ONETOUCH® GlucoTouch™

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/2005/40

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

Summary

Background
OneTouch GlucoTouch is a meter designed for glucose self-measurements by diabetic patients. The meter is produced and supplied in Scandinavia by LifeScan. OneTouch GlucoTouch was launched onto the Norwegian market in 1996.

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 diabetic patients. The evaluation of OneTouch GlucoTouch is done under the direction of SKUP during the spring of 2005.

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

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

Materials and methods
82 diabetic patients took part in the evaluation. 43 participants had two consultations (the "training group") and 39 participants had one consultation (the "postgroup"). At the first consultation the "training group" was given a standardised training about the OneTouch GlucoTouch device before they did a finger prick and performed two measurements on the meter. The biomedical laboratory scientist also took capillary samples of the diabetic patients and measured twice at OneTouch GlucoTouch. In addition, two capillary samples were taken to a designated comparison method. The postgroup received OneTouch GlucoTouch 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 final 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 GlucoTouch.

Results

- OneTouch GlucoTouch shows acceptable precision. The CV is < 5 % under standardised and optimal measuring conditions and between 3 and 7 % when the measurements are performed by diabetic patients.
- 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 diabetic patients, OneTouch GlucoTouch also shows good results. 99 % of these results are within the quality goals set in ISO 15197 and 100 % are within the "adjusted ISO-goal".
- Two of the three lots of test strips that were used showed significantly higher values than the comparison method, and one lot shows significant lower values than the comparison method. All the lots are within the ISO-limits.

- Glucose measurements on OneTouch GlucoTouch seem to be affected by the hematocrit values between 32 – 55 %. Hematocrit outside this range has not been tested.
- The diabetic patients summarise the OneTouch GlucoTouch device as easy to use. As a whole they were pleased with the device. The patients that had used the user manual were satisfied with the manual.

Conclusion

Glucose measurements on OneTouch GlucoTouch 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 diabetic patients are also within the ISO-goal. The glucose results in this evaluation are affected by hematocrit as described in the package insert. The users say that the OneTouch GlucoTouch device is easy to use and they are 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 diabetic patients.

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 GlucoTouch. In October 2004 SKUP gave a written offer, and late in December 2004 a preliminary suggestion regarding how to organise the evaluation was sent. After some discussions, the protocol for the evaluation of OneTouch GlucoTouch 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 GlucoTouch system was launched onto the Norwegian market in 1996. SKUP carried out the user-evaluation of OneTouch GlucoTouch 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*"[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
- An examination of analytical quality among approximately 80 diabetics
- An examination of agreement between OneTouch GlucoTouch 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 teststrips
- An examination to see if hematocrit interferes with the measurements
- An evaluation of user-friendliness of OneTouch GlucoTouch
- An evaluation of the user-manual of OneTouch GlucoTouch

The blood sampling of the diabetics and the measurements on OneTouch GlucoTouch under standardised and optimal conditions, were done by Lise Walberg and Kjersti Hveding, biomedical laboratory scientists and laboratory consultants, 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 Åse Hirsch-Nilsen, 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 GlucoTouch 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 GlucoTouch 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 the 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 GlucoTouch

OneTouch GlucoTouch is a blood glucose monitoring system based on reflectometric 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. The system requires calibration by the user. Code numbers are used to calibrate meters with the test strips to ensure proper operation of the system. The user has to make sure that the code number displayed by the meter when the meter is activated matches the code number printed on the test strip package. An electronic check is performed automatically by pressing a button. The test strip chemistry is glucose oxidase.

When a drop of blood is applied to the pink square of a test strip, glucose in the blood reacts with the reagents on the test strip. Glucose oxidase present in the reagent enables this reaction and provides specificity for glucose. Gluconic acid and hydrogen peroxide are produced from this reaction. The enzyme peroxidase then causes the hydrogen peroxide to react with dyes in the reagent to produce a blue colour when combined with oxygen. This blue colour is visible through the confirmation dot on the back of the test strip and is read by the meter. The darker the blue colour, the higher the glucose level.

The test strips are packed in a plastic bottle with a screw-cap and desiccant. The system requires a blood volume of at least 5 µL. A confirmation dot turns completely blue when enough blood is applied. The result is presented in approximately 30 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. When analysing a OneTouch GlucoTouch Control Solution, the meter has to be told that it is a control. The Penlet Plus adjustable lancing device is used to form a drop of blood on the fingertip. The OneTouch Diabetes Management software is available to download the meter's information to a computer through the meter data port. Technical data from the manufacturer is shown in table 1.

Table 1. Technical data from the manufacturer

TECHNICAL DATA FOR ONETOUCH GLUCOTOUCH	
Ambient temperature	10 – 35 °C
Sample volume	≥ 5 µL
Measuring time	Approximately 30 seconds
Measuring range	0 – 27,8 mmol / L
Hematokrit	25 – 60 %
Memory	150 tests
Power supply	2 × AAA batteries
Operating time	Approximately 1100 tests
Dimensions	W= 89 mm, H= 61 mm, D= 20 mm
Weight	108 g (included the batteries)

4.2.1. Product information, OneTouch GlucoTouch

OneTouch GlucoTouch blood glucose meter system
Manufactured by: LifeScan, Johnson & Johnson
Internett: http://www.lifescaneurope.com/nor/produkter/teststrimler/glucotouch/

Suppliers of OneTouch GlucoTouch 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

During this user-evaluation 86 GlucoTouch blood glucose meters were used.
Serial no. L1142RA00795 (Oslo), L3342RA00072 (Gjøvik) (called meter A) and serial no. L3342RA00070 (Oslo), L0132RA01280 (Gjøvik) (called meter B) were used by the biomedical laboratory scientists under the standardised and optimal conditions.
Attachment 1 gives serial numbers for the 82 meters used by the diabetics.

OneTouch GlucoTouch blood glucose test strips:

Lot-no. A-268518A	Expiry 2006-04
Lot-no. A-271808D	Expiry 2006-07
Lot-no. A-268514A	Expiry 2006-04

OneTouch GlucoTouch Control Solution:

Lot-no. 5D2R05	Expiry 2006-11

UltraSoft with FinePoint lancets (25G)

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

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

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

Centrifuge used for samples for the designated comparison method:
Heraeus Biofuge Pico, Serial no. 291323 (Gjøvik)
Eppendorf Centrifuge Minispin Plus, Serial no. 5453 016501 (Oslo)

4.4. Evaluation procedure

4.4.1. Model for the evaluation

The practical work with the evaluation was carried out during 7 weeks from May to June 2005 (from week number 18 to week number 25) at two hospitals in Norway. The practical work was done by Lise Walberg (Innlandet Hospital, Gjøvik) and Kjersti Hveding (Ullevål Hospital, Oslo). They are biomedical laboratory scientists.

The evaluation consisted of two parallel evaluations. One part of the evaluation was done by two biomedical laboratory scientists 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 interferences 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 GlucoTouch by the users, 82 diabetics tested their blood glucose using OneTouch GlucoTouch. The diabetics were divided into two groups (random distribution). 43 diabetics were called in and received personal training in how to use the blood glucose meter, here called the "training group". 39 diabetics received the blood glucose meter and instructions by post, here called the "postgroup".
The reason for dividing the diabetics into a "training group and a "postgroup" 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.

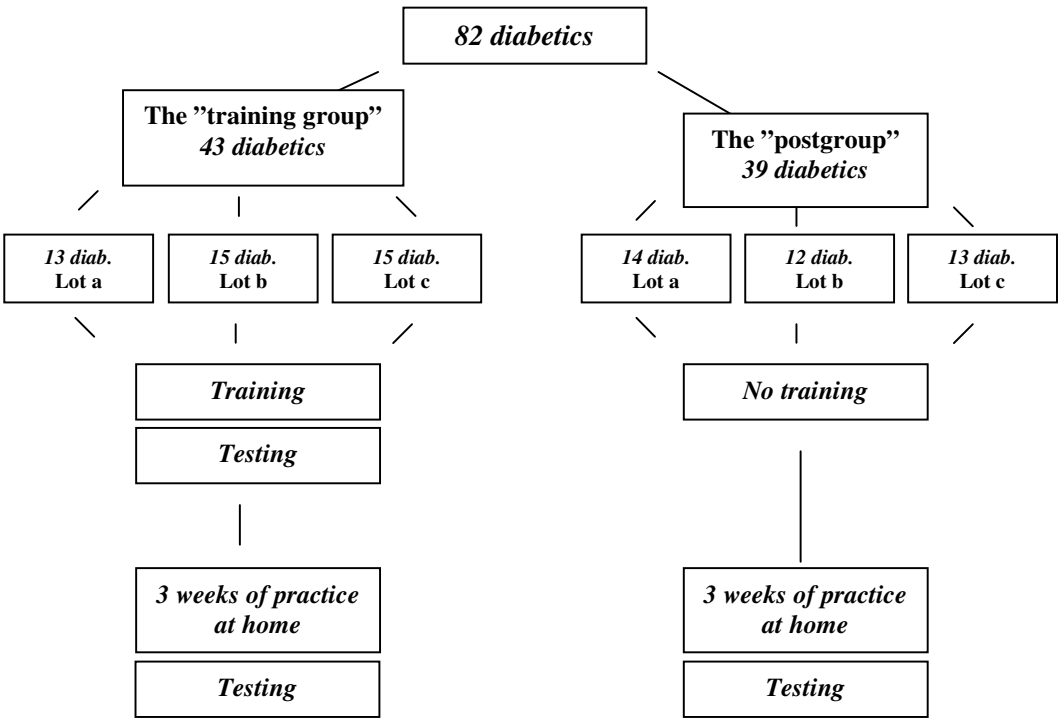

Figure 1. Model for the evaluation

All the diabetics could not participate in the user evaluation during the same weeks. The biomedical laboratory scientists had capacity to receive approximately 25-30 diabetics a week. Therefore the start-up was spread out over 3 weeks, and the final consultation consequently spread out correspondingly.

4.4.2. Recruiting of the diabetics

The OneTouch GlucoTouch glucose meter was tested in use by 82 diabetics (the evaluation started with 82 diabetics, but one diabetic did not carry through). 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). None of the diabetics used OneTouch GlucoTouch at the time. 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).
Patient characteristics of the group are shown in table 2.

Table 2. Characteristics of diabetic patients included in the evaluation (n=82).

		Diabetic patients
Total		82
Sex	Men	46
	Women	36
Age (years), median and range		58 (21-74)
Diabetes	Type 1	34
	Type 2	44
	Don't know	4
Treatment	Insulin	49
	Tablets	27
	Diet	5
	Unspecified	1
Frequency of SMBG	Less than weekly	2
	1 -3 per week	5
	4 – 6 per week	7
	7 – 10 per week	16
	> 10 per week	45
	Doesn't measure	0
	Unspecified	7

Some of the diabetic patients used more than one SMBG-device at home, but only one device is registered here.
The SMBG-devices that the diabetic patients use regularly: Accu-Chek Compact (18), Accu-Chek Sensor (9), Ascensia Breeze (6), Ascensia Contour (5), Ascensia DEX/DEX2 (2), Ascensia Elite (9), OneTouch Ultra (18), Precision Xtra (7), FreeStyle/FreeStyle Mini (7), and unspecified (1).

4.4.3. The training group at the first consultation

The 43 diabetics selected to participate in a training programme were called in two and two at the time. They received the OneTouch GlucoTouch device along with test strips, lancet pen, lancets, user manual and an instruction letter with explanations regarding what to do with the OneTouch GlucoTouch 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 and Kjersti Hveding were in charge of the training of the diabetics, after having been trained themselves by a representative from LifeScan.

Training programme
The training programme covered a simple demonstration of how to use OneTouch GlucoTouch 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 have been trained, the 43 diabetics made duplicate blood glucose tests on OneTouch GlucoTouch. These results were registered for the evaluation. Afterwards they brought the OneTouch GlucoTouch 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 postgroup

39 diabetics received the OneTouch GlucoTouch 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 GlucoTouch 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 final consultation to have two duplicate tests done. The results of these tests were registered.

4.4.5. Use of OneTouch GlucoTouch by the diabetics at home

The diabetics used OneTouch GlucoTouch 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 GlucoTouch 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 GlucoTouch. 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 GlucoTouch 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 GlucoTouch in the evaluation. To document correct functioning on the GlucoTouch-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 82 diabetics were called for, one by one, to a consultation. Each diabetic brought their assigned OneTouch GlucoTouch meter and the remaining test strips to this consultation. They made duplicate blood glucose tests on OneTouch GlucoTouch. 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 GlucoTouch were done, the diabetics filled out two questionnaires. The first questionnaire was about the user-friendliness of the OneTouch GlucoTouch 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 GlucoTouch or return it to the project.

4.4.7. Evaluation under standardised and optimal conditions

The two biomedical laboratory scientists used two OneTouch GlucoTouch blood glucose meters each 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 GlucoTouch		Lot A268514A (n)	Lot A268518A (n)	Lot A271808D (n)
Meter A	1st consultation		43 x 2	
	2nd consultation		81 x 2	
Meter B	1st consultation	13 x 2*	13 x 2*	17 x 2
	2nd consultation	27 x 2	27 x 2	27 x 2
Total		40 x 2	164 x 2	44 x 2

** At one consultation 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 the meters "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 on 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 GlucoTouch 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 GlucoTouch, which recommend hematocrit from 25 – 60 %.

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 10 000 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 GlucoTouch results were excluded for accuracy and trueness calculations. Differences between 4 and 10% are included in the calculations. In spite of this deviation on the comparison method, these results 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 GlucoTouch 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 43 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 GlucoTouch at home for three weeks. One diabetic patient did not meet for the final consultation.
3. Results from 39 diabetics in the "postgroup" who had not participated in the training programme, but who had practised using OneTouch GlucoTouch at home for three weeks.
4. Results from 124 measurements under standardised and optimal conditions
5. Results from 124 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

81 diabetics completed the evaluation. 43 diabetics from the "training group" met at the first consultation, and 42 of those met at the final consultation together with the 39 diabetics from the "postgroup". Blood samples were taken at each consultation. This means that the total number is 124 x 2 (duplicates) x 4 (meter A, meter B, diabetic's meter, comparison method) = 992 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 outliers, some results are missing or excluded for other reasons. They are summarized and explained here:

- ID number 230 is missing in the final consultation because the diabetic patient was unable to meet for this appointment
- ID number 265 is missing for the comparison method at the first consultation because of too little plasma. ID 265 at the first consultation is included in the calculations regarding the imprecision at OneTouch GlucoTouch, but excluded when OneTouch GlucoTouch is compared with the comparison method (accuracy).
- ID number 206 and ID number 250 had a difference > 10 % between the paired results on the comparison method in the final consultation. The difference was confirmed by a re-run. As a consequence of this, the results from ID 206 and ID 250 at the final consultation are included in the calculations regarding the imprecision at OneTouch GlucoTouch, but excluded when OneTouch GlucoTouch is compared with the comparison method (accuracy and trueness).
- ID number 329 is omitted at the final consultation because the sample to the comparison method was handled wrong preanalytically (forgotten in the centrifuge). ID 329 is included in the calculations regarding the imprecision at OneTouch GlucoTouch, but excluded from calculations when OneTouch GlucoTouch is compared with the comparison method (accuracy and trueness).

5.4. Calculation of imprecision based on duplicate results

Two capillary samples were taken of each diabetic patient to the meter A, meter B, 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 significant difference in glucose concentration between the paired measurements on OneTouch GlucoTouch in this evaluation.

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	95 % CI for the mean difference, mmol/L	n
OneTouch GlucoTouch	Meter A	< 7	5,9	5,9	0,01	-0,08 – 0,09	35
		7 – 10	8,3	8,3	-0,03	-0,14 – 0,08	42
		> 10	14,2	14,3	0,12	-0,023 – 0,27	47

5.5. Calculation of trueness

To measure the trueness of the measurements on OneTouch GlucoTouch, 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 GlucoTouch meter A.

5.6. Calculation of accuracy

To evaluate the accuracy of the results at OneTouch GlucoTouch, the agreement between OneTouch GlucoTouch 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 GlucoTouch 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 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 less than 0,5 CV% 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 GlucoTouch

6.2.1. Precision of OneTouch GlucoTouch

All of the OneTouch GlucoTouch 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.

All 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 4

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

OneTouch GlucoTouch	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A	< 7	5,9	35	0	2,9 (2,4-3,8)
Meter B	< 7	6,0	38	0	4,3 (3,5-5,6)
Meter A	7 – 10	8,3	42	0	3,0 (2,5-3,9)
Meter B	7 – 10	8,2	36	0	3,4 (2,8-4,5)
Meter A	> 10	14,3	47	0	2,5 (2,1-3,1)
Meter B	> 10	13,8	50	0	3,3 (2,8-4,1)

Repeatability obtained by the diabetic patients
The repeatability obtained by the diabetic patients 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 "postgroup", 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 diabetic patients 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 diabetic patients' measurements at NOKLUS is shown in attachment 5
Raw data from the diabetic patients' measurements at home is shown in attachment 6

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

OneTouch GlucoTouch	Consultation	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
NOKLUS	1st trained	< 7	6,2	15	0	3,6 (2,6-5,7)
	2nd trained	< 7	6,0	16	0	3,2 (2,4-5,0)
	post group	< 7	5,7	7	0	6,8 (4,4-15,0)
Home		< 7	5,5	145	4	5,0 (4,5-5,6)
NOKLUS	1st trained	7 – 10	8,0	10	0	2,4 (1,6-4,4)
	2nd trained	7 – 10	8,1	12	0	3,9 (2,8-6,7)
	post group	7 – 10	8,8	10	0	5,5 (3,9-10,2)
Home		7 – 10	8,2	143	0	4,1 (3,7-4,7)
NOKLUS	1st trained	> 10	13,2	16	0	1,5 (1,1-2,4)
	2nd trained	> 10	14,3	12	0	3,8 (2,7-6,4)
	post group	> 10	13,8	20	0	3,5 (2,7-5,1)
Home		> 10	13,2	83	0	4,6 (4,0-5,5)

*The "training group", first consultation: ID 88 and ID 295 are excluded. Both are missing duplicate results.
**The "training group", final consultation: ID 107 and ID 268 are excluded. ID 107 is missing duplicate result. ID 268 needed help from biomedical laboratory scientist.
***The "postgroup": ID 159 and ID 279 are excluded. ID 159 is missing duplicate result. ID 279 did one measurement at the wrong side on the test strip.
****"Home": 35 measurements are missing and four outliers are excluded

Reproducibility with Internal Quality Control

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

The reproducibility of OneTouch GlucoTouch at meter A and B is shown in table 10.
The reproducibility at all the meters of the diabetic patients is shown in table 11.
Raw data is shown in attachment 7.

Table 10. OneTouch GlucoTouch – Reproducibility (results with OneTouch GlucoTouch control solution) measured by the biomedical laboratory scientist on meter A and on meter B.

OneTouch GlucoTouch	Lot of strips	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A	A268518A	5,9-8,8	7,7	27	0	3,9 (3,1-5,4)
Meter B	A268514A	5,7-8,6	7,7	15	0	2,8 (2,1-4,5)
	A268518A	5,9-8,8	7,8	15	0	2,3 (1,7-3,7)
	A271808D	5,4-8,1	7,2	16	0	1,9 (1,4-2,9)

Table 11. OneTouch GlucoTouch – Reproducibility (results with OneTouch GlucoTouch control solution) measured by the biomedical laboratory scientist on the diabetic patient's meters.

OneTouch GlucoTouch	Lot of strips	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
1st consultation *						
The diabetic patients' meters	A268514A	5,7-8,6	7,8	13	0	3,7 (2,7-6,1)
	A268518A	5,9-8,8	7,9	15	0	2,9 (2,1-4,6)
	A271808D	5,4-8,1	7,2	13	0	1,9 (1,4-3,2)
2nd consultation **						
The diabetic patients' meters	A268514A	5,7-8,6	7,7	27	0	3,9 (3,1-5,3)
	A268518A	5,9-8,8	7,8	26	0	4,9 (3,9-6,8)
	A271808D	5,4-8,1	7,0	26	0	2,7 (2,1-3,8)

* ID 96 and ID 229 are missing QC-results
**ID 24 and ID 160 are missing QC-results

Discussion
The repeatability at OneTouch GlucoTouch is acceptable when measured with capillary blood samples. The repeatability obtained under standardised and optimal conditions is somewhere between 2,5 and 4,3 % (meter A and meter B).
The repeatability obtained at NOKLUS by the diabetic patients in the "training group" is nearly as good as the precision achieved by the biomedical laboratory scientists. The CV % is between 3 and 4. The precision obtained at NOKLUS by the diabetic patients in the "postgroup" are slightly poorer. The CV% for this group is between 3 and 7. The results at home show that the diabetic patients have been practising with the new system according to the instructions, but one should not make a point of the calculated CV values.

The reproducibility at OneTouch GlucoTouch meter A and B is good when measured with an internal control solution. The CV is approximately 3 %.
The reproducibility was good at the first consultation when the diabetics'meters and test strips were new. The CV was approximately 3 %. The results from the second consultation were not as good as the initial results, but still acceptable with a CV approximately 4 %.

6.2.2. Trueness

The trueness of OneTouch GlucoTouch is calculated from the results done by the biomedical laboratory scientists at the final consultation (the "training group" and the "postgroup") and is shown in table 12. Raw data is shown in attachment 8.

Table 12. Mean difference between OneTouch GlucoTouch 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	5,7	5,9	8,1	8,3	14,2	14,4
% deviation from the comparison method (95 % CI)	3,4 (0,8 – 6,1)		2,7 (0,6 – 4,9)		1,6 (-0,1 – 3,3)	
n	20		25		33	
Outliers	0		0		0	
p-value	0,013		0,015		0,057	

Discussion

The agreement between OneTouch GlucoTouch and the comparison method is good. There is a small, but significant bias between the two methods at two different levels of glucose concentrations. OneTouch GlucoTouch gives slightly higher values than the comparison method. The glucose results at OneTouch GlucoTouch still fulfil the quality goal set by ISO (see chapter 6.2.3).

6.2.3. Accuracy

To evaluate the accuracy of the results at OneTouch GlucoTouch, the agreement between OneTouch GlucoTouch 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 GlucoTouch. 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 diabetic patients.

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 diabetic patients' self-measurements the "adjusted ISO-goal" at 25 % is used.

The accuracy, OneTouch GlucoTouch meter B, under standardised and optimal measuring conditions, with the first measurement at the final consultation is shown in figure 2.
The accuracy, OneTouch GlucoTouch, as measured by the diabetic patients with the first measurement at the final consultation is shown in figure 3.
The results from the two difference plots are summarised in table 13 and discussed afterwards.

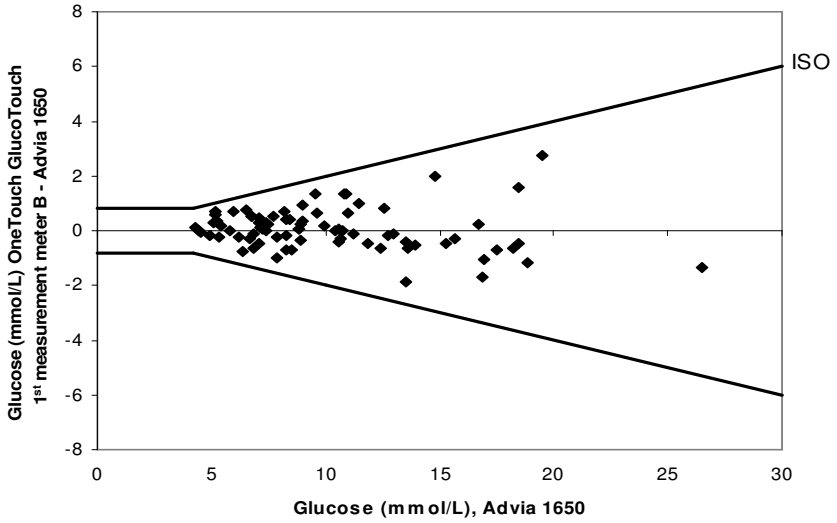

Figure 2. Accuracy. OneTouch GlucoTouch meter B (three lots of test strips) under standardised and optimal measuring conditions at the final consultation. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at OneTouch GlucoTouch and the mean value of the duplicate results at the comparison method. N = 78.

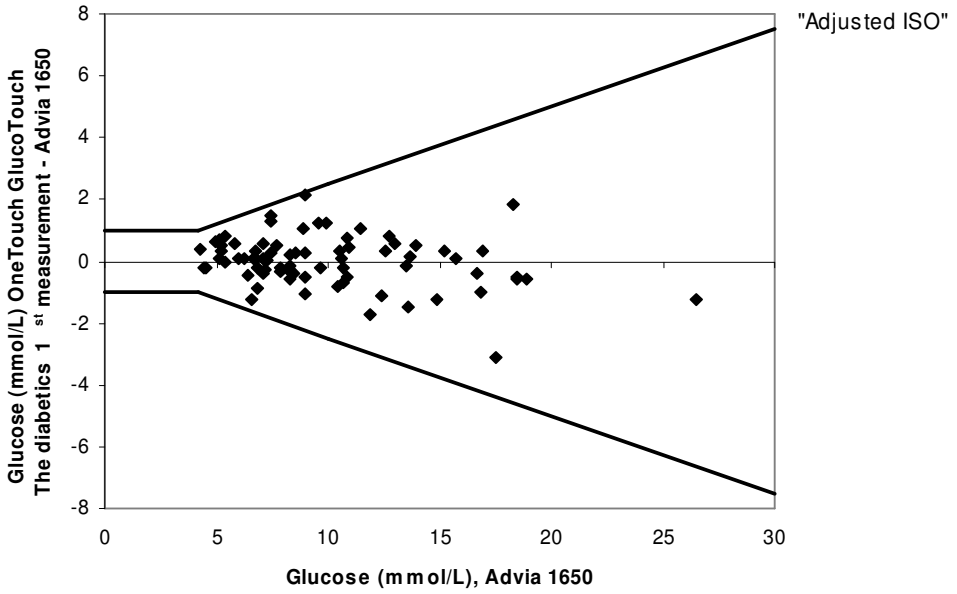

Figure 3. Accuracy. The diabetic patients' self-measurements at the final consultation. Three lots of test strips. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at OneTouch GlucoTouch and the mean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

Table 13. Total error of OneTouch GlucoTouch results compared to the comparison method. Percentage OneTouch GlucoTouch 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	42	88	100		
		B 1st measurement	42	98	100		
Biomedical laboratory scientist	2nd	A 1st measurement	78	92	100		
		B 1st measurement	78	83	100		2
Diabetic patients at NOKLUS	1st	1st measurement	42	88	98	100	
	2nd	1st measurement	76*	76	99	100	3

* One diabetic patient did the measurement technical wrong (ID 279) and one diabetic patient needed help from the biomedical laboratory scientist (ID 268). Both are excluded from the calculation of the accuracy

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, but the results do not fulfil the strict limits recommended by ADA. Figure 3 shows that the diabetic patients' first self-measurements at the final consultation fulfil the "adjusted ISO-goal". The results also fulfil the ISO-goal, as shown in table 13. The results do not fulfil the optimal quality goals from ADA.

Conclusion

The OneTouch GlucoTouch 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 diabetic patients.

6.3. Variation between three lots of test strips

All the measurements on meter A were performed with the same lot. 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 GlucoTouch 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 A268514A**	**The comparison method**	**Meter B Lot A268518A**	**The comparison method**	**Meter B Lot A271808D**
Mean glucose, mmol/L	9,3	9,6	9,6	9,9	11,2	10,8
% deviation from the comparison method (95 % CI)	2,9 (0,5-5,2)		2,8 (0,1-5,4)		-3,5 (-5,5 – (-)1,4)	
n	26		25		27	
Outliers	0		0		0	
p-value	0,029		0,042		0,002	

Discussion

The differences between the comparison method and lot A268514A, A268518A and A271808D are statistically significant. Lot A268514A and A268518A give significantly higher values than the comparison method and lot A271808D gives significantly lower values than the comparison method. All the lots are within the ISO-limits.

7. Effect of hematocrit

The package insert of OneTouch GlucoTouch test strips states that glucose concentrations are affected by hematocrit-values: "At lower hematocrit, results will tend to be higher than laboratory results. At higher hematocrit, results will tend to be lower than laboratory results". To measure the effect of hematocrit at OneTouch GlucoTouch, a venous sample was taken of the diabetic patients (voluntarily) at the final consultation. All the diabetics were willing to have a sample for hematocrit taken. Out off the 81 diabetic patients that met for the final consultation, the sampling to hematocrit was successful in 80 cases.

The measurements on OneTouch GlucoTouch are performed under standardised and optimal measuring conditions. The glucose concentration range in the samples was from 4,4 to 26,8 mmol/L. The hematocrit range was 32 – 55%.

The effect of hematocrit is shown in figure 4 and figure 5 (excluded results are explained in 5.3). The x-axis in the plots shows the hematocrit value, and the y-axis shows the difference in glucose concentration in mmol/L between OneTouch GlucoTouch and the comparison method (OneTouch GlucoTouch – the comparison method). Raw data is shown in attachment 9.

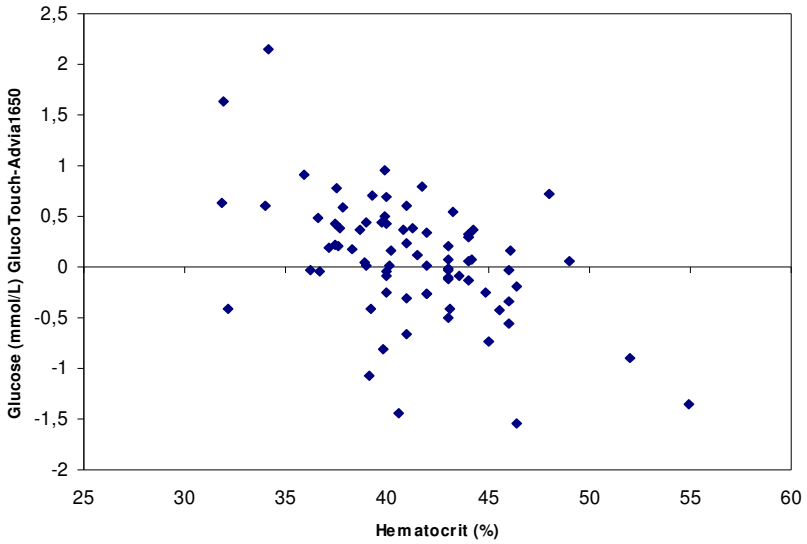

Figure 4. The effect of hematocrit at glucose measurements (in mmol/L) at OneTouch GlucoTouch under standardised and optimal conditions. The x-axis shows the hematocrit value in %. The y-axis shows the difference in glucose concentration between OneTouch GlucoTouch and the comparison method in mmol/L. n= 77

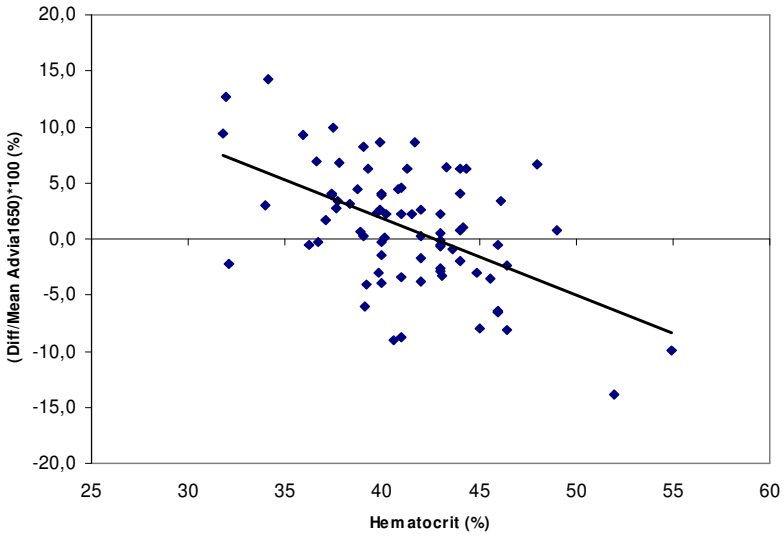

Figure 5. The effect of hematocrit at glucose measurements on OneTouch GlucoTouch under standardised and optimal conditions. The x-axis shows the hematocrit value in %. The y-axis shows the difference in glucose concentration between OneTouch GlucoTouch and the comparison method (OneTouch GlucoTouch – the comparison method) in percent. n=77

Discussion

The trend-line in figure 5 shows that the glucose measurements on OneTouch GlucoTouch are affected with hematocrit value of the samples, as described in the package insert. The glucose values at OneTouch GlucoTouch are over-estimated when the hematocrit is below 40 %, and under-estimated when hematocrit is more than 45 %. In spite of the hematocrit effect, the glucose results at OneTouch GlucoTouch still fulfil the quality goal set by ISO.

8. Evaluation of user friendliness

Each diabetic patient filled out a questionnaire about the user-friendliness and a questionnaire about the user-manual of OneTouch GlucoTouch when they attended the final consultation (n = 81). Some patients 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. Questionnaire about user-friendliness of OneTouch GlucoTouch

The questionnaire about the user-friendliness had 10 questions concerning OneTouch GlucoTouch and one question concerning UltraSoft lancet pen. In addition, each patient should give the name of the blood glucose meter he/she uses generally.
For eight of the questions the patients were asked to rank the answers on a scale from 1 to 6, where 1 is difficult and 6 is simple. The mean is more than 5 for all, but two questions. This indicates that the patients seemed satisfied with calibrating the meter, with inserting the strip into the meter, with reading the figures in the display, with recognizing the meters' sound signal and with operating the meter, all in all. The two questions that the patients ranked with a mean less than 5 had to do with filling blood onto the test strip (mean 4,1) and cleaning the meter (mean 4,9). This indicates that the issue the patients were less satisfied with was filling blood onto the strip. 13 patients have also reported this issue as a disadvantage with the system (see next page). Regarding UltraSoft lancet pen the mean is 5,3, which indicates that the patients were satisfied with the lancet pen. The answers to these questions are summarized in table 15.

Table 15. OneTouch GlucoTouch - Questions about the meter/the test strip and about UltraSoft lancet pen.

Questions about OneTouch GlucoTouch and about UltraSoft 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 calibrate the meter	5,3	1 - 6	2	81
	2. To fill blood onto the test strip	4,1	1 - 6	0	81
	3. To insert the test strip into the meter	5,4	1 - 6	0	81
	4. To read the figures in the display	5,9	1 – 6	0	81
	5. To recognize the meters' sound signal	5,8	2 - 6	1	81
	6. To clean the meter	4,9	1 - 6	19	81
	7. All in all, to operate the meter	5,0	1 - 6	1	81
	8. To operate UltraSoft lancet pen	5,3	1 - 6	15	81

2 % of the patients answered that they had technical problems with the meter during the testing period. However, written comments indicate that the problems were not technical ones.

40 patients reported one or more advantages with OneTouch GlucoTouch. The reported advantages are distinctly grouped as follows:
1. large display with large and distinct figures (18)
2. simple operating of the meter (7)
3. PC connection/memory feature (5)
4. large size of the test strip (4)
5. the possibility of visual reading of the result (2)

Singly, reported advantages are that the meter seems robust, that the carrying case is O.K. and that the meter has a simple calibration and simple cleaning procedure.

62 patients reported one or more disadvantages with OneTouch GlucoTouch. With 81 participating patients this means that many of the same patients who reported one ore more advantages also report one or more disadvantages. The reported disadvantages are distinctly grouped as follows:
1. the meter/strip needs large blood sample volume (30)
2. the meter has long measuring time (20)
3. the meter has large size/is heavy (14)
4. difficult application of blood onto the strip (13)
5. box with strips (6)
6. complicated operating of the meter (5)
7. the meter needs cleaning procedure (4)
8. application of blood onto the strip before insertion of the strip into the meter (3)
9. manually calibration of the meter (2)

Singly, reported disadvantages are that the meter has a low signal volume, that it is difficult to find the stored results in the meter memory and that the carrying case is too large.

The interesting fact is that one of the mentioned advantages also is reported as a disadvantage. This refers to the operating of the meter, which seems simple for some and complicated for others. The disadvantages most frequently reported are that the meter/strip needs large blood sample volume (≥ 5 μL), that the meter has a long measuring time (approximately 30 seconds), that the meter is large, heavy and that the application of blood onto the strip is difficult. Comments from patients who have reported the box with strips as a disadvantage are that the box is large, that it is more convenient with individually packed test strips or that the strips have to be inserted manually into the meter. The last group is patients that generally use meters with loading several strips at a time (Accu-Chek Compact, Ascensia DEX2 or Ascensia Breeze).

8.2. Questionnaire about the user manual for OneTouch GlucoTouch

On the questionnaire about the user manual each patient 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 16 shows that 78 % of the patients had used the user manual, i.e. 63 of the 81 patients that participated in the study. 11 % (9 of the 81 patients) did answer neither this question nor the rest of the questionnaire. These nine patients have probably not used the user-manual. Therefore the rest of the questions are answers from the 63 patients who answered "yes" on the first question.

Approximately 40 % of them had read the entire manual and approximately 80 % had consulted the manual when needed. The 63 patients that had been reading in the user manual seemed satisfied with the manual. 92 % answered they were satisfied with the description of how to perform a blood glucose measurement with this meter. Eight percent thought the manual had essential shortcomings. Only one of these patients commented this issue, and he/she reported that the user manual was little educational. 92 % were quite satisfied with the user manual, all in all. Otherwise three patients gave negative comments to that the Norwegian user manual also has incorporated a Danish translation.

Table 16. OneTouch GlucoTouch– Questions about the user manual.

Questions about the user manual	Yes (%)	No (%)	Not answered (%)	Number
Have you been reading in the user manual?	78	11	11	81
If yes, did you read the entire user manual?	44	40	16	63
And/or did you only consult the user manual when needed?	78	11	11	63
1. Are you satisfied with the description of how to perform a blood glucose measurement with this meter?	92	6	2	63
2. Do you think the user manual has essential shortcomings?	8	89	3	63
3. All in all, are you satisfied with the user manual?	92	5	3	63

The two biomedical laboratory scientists agreed with the diabetics in most of their answers. The advantages are the large size of the test strip and that it was easy to see if the test strip was filled with enough blood. The negative comments were that the test strip needed a large blood sample volume and that the measuring time was long. The biomedical laboratory scientists had been reading the entire user manual and were satisfied with the manual.

9. References

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10. Attachments

1. Serial numbers, OneTouch GlucoTouch meters
2. Information letter to the diabetic patients (in Norwegian)
3. Raw data, internal quality control, Advia
4. Raw data, OneTouch GlucoTouch results under standardised conditions, meter A and B
5. Raw data, OneTouch GlucoTouch results, the diabetics measurements at NOKLUS
6. Raw data, OneTouch GlucoTouch results, the diabetics measurements at home
7. Raw data, internal quality control, OneTouch GlucoTouch
8. Raw data, Advia results, diabetic patients
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.