples in higher degree than described in the package insert. Glucose values are over-estimated when the hematocrit is below 30 %. With hematocrit values over approximately 40 % the glucose values are under-estimated.
- The diabetics summarise the OneTouch Ultra device as easy to use. As a whole they were pleased with the device. The diabetics that had used the user manual were satisfied with the manual.

Conclusion

Glucose measurements on OneTouch Ultra have acceptable precision. The results obtained under optimal measuring conditions are within the quality goals set in the ISO-guide 15197. The measurements performed by the diabetics are within the “adjusted” quality goals set in the ISO-guide 15197 and also within the ISO-goal. The three lots used in this evaluation showed significantly lower values than the comparison method. The glucose results in this evaluation are affected by hematocrit in a higher degree than described in the package insert. In spite of the hematocrit effect, the glucose results still fulfil the quality goal set by ISO. The users find the OneTouch Ultra device easy to use and they are quite satisfied with the device.

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

1. The organisation of SKUP

Scandinavian evaluation of laboratory equipment for primary health care, SKUP, is a cooperative venture by Norway, Sweden and Denmark. SKUP was established in the autumn of 1997 at the initiative of professionals and health authorities in the three countries. SKUP is led by a Scandinavian expert group. The secretariat is located at NOKLUS Centre in Bergen, Norway.

The goal of SKUP is to produce objective and independent information concerning the quality and user-friendliness of laboratory equipment for physicians' offices outside the hospital. This information is generated by organizing SKUP's own evaluation program.

The SKUP evaluation is standardised according to SKUP's general evaluation guidelines. The evaluation follows a protocol based on these guidelines, but the protocol is always adjusted to the actual evaluation in cooperation with the supplier. The SKUP evaluation consists of two comparable parts. One part of the evaluation is done under standardised and optimal measuring conditions and the other part is performed by the users the equipment is produced for. Primarily, SKUP evaluates equipment intended for the primary health care, but SKUP can also offer evaluations of equipment for self monitoring blood glucose (SMBG). The evaluations of SMBG are conducted under standardised and optimal conditions and among diabetics.

SKUP personnel are financed with funds from their respective countries, while the actual testing is funded by the equipment suppliers. For suppliers this offers an opportunity to have their equipment subjected to standardised testing all over Scandinavia. For consumers it means easy access to objective information on equipment, and health care authorities will be able to gain an overview of the equipment (and its quality) available on the market at any given time.

SKUP distributes information about evaluated equipment to physicians' offices, laboratory medical councils, laboratory advisors and health political authorities. The evaluation reports are presented at www.skup.nu.

A unique evaluation code number is assigned to every SKUP evaluation report. The code is composed of the name SKUP, and the year and number of the evaluation. This applies for all evaluations following the complete SKUP standard evaluation procedure. Pre marketing evaluations, evaluations without the user's contribution, supplementary evaluations and special evaluations on request from the producer/supplier are in addition marked with a star in connection to the evaluation number. If the company makes use of SKUP's name in the marketing of an instrument, they have to refer to www.skup.nu and the actual evaluation number at the same time. If required, the company can get access to a SKUP logo where this information is an integral part.

2. Planning of the evaluation

Ellen Ahlmann-Ohlsen from LifeScan, Denmark, applied to SKUP in the autumn of 2004 for an evaluation of the glucose meter OneTouch Ultra. In October 2004 SKUP gave a written offer, and late in December 2004 a preliminary suggestion regarding how to organise the evaluation was sent. The protocol for the evaluation of OneTouch Ultra was accepted by LifeScan in April 2005. A contract was set up between LifeScan and SKUP in May 2005. The Laboratory at Haraldsplass Diaconal Hospital (HDH) accepted to carry out the analytical part of the evaluation dealing with the reference samples. During the planning of the evaluation, a meeting was held at NOKLUS Centre (November 11th, 2004). Ellen Ahlmann-Ohlsen, Denmark, and Bernt Erik Bibow, Norway, participated from LifeScan.

The OneTouch Ultra system was launched onto the Norwegian market in the autumn of 2002. SKUP carried out the user-evaluation of OneTouch Ultra blood glucose meter system during the spring of 2005.

SKUP evaluations are made according to guidelines in the book "*Evaluation of analytical instruments. A guide particularly designed for evaluations of instruments in primary health care*" (Christensen, Monsen et al. 1997) [1]. The evaluation of a self-monitoring blood glucose device follows the guidelines in the book, but the evaluation in primary health care is replaced by a user-evaluation conducted among diabetics, based on the model by the NOKLUS-project "*Diabetes-Self-measurements*" [2].

The evaluation comprises the following studies:

- An examination of analytical quality under standardised and optimal conditions done by a biomedical laboratory scientist (see chapter 4.1.1.)
- An examination of analytical quality amongst approximately 80 diabetics
- An examination of agreement between OneTouch Ultra and a designated comparison method
- A comparison of analytical quality among diabetics with and without training programme
- A comparison of analytical quality among diabetics before and after three weeks of practise
- An examination of variation between three lots of test strips
- An examination to see if hematocrit interferes with the measurements
- An evaluation of user-friendliness of OneTouch Ultra
- An evaluation of the user-manual of OneTouch Ultra

The blood sampling of the diabetics and the measurements on OneTouch Ultra under standardised and optimal conditions, were done by Lise Walberg, biomedical laboratory scientist and laboratory consultant, SKUP/NOKLUS. Two biomedical laboratory scientists, Wenche Eilifsen Hauge and Kjersti Østrem, were given the responsibility for the practical work with the comparison method at the laboratory at HDH. The statistical calculations and the report writing are done by Marianne Risa, SKUP/NOKLUS Centre.

3. Analytical quality specifications

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. OneTouch Ultra is designed for monitoring blood glucose, and the quality goals must be set according to this.

Precision
For glucose meters designed for monitoring blood glucose one should point out the need of a method with good precision [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].

Accuracy
According to ADA the total error for meters designed for self monitoring and point of care testing of glucose should not exceed 10 % in the range 1,67 – 22,2 mmol/L. The quality goal from ADA must be seen as an optimal goal for the analytical quality of these meters.

The quality goal for the total error of OneTouch Ultra is found in ISO 15197, *In vitro diagnostic test systems – Requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus* [6]. The ISO-guide is an international protocol for evaluating meters designed for glucose monitoring systems.

ISO 15197 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.

This is a quality goal for measurements by trained laboratory staff. Ideally, the same quality requirement should apply for measurements by the diabetics. Previous investigations under the direction of the NOKLUS-project ”Diabetes-Self-measurements” [5,7], and results from evaluations under the direction of SKUP, have showed that few of the self-monitoring glucose meters that were tested met the ISO-requirements. The results by the diabetics therefore have to be discussed towards a *modified* goal suggested by NOKLUS, with a total error of 25 %. This modified goal has wide, and not ideal, limits. The modified requirements for diabetics will be tightened up over time as the meters improve due to technological development.

Quality demands, adjusted to the diabetics self-measurements:

Ninety-five percent (95 %) of the individual glucose results shall fall within ± 1,0 mmol/L of the results of the comparison method at glucose concentrations < 4,2 mmol/L and within ± 25 % at glucose concentrations ≥ 4,2 mmol/L.

4. Materials and methods

4.1. Statistical terms and expressions

4.1.1. Precision

The common used terms within-series imprecision and between-series imprecision are often misinterpreted. Especially the terms between-series and between-day imprecision are often not precisely defined. In this report, the terms are replaced by the precisely defined terms *repeatability and reproducibility*. Repeatability is the agreement between the results of consecutive measurements of the same component carried out under identical measuring conditions (within the measuring series). Reproducibility is the agreement between the results of discontinuous measurements of the same component carried out under changing measuring conditions over time. The reproducibility includes the repeatability. The two terms are measured as imprecision and are expressed by means of the standard deviation (SD) or coefficient of variation (CV). Precision is descriptive in general terms (good, poor), whereas imprecision is an estimate, reported in the same unit as the analytical result (SD) or in % (CV). The imprecision will be summarised in tables.

4.1.2. Accuracy

Accuracy is the closeness of agreement between the result of one measurement and the true value. Inaccuracy is a measure of a single measurements deviation from a true value, and implies a combination of random and systematic error (analytical imprecision and bias). Inaccuracy, as defined by a single measurement, is not sufficient to distinguish between random and systematic errors in the measuring system. Inaccuracy can be expressed as total error. The inaccuracy will be illustrated by difference plots with quality goals for the total error shown as deviation limits in percent.

4.1.3. Trueness

Trueness is the agreement between an average value obtained from a large number of measuring results and a true value. Trueness is measured as bias (systematic errors). Trueness is descriptive in general terms (good, poor), whereas bias is the estimate, reported in the same unit as the analytical result or in %. The bias at different glucose concentration levels will be summarised in tables.

4.2. OneTouch Ultra

One Touch Ultra is a blood glucose monitoring system based on electrochemical technology. The system consists of a meter and dry reagent test strips designed for capillary blood glucose testing by people with diabetes or by health care professionals. The system is calibrated to report glucose plasma values. An electronic check is performed automatically when the meter is turned on by insertion of an OneTouch Ultra test strip. The system requires manual calibration, i.e. the user has to set code number in the meter display identical to the code number printed on the test strip vial. The test strip uses glucose oxidase enzyme chemistry. Glucose oxidase is highly specific for D-glucose. The glucose oxidase enzyme catalizes glucose oxidation yielding gluconolactone, resulting in the reduction of glucose oxidase. The OneTouch Ultra System incorporates this enzymatic assay with a redox (reduction-oxidation) chemical "mediator" (potassium ferricyanide) reaction to generate an electrical current proportional to the glucose concentration in the blood sample.

The test strips are packed in a plastic bottle with snap-top closure and desiccant. The system requires a blood volume of 1 µL and provides a result in 5 seconds. The meter has the capability of storing 150 results in memory and can calculate the average blood glucose for the last 14 and 30 days. OneTouch Ultra can be used for testing blood either from a fingertip or the arm. LifeScan recommends consulting health care professionals before testing on the arm. The OneTouch Ultra Soft adjustable lancet pen is used to form a drop of blood on the fingertip. If arm-testing, a special cap has to be used on the lancing device. The meter information can be downloaded to a computer through the meter's data port by using software and computer-cable from LifeScan. Technical data from the manufacturer is shown in table 1.

Table 1. Technical data from the manufacturer.

TECHNICAL DATA FOR ONE TOUCH ULTRA	
Ambient temperature	6 - 44º C
Sample volume	1 µl
Measuring time	5 s
Measuring range	1,1 - 33,3 mmol/L (20 - 600 mg/dL)
Hematocrit	30 – 55 %
Memory capacity	150 tests
Power supply	1×3V lithium battery supply (DL or CR2032)
Operating time	Approximately 1000 tests (1 year consumption)
Dimension	W= 57 mm, H= 79 mm, D= 21,5 mm
Weight	42,5 g (included the battery)

4.2.1. Product information, OneTouch Ultra

OneTouch Ultra blood glucose meter system
Manufactured by: LifeScan, Johnson & Johnson
Internet: http://www.LifeScan.com

Suppliers of OneTouch Ultra in Scandinavian countries:

Sweden:	Denmark:	Norway:
LifeScan Sweden	LifeScan Denmark	LifeScan Norway
Johnson & Johnson AB	Johnson & Johnson	Johnson & Johnson AB
Staffans väg 2	Blokken 39	Nesbruvn.75. Postboks 34
S-191 84 Sollentuna	DK-3460 Birkerød	N-1396 Billingstad
Sweden	Denmark	Norway
www.lifescaneurope.com/swe/	www.lifescaneurope.com/den/	www.lifescaneurope.com/nor/
Phone: +46 86 26 22 00	Phone: +45 45 94 28 00	Phone: +47 66 98 10 30

79 OneTouch Ultra blood glucose meters were used in this evaluation.
Serial no.SNG8777RT and serial no. RJS166BQT (called meter A and B) were used by the biomedical laboratory scientist under standardised and optimal conditions.
Attachment 1 gives serial numbers for the 77 meters that were used by the diabetics.

OneTouch Ultra teststrips:

Lot-no. 2537329	Expiry 2006-07
Lot-no. 2538128	Expiry 2006-08
Lot-no. 2561201	Expiry 2006-08

OneTouch Ultra Control Solution:

Lot-no. 4A2R07	Expiry 2006-01
Lot-no. 4A2R12	Expiry 2006-06

4.3. Designated comparison method

Definition
A designated comparison method is a fully specified method, which, in the absence of a reference method, serves at the common basis for the comparison of a field method.

Verifying of trueness
The results from SMBG-devices must be compared with a recognized comparison method. The comparison method should be a plasma method, hexokinase by preference. The method has to show traceability equivalent to that of an internationally accepted reference solution, such as the standards supplied by the National Institute of Standards & Technology, NIST. The NIST-standard SRM 965a with four levels of glucose concentrations was used in this evaluation. In addition, freshly frozen, human serum controls from NOKLUS with glucose concentrations at two levels were analysed. The NOKLUS-controls have target values determined with an isotope-dilution gas chromatography/mass spectrometry method at a Reference laboratory in Belgium; Laboratory for Analytical Chemistry, University of Gent, Belgium [8]. The results are summarized in chapter 6.1.2.

The designated comparison method in this evaluation
In this evaluation, the routine method for quantitative determination of glucose in human serum, plasma (lithium heparin) and urine at the Laboratory at Haraldsplass Diaconal Hospital was used as the designated comparison method. The method will be called *the comparison method* in this report. The comparison method is a photometric enzymatic method based on the method by Slein, utilising hexokinase and glucose-6-phosphate dehydrogenase enzymes. The method is implemented on the Advia 1650 Chemistry System from Bayer, with reagents and calibrators from Bayer. The Advia 1650 Chemistry System Glucose Hexokinase II method is a two-component reagent. Sample is added to Reagent 1, which contains buffer, ATP and NAD. Absorbance readings of the sample in Reagent 1 are used to correct for interfering substances in the sample. Reagent 2 is added, which initiates the conversion of glucose and the development of an absorbance at 340 nm. The difference between the absorbance in Reagent 1 and Reagent 2 is proportional to the glucose concentration. The measuring principle in the Advia 1650 is as follows: Glucose is phosphorylated by ATP in the presence of hexokinase. The glucose-6-phosphate that forms is oxidised in the presence of glucose-6-phosphate dehydrogenate causing the reduction of NAD to NADH. The absorbance of NADH is measured as an endpoint reaction at 340 nm.

Internal quality assurance of the Advia 1650 comparison method during the evaluation period
The Autonorm Human Liquid Control Solutions at two levels from Sero AS were part of all the measuring series for this evaluation. The controls were measured as the first and the last samples in all the series. The results are summarised in table 5.

4.3.1. Product information, comparison method

Designated comparison method Advia 1650
Manufactured by: Bayer AS
Serial no. CA 175524-196

Reagents
Bayer Glucose Hexokinase method II (B01-4597-01)
Lot-no. 0581X

Calibrator
Chemistry Cal Bayer
Lot-no. 179747 Expiry 2005-10 Reference value = 13.5 mmol/L

Internal control
Seronorm Autonorm Human Liquid 1 and 2, Sero AS
Liquid 1: Value = 5.2 ± 0,36 mmol/L Lot-no. NO3588 Expiry 2006-01
Liquid 2: Value = 15.0 ± 1.05 mmol/L Lot-no. MI4298 Expiry 2006-07

NOKLUS control
(ID-GCMS method; reference value from Laboratory for Analytical Chemistry, University of Gent, Belgium)
Level 1: Value = 3.20 ± 0,010 mmol/L
Level 2: Value = 7.78 ± 0,026 mmol/L

NIST standards
Standard Reference Material® 965a, National Institute of Standards & Technology
Level 1: Value = 1.918 ± 0.020 mmol/L
Level 2: Value = 4.357 ± 0.048 mmol/L
Level 3: Value = 6.777 ± 0.073 mmol/L
Level 4: Value = 16.24 ± 0.19 mmol/L

Blood sampling device
Accu-Chek SoftClix Pro: Lot-no. WIP 011
Accu-Chek SoftClix Pro lancets: Lot-no. WIP 45 G 3 Expiry 2008-12-31

Tubes used for sampling for the designated comparison method
Microvette CB 300 LH (litium-heparin) manufactured by Sarstedt AS
Lot-no. 4074301 Expiry 2007-11

Centrifuge used for samples for the designated comparison method
Heraeus Biofuge Pico
Serial no. 291323

4.4. Evaluation procedure

4.4.1. Model for the evaluation

The practical work with the evaluation was carried out during 10 weeks from April to June 2005 (from week number 17 to week number 26) at Innlandet Hospital, Gjøvik, in Norway. The practical work was done by Lise Walberg. She is a biomedical laboratory scientist.

The evaluation consisted of two parallel evaluations. One part of the evaluation was done by the biomedical laboratory scientist under standardised and optimal conditions. This part of the evaluation is done by laboratory educated personnel, completely according to the protocol and user manual after having received thoroughly training. All possibilities for disturbance of, and interference with, the measurements will be tried kept at a minimum. The evaluation under standardised and optimal conditions documents the quality of the system under best possible conditions. The other part of the evaluation was done by diabetics. In order to determine the analytical quality of OneTouch Ultra by the users, 77 diabetics tested their blood glucose using OneTouch Ultra. The diabetics were divided into two groups (random distribution). 39 diabetics were called in and received personal training in how to use the blood glucose meter, here called the "training group". 38 diabetics received the blood glucose meter and instructions by post, here called the "post group".
The reason for dividing the diabetics into a "training group and a "post group" is that this reflects the actual market situation regarding training when diabetics acquire blood glucose meters [2].
The model for the evaluation is shown in figure 1.

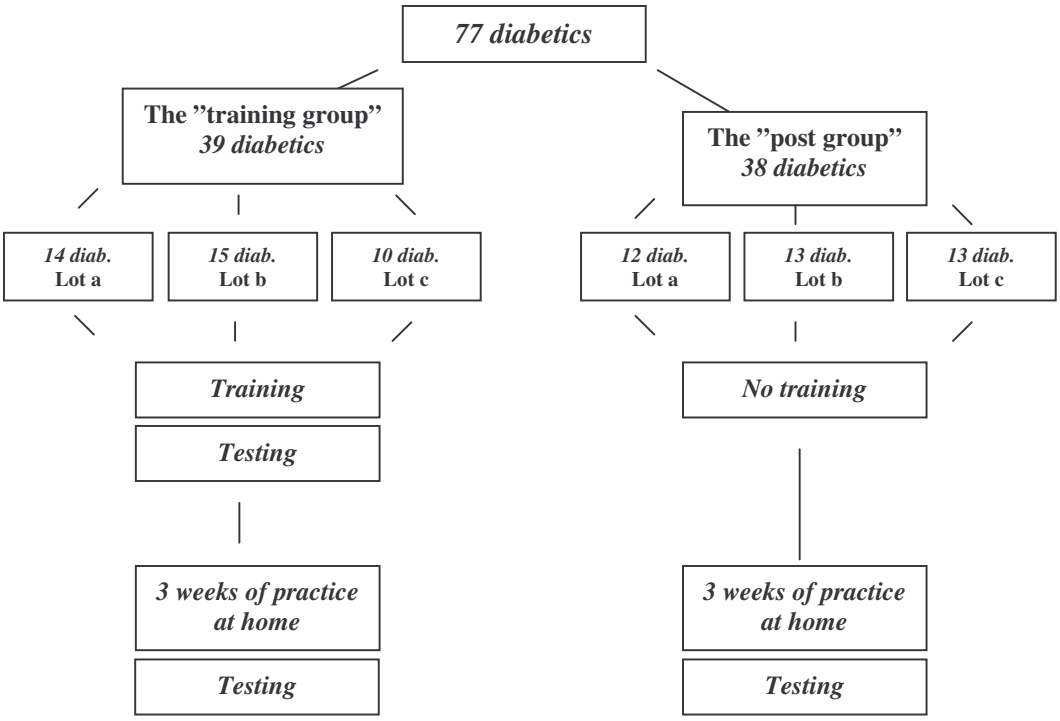

Figure 1. Model for the evaluation

All the diabetics could not participate in the user evaluation during the same weeks. The biomedical laboratory scientist had capacity to receive approximately 25-30 diabetics a week. Therefore the start-up was spread out over 4 weeks, and the final consultation consequently spread out correspondingly.

4.4.2. Recruiting of the diabetics

The OneTouch Ultra glucose meter was tested in use by 77 diabetics. The evaluation started with 85 diabetics, but due to illness and other different reasons only 77 diabetics completed. The diabetics were recruited through advertisement in the daily press and by mail inquiry sent to members of the local branch of the Norwegian Diabetes Association. The group of diabetics was representative for diabetics who carry out self-monitoring of blood glucose (SMBG). The group included diabetics from across a range of self-monitoring frequencies, i.e. diabetics who performed self-monitoring often (one or more times a day) and those who performed self-monitoring less frequently (once a week). None of the diabetics used OneTouch Ultra at the time, but at the end of the evaluation, at the final consultation, 6 diabetics answered that they used OneTouch/OneTouch Ultra/Ultra Smart/InDuo.
Characteristics of the diabetics in the group are shown in table 2.

Table 2. Characteristics of diabetics included in the evaluation (n=77).

		Diabetics
Total		77
Sex	Men	44
	Women	33
Age (years), median and range		54 (25 – 74)
Diabetes	Type 1	28
	Type 2	46
	Don't know	3
Treatment	Insulin	39
	Tablets	18
	Insulin and tablets	7
	Diet	8
	Unspecified	5
Frequency of SMBG	1 – 3 per month	4
	1 – 3 per week	15
	4 – 6 per week	5
	7 – 10 per week	10
	> 10 per week	33
	Doesn't measure	1
	Unspecified	9

Some of the diabetics used more than one SMBG-device at home, but only one device is registered here.
The SMBG-devices that the diabetics use regularly: Accu-Chek (2), Accu-Chek Compact (15), Accu-Chek Sensor/Accutrend Sensor (6), Ascensia Contour (5), Ascensia DEX/DEX2/Breeze (13), Ascensia Elite (2), OneTouch (1), OneTouch Ultra/Ultra Smart/InDuo (5), GlucoTouch (2), EuroFlash (2), MediSense Precision/Precision Xtra (7), MediSense Companion2 (1), FreeStyle/FreeStyle Mini (6), GlucoMen (1), Glucometer Elite (3), SoftSense (1), doesn't do SMBG (2) and unspecified (3).

4.4.3. The training group at the first consultation

The 39 diabetics selected to participate in a training programme were called in two and two at the time. They received the OneTouch Ultra device along with test strips, lancet pen, lancets, user manual, and an instruction letter with explanations regarding what to do with the OneTouch Ultra device during the period at home. The instruction letter is attached to the report (in Norwegian). See attachment 2. The responsibility for the training programme was undertaken by SKUP. Lise Walberg was in charge of the training of the diabetics, after having been trained herself by a representative from LifeScan.

Training programme
The training programme covered a simple demonstration of how to use OneTouch Ultra with an explanation of the display and error messages, insertion of the test strips, blood sampling and drawing of blood into the test strip, as well as precautions for storage and the shelf-life of test strips, etc. The training programme was standardised to make sure that all the diabetics received the same instruction.

Blood sampling
After having been trained, the 39 diabetics made duplicate blood glucose tests on OneTouch Ultra. These results were registered for the evaluation. Afterwards they brought the OneTouch Ultra blood glucose meter home to use the meter over a three-week period. After this period, they attended a final consultation and made two new duplicate blood glucose tests, which were registered.

4.4.4. The post group

The 38 diabetics in the "post group" received the OneTouch Ultra device by post, along with test strips, lancet pen, lancets, user manual and an instruction letter with explanations regarding what to do with the OneTouch Ultra device during the period at home. No training was given. They used the meter over a three-week period at home. After this period, they attended a consultation where two duplicate tests were done. The results of these tests were registered.

4.4.5. Use of OneTouch Ultra by the diabetics at home

The diabetics used OneTouch Ultra at home for three weeks. The length of this practice period ought not to exceed three weeks by more than a few days. Most users read the user manual at once when they receive the meter. As the diabetics should evaluate the user manual at the final consultation, it would be unfortunate if the practice period at home was too long. During the practice period the diabetics used OneTouch Ultra in addition to their own glucose meter and they continued to carry out self-measurements with their own meter as normal.

The first and the second week
The diabetics familiarised themselves with the new device during the first two weeks. Each diabetic used approximately 25 test strips to measure his/her blood glucose with OneTouch Ultra. They could choose when to do the measurements themselves. Fasting was not necessary. If more convenient to them, they could perform the measurement at the same time as they measured their blood glucose with their own meter.

The third week
During the third week the diabetics performed five measurements in duplicate on OneTouch Ultra on different days. The results were recorded on a provided form. They pricked a finger and made two consecutive measurements with blood from the same prick. If necessary they pricked another finger for the second measurement. They were free to choose when to perform the measurements, and it was not necessary to be fasting. They could choose whether to use the lancets provided for the evaluation, or the lancets they use ordinarily.

Internal quality control
The diabetics are not familiar with control solutions for self-measurements. Therefore they were not instructed to use control solution on OneTouch Ultra in the evaluation. To document correct functioning on the OneTouch Ultra-meters used by the diabetics during the test period, the biomedical laboratory scientist in charge of the practical work controlled the meters when the diabetics were called for the consultations.

4.4.6. The final consultation

Blood sampling
After the three week practice period at home, the 77 diabetics were called for, one by one, to a consultation. Each diabetic brought their assigned OneTouch Ultra meter and the remaining test strips to this consultation. They made duplicate blood glucose tests on OneTouch Ultra. These results were registered for the evaluation. Finally, a venous sample for hematocrit was taken.

The questionnaires
After all the blood samples were collected and the measurements on OneTouch Ultra were done, the diabetics filled out two questionnaires. The first questionnaire was about the user-friendliness of the OneTouch Ultra device, the second about the user-manual. The questionnaires (in Norwegian) are attached to the report. After the evaluation, the diabetics could choose whether to keep OneTouch Ultra or return it to the project.

4.4.7. Evaluation under standardised and optimal conditions

The biomedical laboratory scientist used two OneTouch Ultra blood glucose meters for the evaluation (meter "A" and meter "B"). Meter "A" was used for one lot of test strips for all measurements on all the diabetics. Meter "B" was used for the same three lots as distributed among the diabetics. In this way, the variation between the three lots, or more precisely, the agreement of the three lots to the comparison method, can be assessed. The number of samples for each lot of strips measured under standardised and optimal conditions is shown in table 3.

Table 3. The number of samples (n) for each lot of strips measured under standard and optimal conditions.

OneTouch Ultra		Lot 2537329 (n)	Lot 2538128 (n)	Lot 2561201 (n)
Meter A	1st consultation		39 x 2	
	2nd consultation		77 x 2	
Meter B	1st consultation*	27 x 2		12 x 2
	2nd consultation*	25 x 2	15 x 2	35 x 2
Total		52 x 2	130 x 2	47 x 2

* At two consultations the lot was not registered.

Blood sampling

Meter "A" and meter "B" were checked by means of the manufacturer's control solution every day they were used.

The blood sampling and analysis were done in the following order:

1. The biomedical laboratory scientist took a sample for the comparison method
2. The diabetic took duplicate samples for their assigned meter
3. The biomedical laboratory scientist took samples and analysed on meter "A", "B", "A", and "B"
4. The biomedical scientist took a new sample for the comparison method
5. The biomedical laboratory scientist measured internal quality control at the diabetic's meter

The duration of the sampling should not exceed 10 minutes.

The order of meter "A" and "B" was changed between each diabetic, but the blood samples for the comparison method were always taken first and last in accordance with ISO 15197. The biomedical laboratory scientist registered whether the diabetic had set the right or wrong calibration code in the blood glucose meter, used correct cleaning, drying, and skin puncture procedure, applied the blood sample correctly to the test strip, and otherwise followed manufacturer's instructions for performing a glucose meter test.

At the final consultation, i.e. after the period with use of OneTouch Ultra at home, a venous sample for hematocrit determination was taken. Hematocrit may influence blood glucose readings, especially in meters designed for self-monitoring. This also applies to OneTouch Ultra. In the package insert hematocrit from 30 – 55 % is recommended.

Handling of the samples for the comparison method
The samples for the comparison method were capillary taken using a Microvette Li-heparin tube from Sarstedt. The samples were centrifuged immediately for three minutes at 13 000 g, and plasma was separated into sample vials for Advia 1650. The samples were frozen directly as the plasma was separated and the plasma was stored at minus 80 °C. The samples were gathered and sent frozen in a quantity of about 80 samples at a time. The samples were transported under cold storage (minus 18 °C to minus 24 °C) to NOKLUS Centre in Bergen where they were kept at minus 80 °C until the analysis took place.

Analysing the samples for the comparison method
The samples were analysed with Advia 1650. The samples were thawed at NOKLUS Centre just before they were analysed. The first and the second sample for the comparison method, taken at the start and at the end of each blood sampling, reflect the stability of the glucose concentration during the sampling time. The difference between the first and the second comparative reading was not allowed to be more than 4 % or 0.22 mmol/L (per ISO 15197 Section 7.3.2.). If the difference between any paired results exceeded these limits, the samples were re-analysed. If the result from the re-run confirmed the difference, the difference was looked upon as a real difference in the glucose concentration in the two samples. Deviations > 10 % were regarded as not acceptable and such results would be excluded. As a consequence of this, the matching OneTouch Ultra results were excluded for accuracy and trueness calculations. Differences between 4 and 10% are included in the calculations. In spite of these deviations on the comparison method, the corresponding results at OneTouch Ultra still fulfil the quality goals. If the deviation between the two results was not confirmed by the re-run, the result from the re-run was used as the accepted result. Recommended minimum volume for analysis of glucose on Advia 1650 in this evaluation was 120 µL plasma.

The questionnaires
The biomedical laboratory scientist evaluated the user-friendliness of OneTouch Ultra and the user-manual. The biomedical laboratory scientist provided a description in the form of key words and looked for any defects and deficiencies or whether there was anything in the system that did not function optimally.

4.4.8. Evaluation of analytical quality

The following sets of data give the basis for the evaluation of the analytical quality:

1. Results from 39 diabetics in the "training group" who had participated in the training programme, but not practised using the blood glucose meter at home.
2. Results from the same diabetics after they had practised using OneTouch Ultra at home for three weeks.
3. Results from 38 diabetics in the "post group" who had not participated in the training programme, but who had practised using OneTouch Ultra at home for three weeks.
4. Results from 116 measurements under standardised and optimal conditions
5. Results from 116 measurements from the comparison method.

The results from the group with and without training were compared (group 2 and 3) and the results from the group with and without practise at home (group 1 and 2) were also compared. All the diabetic measurements were evaluated against the results achieved under standardised and optimal conditions. User-friendliness and user-manual were evaluated by means of questionnaires.
The three lots of test strips were distributed evenly between the diabetics in the group with and without training (random distribution in each group). Each lot was used by approximately 13 diabetics in each group (see figure 1).

5. Statistical calculations

5.1. Number of samples

77 diabetics completed the evaluation. The 39 diabetics in the "training group" met at two consultations and the 38 diabetics in the "post group" met at one consultation. Blood samples were taken at each consultation. This means that the total number of samples is
116 x 2 (duplicates) x 4 (meter A, meter B, diabetic's meter, comparison method) = 928 samples.

5.2. Statistical outliers

All results are checked for outliers according to Burnett [9], with repeated truncations. The model takes into consideration the number of observations together with the statistical significance level for the test. The significance level is often set to 5 %, so also in this evaluation. Where the results are classified according to different glucose concentration levels, the outlier-testing is done at each level separately. Statistical outliers are excluded from all calculations. Possible outliers will be commented on under each table.

5.3. Missing or excluded results

Besides the statistical outliers, some results are missing or excluded for other reasons. They are summarized and explained here:

- ID 57 at the first consultation and ID 100 at the final consultation had a difference > 10 % between the paired results on the comparison method. The difference was confirmed by a re-run. As a consequence of this, the results for ID 57 at the first consultation and the results for ID 100 at the final consultation are excluded when OneTouch Ultra is compared with the comparison method (accuracy and trueness). These results are included in the calculations regarding the imprecision at OneTouch Ultra because each set of duplicate measurements on OneTouch Ultra is completed in less then a minute.
- ID 100 at the final consultation is excluded from calculation regarding the effect of hematocrit because of a difference > 10 % between the paired results on the comparison method
- ID 108 had only one measurement on the assigned OneTouch Ultra at the final consultation. ID 108 is therefore excluded from the calculation of repeatability based on the diabetics' measurements.
- In calculation of repeatability based on diabetics' measurements at home some measurements had to be excluded. ID 67 had not done measurements at home. ID 60 had only 4 duplicated measurements. ID 15, ID 97, ID 132 and ID 135 had only one measurement at one day each, and ID 5 had only one measurement at two days. These results were excluded.

5.4. Calculations of imprecision based on duplicate results

Two capillary samples were taken of each diabetic to meter A, meter B, the diabetic's meter and to the comparison method at each consultation. The imprecision was calculated by use of paired measurements, based on the following formula:

$SD = \sqrt{\frac{\sum d^2}{2n}}$, d = difference between two paired measurements, n = number of differences

The assumption for using this formula is that there must be no systematic difference between the 1st and the 2nd measurement. Table 4 shows that there is no systematic difference in glucose concentration between the paired measurements on OneTouch Ultra in this evaluation (see comments below).

Table 4. No systematic differences between the 1st and the 2nd measurement. T-test for paired values.

		Glucose level mmol/L	Mean 1st measurement mmol/L	Mean 2nd measurement mmol/L	Mean difference 2nd – 1st measurement mmol/L	P	n
OneTouch Ultra	Meter A	< 7	5,3	5,4	0,11	0,004	36
		7 – 10	8,3	8,3	-0,04	0,525	45
		> 10	14,1	14,0	-0,12	0,442	33
	Meter B	< 7	5,3	5,4	0,07	0,097	35
		7 – 10	8,2	8,3	0,07	0,367	43
		> 10	13,7	13,7	0,02	0,904	33

Comments
The difference in glucose concentration between the first and the second measurement of the paired results is neglect able. Five of the six differences are not significant. At the glucose concentration level < 7 mmol/L at meter A there is a small and statistical significant difference, but the difference is of no importance here.

5.5. Calculation of trueness

To measure the trueness of the measurements on OneTouch Ultra, the average bias at three glucose concentration levels is calculated based on the results obtained under standardised and optimal measuring conditions. A paired t-test is used with the mean values of the duplicate results at the comparison method and the mean result at OneTouch Ultra meter A.

5.6. Calculation of accuracy

To evaluate the accuracy of the results at OneTouch Ultra, the agreement between OneTouch Ultra and the comparison method is illustrated in difference plots. In the plots the x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at OneTouch Ultra and the mean value of the duplicate results at the comparison method.

6. Results and discussion

6.1. Precision and trueness of the designated comparison method

6.1.1. The precision of the comparison method

The repeatability of the comparison method is shown in table 6 and table 7. The results are obtained with the SRM 965a standards supplied by the National Institute of Standards & Technology, NIST, and freshly frozen, human serum controls from NOKLUS. The repeatability is calculated as a combined CV %.

The reproducibility of the comparison method is shown in table 5. The results are obtained with the internal control solution at two levels of glucose concentrations. The controls were analysed in duplicate in the beginning and at the end of each series of samples, giving a total number of more than 100 results. In table 5 only the first result in each series is included.
All the results are shown in attachment 3.

Table 5. The comparison method – Reproducibility (results with internal control solutions).

Control Solution	Target value glucose (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Autonorm 1	5,2 ± 0,36	5,2	52	0	0,6 (0,5-0,7)
Autonorm 2	15,0 ± 1,05	15,1	52	0	0,6 (0,5-0,8)

Discussion
The precision of the comparison method is good. The repeatability is approximately 0,5 CV% (see table 6 and 7) and the reproducibility is less than 1 CV%.

6.1.2. The trueness of the comparison method

In order to demonstrate the trueness of the comparison method, the SRM 965a standards supplied by the National Institute of Standards & Technology, NIST, were analysed at several occasions during the evaluation period. SRM 965a consists of ampoules with human serum with certified concentrations and uncertainties for glucose at four concentrations. The SRM 965a materials cover a glucose concentration range from 1,9 to 16,2 mmol/L.

The agreement between the comparison method and the NIST-standards is shown in table 6.

Table 6. The comparison method – Standard Reference Material (SRM 965a) measured on the comparison method during the evaluation period.

SRM 965a	Date	Certified glucose concentration mmol/L (uncertainty)	Mean value glucose (mmol/L)	n	Combined CV % (95 % CI)	% deviation from target value
Level 1	14.06.05	**1,918** (1,898 - 1,938)	1,98	5	0,6 (0,4 - 1,1)	+3,3
	04.07.05		1,97	6		+2,8
	Total		**1,98**	**11**		**+3,0**
Level 2	14.06.05	**4,357** (4,309 - 4,405)	4,43	5	0,5 (0,4 - 0,9)	+1,7
	06.07.05		4,46	6		+2,4
	Total		**4,45**	**11**		**+2,1**
Level 3	15.06.05	**6,777** (6,704 - 6,850)	6,94	5	0,3 (0,2 - 0,5)	+2,3
	06.07.05		6,97	6		+2,8
	Total		**6,95**	**11**		**+2,6**
Level 4	15.06.05	**16,24** (16,05 - 16,43)	16,44	5	0,4 (0,3 - 0,7)	+1,2
	11.07.05		16,48	6		+1,5
	Total		**16,46**	**11**		**+1,4**

Table 6 reveals that glucose results at Advia 1650 are approximately 2 % higher than the target values from NIST. Even though the obtained results are only just outside the given uncertainty limits for the Reference Material, it was decided that all results from Advia should be adjusted according to the findings presented in the table above. The adjustment was done by means of the following regression equation ($R^2 = 1,0$):

$y = 0,9892x – 0,0555$

From now on in this report, whenever any result from Advia is presented, the result has already been adjusted according to this equation.

To verify the trueness of the comparison method, freshly frozen, human serum controls from NOKLUS with glucose concentrations at two levels were analysed. The NOKLUS-controls have target values determined with an isotope-dilution gas chromatography/mass spectrometry method at a Reference laboratory in Belgium; Laboratory for Analytical Chemistry, University of Gent, Belgium [8].
The agreement with target values from the reference laboratory in Belgium is shown in table 7.

Table 7. The comparison method – Control samples from NOKLUS's External Quality Assessment program, measured on the comparison method during the test period.

Control solution	Date	Target value from Reference lab. in Belgium (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	Combined CV% (95% CI)	% deviation from target value
NOKLUS 1	10.06.05	3,20	3,15	7		0,4 (0,3-0,6)	-1,5
	16.06.05		3,15	6			-1,4
	28.06.05		3,15	6			-1,6
	Total		**3,15**	**19**	**0**		**-1,5**
NOKLUS 2	10.06.05	7,78	7,78	7		0,3 (0,2-0,4)	-0,3
	17.06.05		7,72	6			-0,8
	29.06.05		7,72	6			-0,8
	Total		**7,73**	**19**	**0**		**-0,6**

Discussion
The trueness of the comparison method is very satisfactory.

6.2. Precision, trueness and accuracy of OneTouch Ultra

6.2.1. Precision of OneTouch Ultra

The OneTouch Ultra meters in the user evaluation were checked by the biomedical laboratory scientists with the manufacturer's control solution. All of the results were inside the limits of the control.

The results from the calculations of the precision are discussed at the end of this chapter.

Repeatability under standardised and optimal measuring conditions
The repeatability obtained under standardised and optimal conditions with capillary blood samples is shown in table 8. The table gives the results from the biomedical laboratory scientists' measurements at the first and the final consultation together. Raw data is shown in attachment 6.

Table 8. OneTouch Ultra – Repeatability (results with patient samples) measured under standard and optimal conditions.

OneTouch Ultra	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A	< 7	5,3	38	0	3,7 (3,1 – 4,8)
Meter B	< 7	5,3	37	3*	3,4 (2,7 – 4,4)
Meter A	7 – 10	8,3	45	0	3,7 (3,1 – 4,7)
Meter B	7 – 10	8,3	43	0	4,3 (3,5 – 5,4)
Meter A	> 10	14,0	33	0	4,5 (3,6 – 5,9)
Meter B	> 10	13,7	33	0	4,4 (3,5 – 5,8)

* The 3 outliers are excluded one by one by three truncations.

Repeatability obtained by the diabetics
The repeatability obtained by the diabetics with capillary blood samples is shown in table 9. The table gives the results from the measurements at the first and second consultation for the "training group", the consultation for the "post group", together with the results they obtained at home. The results obtained at home of course have a higher degree of uncertainty since it is impossible to control what has actually been done. The reporting of these home-values also reveals that some of the diabetics did not quite understand "the recipe" on how to perform and report the five duplicate measurements they were supposed to carry out according to the written instruction they had received.

Raw data from the diabetics' measurements at NOKLUS is shown in attachment 7.
Raw data from the diabetics' measurements at home is shown in attachment 8.

Table 9. OneTouch Ultra – Repeatability (results with patient samples) measured by the "training group" and the "post group".

OneTouch Ultra	Consultation	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
At NOKLUS	1st training	< 7	5,0	13	0	4,6 (3,3 – 7,6)
	2nd training	< 7	5,1	8	0	3,9 (2,6 – 8,0)
	Post group	< 7	5,5	10	0	2,1 (1,5 – 3,9)
At home		< 7	5,5	132	1	5,8 (5,2 – 6,6)
At NOKLUS	1st training	7 – 10	8,2	20	0	5,8 (4,4 – 8,5)
	2nd training*	7 – 10	8,5	13	0	6,1 (4,4 – 10,1)
	Post group	7 – 10	8,5	14	0	4,3 (3,1 – 7,0)
At home		7 – 10	8,4	147	0	6,0 (5,4 – 6,7)
At NOKLUS	1st training	> 10	14,0	6	0	5,5 (3,4 – 13,4)
	2nd training	> 10	14,1	17	0	5,2 (3,9 – 7,9)
	Post group**	> 10	14,1	13	1	2,4 (1,7 – 3,9)
At home ***		> 10	13,5	89	2	9,6 (8,3 – 11,2)

* ID 108 is excluded because of missing duplicate results.
** 1 outlier is excluded.
** 14 home measurements are missing and 3 outliers among the home measurements are excluded.

As mentioned above the results obtained at home have a higher degree of uncertainty. At the highest glucose level at the home measurements, no results were outliers according to Burnett. Nevertheless, two results were chosen to be excluded as outliers since the difference between the two duplicates were large (-7,5 and -6,9 mmol/L).

Reproducibility with Internal Quality Control
The results for reproducibility are obtained with the OneTouch Ultra Control Solution. The measurements are carried out on meter A and B during the whole evaluation period and at all the meters in use by the diabetics. All the control measurements are done by the biomedical laboratory scientist. The control measurements on the diabetics' meters were done with the test strips that were distributed to each diabetic. The control solution was kept at NOKLUS during the evaluation period.

The reproducibility of OneTouch Ultra at meter A and B is shown in table 10.
The reproducibility at all the meters of the diabetics is shown in table 11.
Raw data is shown in attachment 5.

Table 10. OneTouch Ultra – Reproducibility (results with OneTouch Ultra Control Solution) measured by the biomedical laboratory scientist on meter A and meter B.

OneTouch Ultra	Lot of strips	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A	2538128	5,3 – 7,2	6,7	22	0	4,1 (3,1 – 5,8)
Meter B	2537329	5,4 – 7,3	6,8	11	0	5,2 (3,7 – 9,2)
	2538128	5,3 – 7,2	6,7	7	0	2,6 (1,6 – 5,6)
	2561201	5,4 – 7,3	6,7	8	0	3,8 (2,5 – 7,8)

Table 11. OneTouch Ultra – Reproducibility (results with OneTouch Ultra Control Solution) measured by the biomedical laboratory scientist on the diabetics' meters.

OneTouch Ultra	Lot of strips	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
1st consultation*						
The diabetics' meters	2537329	5,4 – 7,3	6,7	12	0	3,5 (2,5 – 6,0)
	2538128	5,3 – 7,2	6,7	15	0	3,2 (2,4 – 5,1)
	2561201	5,4 – 7,3	6,8	9	0	2,8 (1,9 – 5,4)
2nd consultation**						
The diabetics' meters	2537329	5,4 – 7,3	6,9	25	0	4,0 (3,1 – 5,5)
	2538128	5,3 – 7,2	6,8	28	0	3,9 (3,1 – 5,3)
	2561201	5,4 – 7,3	6,9	21	1***	3,1 (2,4 – 4,5)

* ID 19, ID 63 and ID 69 are missing QC-results.
** ID 72 is missing QC-result. ID 130 had wrong code when analysing QC and is excluded.
*** The reason for the outlier is that the diabetic's box with test strips had got some jam in it.

Discussion

The precision at OneTouch Ultra is acceptable. The repeatability obtained under standardised and optimal conditions is approximately 4 %. The repeatability obtained at NOKLUS by the diabetics is acceptable with a CV between 2 and 6 %. Table 9 shows that measurements done by the post group surprisingly have a *better* repeatability than measurements done by the training group. This has also been seen in some evaluations done by SKUP earlier. This result indicates that OneTouch Ultra is a robust meter, easy to use, and that training therefore is not essential for a good result. This finding can also be explained by the fact that the diabetics in the post group had to take more responsibility themselves because they did not get any training. They have to read the instructions more carefully in order to understand what to do and how to do it.

The reproducibility at OneTouch Ultra meter A and B was good when measured with an internal control solution. The CV was approximately 4 %.

6.2.2. Trueness

The trueness of OneTouch Ultra is calculated from the results done by the biomedical laboratory scientist at the final consultation (the "training group" and the "post group") and is shown in table 12.

Table 12. Mean difference between OneTouch Ultra and the comparison method. Results under standardised and optimal conditions from the final consultation.

	< 7 mmol/L		**7 – 10 mmol/L**		**> 10 mmol/L**	
	The comparison method	**Meter A**	**The comparison method**	**Meter A**	**The comparison method**	**Meter A**
Mean glucose, mmol/L	5,4	5,1	8,6	7,8	13,6	12,7
Mean deviation from the comparison method, mmol/L (95 % CI)	-0,3 (-0,4 – (-0,2))		-0,7 (-0,9 – (-0,6))		-0,9 (-1,1 – (-0,6))	
n	16		26		33	
Outliers	0		0		1	
p-value	<<0,05		<<0,05		<<0,05	

* ID 100 had a difference > 10 % between the paired results at the comparison method and is excluded.

Discussion

Table 12 shows that meter A shows significantly lower glucose values than the comparison method at all three levels. The difference is between -0,3 and -0,9 mmol/L, but the results still fulfil the quality goal set by ISO.

6.2.3. Accuracy

To evaluate the accuracy of the results at OneTouch Ultra, the agreement between OneTouch Ultra and the comparison method is illustrated in two difference plots. The difference plots give a picture of both random and systematic deviation and reflect the total measuring error at OneTouch Ultra. The total error is demonstrated for the first measurements of the paired results, only. At meter A only one lot of test strips were used. At meter B three different lots were used. The same three lots were randomly distributed between the diabetics.

The limits in the plots are based upon the quality goals discussed in a previous chapter of this report. Under standardised and optimal measuring conditions the ISO-goal at 20 % is used. For the diabetics' self-measurements the "adjusted ISO-goal" at 25 % is used.

The accuracy, OneTouch Ultra meter B, under standardised and optimal measuring conditions, with the first measurements at the final consultation is shown in figure 2.
The accuracy, OneTouch Ultra, as measured by the diabetics with the first measurement at the final consultation is shown in figure 3.
The accuracy is summarised in table 13 and discussed afterwards.

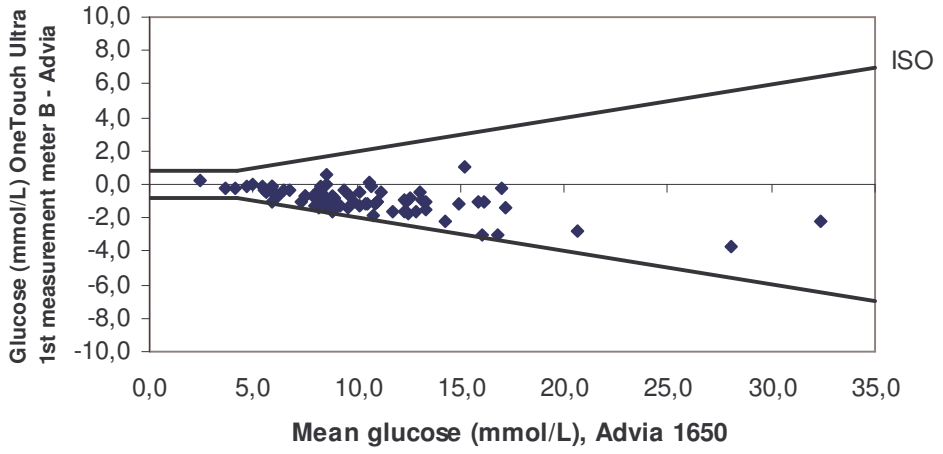

Figure 2. Accuracy. OneTouch Ultra meter B (three lots of test strips) under standardised and optimal measuring conditions at the final consultation. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at OneTouch Ultra and the mean value of the duplicate results at the comparison method. n = 76.

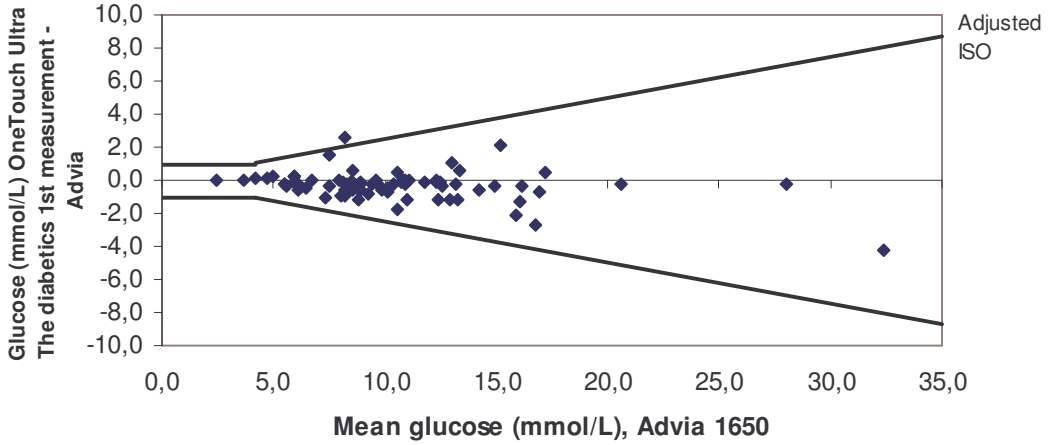

Figure 3. Accuracy. The diabetics' self-measurements at the final consultation. Three lots of test strips.
The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at OneTouch Ultra and the mean value of the duplicate results at the comparison method. n = 76.

Table 13. Total error of OneTouch Ultra results compared to the comparison method. Percentage OneTouch Ultra results within the limits.

Measurements done by	Consultation	Meter	n	Number of results (%)			Shown in figure
				< ADA (< ± 10 %)	**< ISO** < ± 20 % (and < ± 0,83 mmol/L at consentrations ≤ 4,2)	**< "adjusted ISO"** < ± 25 % (and < ± 1,0 mmol/L at consentrations ≤ 4,2)	
Biomedical laboratory scientist	1st	A 1st measurement	38	71	100		
		B 1st measurement	38	74	97,4		
Biomedical laboratory scientist	2nd	A 1st measurement	76	66	100		
		B 1st measurement	76	59	100		2
Diabetics at NOKLUS	1st	1st measurement	38	82	100	100	
	2nd	1st measurement	76	84,2	97,4	98,7	3

- ID 57 at the first consultation and ID 100 at the final consultation had a difference > 10 % between the paired results on the comparison method and are excluded.

Discussion

Figure 2 shows that all the results obtained under standardised and optimal measuring conditions are within the ISO-limits. The summing up in table 13 shows that all the first measurements at the first and the final consultation are within the ISO-limits. Figure 3 shows that the diabetics' first self-measurements at the final consultation fulfil the "adjusted ISO-goal". The results also fulfil the ISO-goal, as shown in table 13. 97,4 % of the results are within the ISO-goal and 98,7 % are within the "adjusted ISO-goal".

Conclusion

The OneTouch Ultra device fulfils the quality goals set in the ISO 15197 when used under standardised and optimal conditions. The quality goals are also met by the measurements of the diabetics.

6.3. Variation between three lots of test strips

All the measurements on meter A were performed with one lot of test strips. The measurements on meter B were performed with three different lot numbers of test strips, on three different groups of diabetics. The three lots can not be compared with each other because the mean glucose concentrations in the three groups of diabetics are different. To measure the variation between the three lots, all the mean glucose results at OneTouch Ultra obtained under standardised and optimal conditions at meter B were compared with the mean of the paired values from the comparison method (paired t-test). The results are shown in table 14.

Table 14. Variation between three lots of test strips. T-test for paired values between three lots at meter B and the comparison method under standardised and optimal conditions at the final consultation.

	The comparison method	**Meter B Lot 2537329**	**The comparison method**	**Meter B Lot 2538128**	**The comparison method**	**Meter B Lot 2561201**
Mean glucose, mmol/L	9,8	9,0	9,5	8,9	10,6	9,7
Mean deviation, mmol/L OneTouch Ultra - The comparison method (95 % CI)	-0,8 (-1,0 – (-0,6))		-0,6 (-0,9 – (-0,4))		-0,9 (-1,3 – (-0,6))	
n	24		15		33	
Outliers	1		0		0	
p-value	<<0,05		<<0,05		<<0,05	

- ID 100 had a difference > 10 % between the paired results on the comparison method and is excluded.
- Missing lot.no at three consultations, these results are excluded.

Discussion

The differences between the comparison method and all the three lots are statistically significant. The three lots gives significantly lower values than the comparison method. In spite of these systematic deviations, the results attain the quality goal set in ISO 15197.

7. Effect of hematocrit

The package insert of OneTouch Ultra test strips states that the glucose concentrations are not affected by hematocrit values between 30 and 55 %. To measure the effect of hematocrit at OneTouch Ultra, a venous sample was taken of the diabetics (voluntary) at the second consultation. All the diabetics were willing to have a sample for hematocrit taken.

The measurements on OneTouch Ultra are performed under standardised and optimal measuring conditions. The glucose concentration range in the samples was from 2,5 to 28,0 mmol/L. The hematocrit range was 32 – 50%.

The effect of hematocrit is shown in figure 4 and figure 5. The x-axis in the plots shows the hematocrit value and the y-axis shows the difference in glucose concentration between OneTouch Ultra and the comparison method (OneTouch Ultra – the comparison method). In figure 4 the difference in glucose concentration is shown in mmol/L, and in figure 5 the difference is shown in %. Raw data is shown in attachment 9.

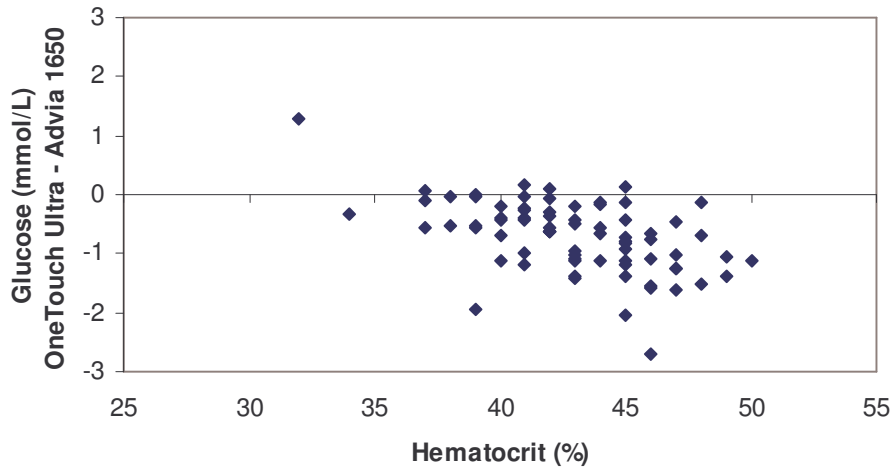

Figure 4. The effect of hematocrit at glucose measurements (in mmol/L) at OneTouch Ultra under standardised and optimal conditions. The x-axis shows the hematocrit value in %. The y-axis shows the difference in glucose concentration between OneTouch Ultra and the comparison method in mmol/L. n= 75

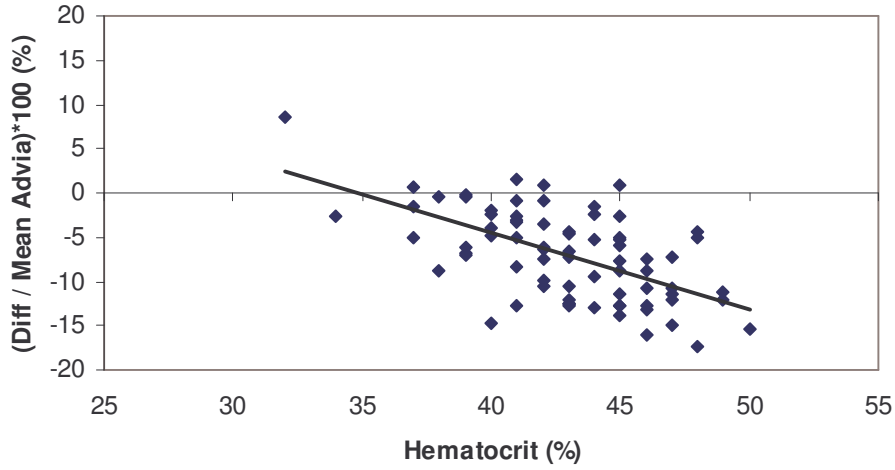

Figure 5. The effect of hematocrit at glucose measurements on OneTouch Ultra under standardised and optimal conditions. The x-axis shows the hematocrit value in %. The y-axis shows the difference in glucose concentration between OneTouch Ultra and the comparison method (OneTouch Ultra – the comparison method) in percent. n=75

- ID 100 had a difference > 10 % between the paired results on the comparison method and is excluded.
- Result from one diabetic showed big difference between OneTouch Ultra and the comparison method (-4,4 mmol/L). This result is excluded from the calculation.

Discussion

Glucose measurements on OneTouch Ultra are affected by the hematocrit values of the samples. The trend-line in figure 5 shows that glucose values at OneTouch Ultra are over-estimated when the hematocrit is below 30 %. With hematocrit values over approximately 40 % the glucose values are under-estimated. In spite of the hematocrit effect, the glucose results still fulfil the quality goal set by ISO.

8. Practical points of view

Questionnaires

Each diabetic filled out a questionnaire about the user-friendliness and a questionnaire about the user manual of OneTouch Ultra when they attended the final consultation (n = 77). Some diabetics needed assistance in filling out the questionnaires.

Questionnaire about the user-friendliness (in Norwegian), see attachment 10.
Questionnaire about the user manual (in Norwegian), see attachment 11.

8.1. Evaluation of user-friendliness of OneTouch Ultra

The questionnaire about the user-friendliness had eight questions concerning OneTouch Ultra and one question concerning the OneTouch Ultra Soft lancet pen. In addition, each diabetic should give the name of the blood glucose meter he/she uses ordinarily on the same questionnaire.
Table 15 summarizes six questions where the diabetics were asked to rank the answers on a scale from 1 to 6, where 1 is difficult and 6 is simple. The mean is 5,3 and 5,7 on the questions about inserting a strip into the meter and about filling the strip with blood, respectively. This indicates that the diabetics seemed satisfied with the use of the test strip.
The diabetics also seemed satisfied with use of the meter. The mean is between 5,1 and 5,8 on the questions about coding the meter, reading the figures in the display, and operating the meter, all in all. Regarding OneTouch Ultra Soft lancet pen the mean is 5,5, which indicates that the diabetics were satisfied with the lancet pen, too. The answers to these questions are summarized in table 15 and 16.

Table 15. OneTouch Ultra - Questions about the meter and about OneTouch Ultra Soft lancet pen

Questions about OneTouch Ultra and about OneTouch Ultra Soft lancet pen		mean	range	Not answered (% of total)	Total number
How will you rank the following questions on a scale from 1 to 6, where 1 is difficult and 6 is simple:	1. To insert a strip into the meter	5,3	1 – 6	3	77
	2. To fill the strip with blood	5,7	3 – 6	3	77
	3. To code the meter	5,1	1 – 6	6	77
	4. To read the figures in the display	5,8	3 – 6	4	77
	5. All in all, to operate the meter	5,4	1 – 6	3	77
	6. To operate OneTouch Ultra Soft lancet pen	5,5	1 – 6	13	77

Table 16 shows the answers to the last question about OneTouch Ultra. 4 % of the diabetics answered that they had technical problems with the meter during the testing period. Written comments indicate that these problems were not technical ones.

Table 16. OneTouch Ultra – Questions about the meter.

Question about OneTouch Ultra	Yes (%)	No (%)	Not answered (%)	Total number
Did you have any technical problems with the meter during the testing period?	4	90	6	77

Positive comments
62 diabetics reported one or more advantages with OneTouch Ultra. The reported advantages are distinctly grouped as follows:
1. simple operating of the meter (20)
2. the meter/strip needs little blood sample volume (10)
3. the meter has short measuring time (42)
4. the small size of the meter (17)
5. to read the figures in the display/good display (10)
6. practical carrying case (3)
7. the meter can be used without taking it out of the carrying case (1)

Negative comments
40 diabetics reported one or more disadvantages with OneTouch Ultra. 17 of the diabetics reported disadvantage with the test strips. Some of the diabetics indicated that it is difficult to get the strips out of the bottle and others indicated that it is more convenient with individually packed test strips. 16 of these 17 diabetics usually use meters with drums or single-packed test strips. The other reported disadvantages are not distinctly grouped. 4 diabetics mean it's a disadvantage that the meter has to be coded. One diabetic mentions that it's an edge inside the meter which sometimes can be hit by the strip, and another diabetic would suggest that the place where the strip is to be placed, should be marked with brighter colour and therefore make it easier for weak-sighted.

8.2. Evaluation of the user manual for OneTouch Ultra

On the questionnaire about the user manual each diabetic first was asked whether he/she had used the manual. If not, they were to ignore the rest of the questions in the questionnaire.

Table 17 shows that 94 % of the diabetics had used the user manual, i.e. 72 of the 77 diabetics that participated in the study. 97 % answered they were satisfied with the description of how to perform a blood glucose measurement with this meter. 3 % of them thought the manual had essential shortcomings. One of the diabetics wants a list with cue words. 97 % of the diabetics were quite satisfied with the user manual.

Table 17. OneTouch Ultra – Questions about the user manual.

Questions about the user manual	Yes (%)	No (%)	Not answered (%)	Number
Have you been reading in the user manual?	94	5	1	77
If yes, did you read the entire user manual?	56	32	13	72
And/or did you consult the user manual when needed?	60	6	35	72
1. Are you satisfied with the description of how to perform a blood glucose measurement with this meter?	97	3	0	72
2. Do you think the user manual has essential shortcomings?	3	94	3	72
3. All in all, are you satisfied with the user manual?	97	1	1	72

The biomedical laboratory scientist agreed with the diabetics in most of their answers. She thought the meter was small and easy to bring along, it was fast to get a result, easy to use and easy to see whether the test strip was filled or not. Her negative comments were, as the diabetics', about the test strips. She thought they sometimes could be difficult to get out from the box and that they sometimes filled slowly. She detected that the meter sometimes started to measure before the test strip was completely filled and she felt that the result from such measurements were too high in proportion to the paired result. By these occasions a new test was always performed. The biomedical laboratory scientist had been reading the entire user manual and was satisfied with the manual.

9. References

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10. Attachments

1. Serial numbers, OneTouch Ultra meters
2. Information letter to the diabetics (in Norwegian)
3. Raw data, internal quality control, Advia
4. Raw data, OneTouch Ultra results under standardised conditions, meter A and B
5. Raw data, OneTouch Ultra results, the diabetics measurements at NOKLUS
6. Raw data, OneTouch Ultra results, the diabetics measurements at home
7. Raw data, internal quality control, OneTouch Ultra
8. Raw data, Advia results, diabetics
9. Raw data, hematocrit
10. Questionnaire, user-friendliness (in Norwegian)
11. Questionnaire, user manual (in Norwegian)

Attachments with raw data are included only in the report to LifeScan, Johnson & Johnson.