Precision Xtra™ Plus (G3c)

Precision Xceed

Test strips and meter designed for glucose self-measurement manufactured by Abbott

Report from an evaluation organised by

SKUP

The evaluation was ordered by Abbott Norge as

SKUP/2006/49

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

Summary

Background
The Precision-system is designed for glucose self-measurements by diabetics. Precision is produced and supplied by Abbott. The Precision Xtra Plus (G3c) is a third generation test strip with "True Measure Technology" from Abbott. In this evaluation the test strip is used with the Precision Xceed meter. The Precision Xtra Plus (G3c) test strip has not yet been launched onto the Norwegian market. The Precision Xceed meter was launched onto the Norwegian market in December 2004.

In order to give reimbursement for glucose test strips in Norway, The National Social Insurance Office (*Rikstrygdeverket*) instructs the companies to carry out an evaluation that includes a user-evaluation among diabetics. A user-evaluation of Precision Xtra Plus test strip was done under the direction of SKUP during the winter of 2005/2006. A supplementary user-evaluation was done during the summer of 2006.

The aim of the user-evaluation
The aim of the user-evaluation of Precision Xtra Plus test strips at Precision Xceed was to

- reflect the analytical quality under standardised and optimal conditions (performed by biomedical laboratory scientists)
- reflect the analytical quality by the users
- 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 Precision Xtra Plus/Precision Xceed regarding user-friendliness
- evaluate the Precision Xceed user-manual

Materials and methods
The evaluation of Precision Xtra plus test strip has been performed twice and includes a first user-evaluation and a supplementary user-evaluation.
77 diabetics took part in the first evaluation; 40 of the participants had two consultations (the "training group") and the rest had one consultation (the "mail group"). At the first consultation the diabetics in the training group were given a standardised instruction about the Precision-system before they did a finger prick and performed two measurements on the meter. The biomedical laboratory scientist also took samples from a finger capillary of the diabetics and measured twice with the system. In addition, two samples from a finger capillary were taken to a designated comparison method. The diabetics in the mail group received the Precision-system through the 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 of Precision Xtra Plus/Precision Xceed and the user-manual of Precision Xceed.
81 diabetics participated in the supplementary user-evaluation, 48 of these diabetics were recruited from the first user-evaluation and 33 diabetics were recruited through Sørlandet Hospital. The diabetics in the supplementary evaluation had only one consultation. The measuring procedure was similar to the procedure in the first user-evaluation.

Results
The results from the first user-evaluation are presented in attachment 12.
The results from the supplementary user-evaluation:

- Under standardised and optimal measuring conditions, the repeatability of Precision Xtra Plus at Precision Xceed is approximately 6 %. The imprecision is a little higher for glucose concentrations below 7 mmol/L. When measured by the diabetics, the precision is acceptable with a CV of approximately 5 % for glucose concentrations above 7 mmol/L. As a whole the imprecision is not significantly more than 5 %.
- The Precision Xtra Plus gives slightly higher glucose results than the comparison method. The positive bias is approximately 4 to 5 % for glucose values < 10 mmol/L.
- Two of the three lots of test strips showed significantly higher values than the comparison method. The deviation was approximately 4 %.
- The quality goal set in the ISO 15197 is achieved under standardised and optimal measuring conditions. The results achieved by the diabetics also fulfil the goals set in ISO 15197.
- Glucose measurements at Precision Xtra Plus test strips at Precision Xceed do not seem to be affected by hematocrit values between 35 and 49 %.
- The diabetics summarise the Precision-device as easy to use. 26 (34 %) of the diabetics reported that they had technical problems with the meter during the testing period. For 16 of these diabetics the written comments indicated problems with the meter not turning on at all, or turning off too quickly. The diabetics that had used the user manual were satisfied with the manual.

Conclusion
The imprecision of Precision Xtra Plus test strips at Precision Xceed under standardised and optimal measuring conditions and in use by the diabetics is just over 5 % as a whole. Glucose results at Precision Xtra Plus are approximately 4 to 5 % higher than at the comparison method for glucose values < 10 mmol/L. The quality goal set in the ISO-guide 15197 is achieved, both under standardised and optimal measuring conditions and by the measurements of the diabetics. The glucose measurements do not seem to be affected by hematocrit-values between 35 and 49 %. The users find the Precision-device simple to use.

Response from Abbott Diabetes Care
Response from Abbott is found in attachment 19.

Table of contents

Attachments with raw data are included only in the copy to Abbott Norge AS.

1. The organisation of SKUP

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

The goal of SKUP is to produce reliable, objective and independent information about analytical quality and user-friendliness of laboratory equipment for primary healthcare. This information is generated by organising *SKUP evaluations*.

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

There are *general guidelines* for all SKUP evaluations and for each evaluation a specific *SKUP protocol* is worked out in co-operation with the manufacturer or their representative. SKUP signs *contracts* both with the requesting company and with the evaluating laboratories. A *complete evaluation* requires both one part performed by experienced laboratory personnel and one part performed by the intended users.

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

SKUP reports are published at www.skup.nu and summaries are distributed to physicians' offices, councils for laboratory medicine, laboratory instructors and healthcare authorities.

For a detailed list of previous SKUP evaluations, please see attachment 18 of this report.

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[1] NOKLUS (Norwegian Quality Improvement of Primary Care Laboratories) is an organisation attached to "Seksjon for Allmennmedisin" (Section for General Practice) at the University of Bergen, in Bergen, Norway.

[2] "Afdeling KKA" is the Department for Clinical Chemistry at the University Hospital in Odense, Denmark. "Afdeling KKA" in Odense and the national "Fagligt Udvalg vedrørende Almen Praksis" (Professional Committee for General Practice) have through an agreement created "the SKUP-division in Denmark". "Fagligt Udvalg vedrørende Almen Praksis"is a joint committee for "PLO", "Praktiserende Lægers Organisation" (General Practioners Organisation) and "Sygesikringens Forhandlingsudvalg" (Committee for Negotiations within the General Health Insurance System).

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

2. The planning of the evaluation

The first user-evaluation
Ingrid E. Stiff Aamlid from Abbott Norway applied to SKUP in the spring of 2005 for an evaluation of the blood glucose test strip Precision Xtra Plus. In June 2005 SKUP gave a written offer, and August 26th 2005 a preliminary suggestion regarding how to organise the evaluation was sent from SKUP to Abbott. The protocol for the evaluation of Precision Xtra Plus was accepted October 3rd 2005. A contract was set up between Abbott and SKUP in October 2005. The Laboratory at Haraldsplass Diaconal Hospital (HDH) accepted to carry out the analytical part of the evaluation dealing with the samples for the comparison method.

Precision Xtra Plus/Precision Xceed is produced and supplied by Abbott. The Precision Xtra Plus (G3c) test strip has not yet been launched onto the Norwegian market. Precision Xceed glucose meter was launched onto the Norwegian market in December 2004. SKUP carried out a user-evaluation of Precision Xtra Plus/Precision Xceed during the winter of 2005/2006.

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 user-evaluation comprises the following studies:

- An examination of analytical quality under standardised and optimal conditions done by biomedical laboratory scientists
- An examination of analytical quality among approximately 80 diabetics
- An examination of agreement between Precision Xtra Plus/Precision Xceed and a designated comparison method
- A comparison of analytical quality among diabetics with and without a 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 Precision Xtra Plus/Precision Xceed
- An evaluation of the user-manual of Precision Xceed

Reasons for a supplementary user- evaluation
Precision Xtra Plus strips are calibrated to the Yellow Springs Instruments (YSI), while the designated comparison method is a hexokinase based method. According to Abbott Diabetes Care (ADC) the YSI method is known to give glucose results between 4 and 8 %, or even 10 %, lower than hexokinase methods. ADC refers to published literature which indicates that external bodies confirm this. In the first user-evaluation SKUP pointed out a negative bias between 8 and

18 % for Precision Xtra Plus compared with the comparison method. According to the initial response from ADC to SKUP regarding the preliminary report from the first user-evaluation, the three lots of test strips that were used in this evaluation were amongst the very first batches manufactured. During the period in which these lots were manufactured, a drop in the accuracy had been observed for lots tested in clinical studies as part of ADC's standard Post Market Surveillance Programme. The reported negative bias was reduced by a calibration adjustment applied in manufacturing all subsequent lots. ADC therefore firmly believed that the results in the first SKUP-evaluation were not representative for the analytical quality for the adjusted product. Therefore Abbott wanted to have a new user-evaluation performed. Three lots of test strips with improved analytical quality were to be used in a supplementary user-evaluation. The protocol for the supplementary user-evaluation of Precision Xtra Plus was accepted in June 2006. A contract was set up between Abbott and SKUP in June 2006. SKUP carried out the supplementary user-evaluation during the summer of 2006.

The supplementary user-evaluation comprises the following studies:

- An examination of the analytical accuracy to see if the measurements under standardised and optimal conditions done by biomedical laboratory scientists have improved and fulfil the ISO-goal
- An examination to see if the analytical quality of the diabetics measurements have improved with use of three new lot of test strips (approximately 50 diabetics)
- An examination of agreement between Precision Xtra Plus/Precision Xceed and a designated comparison method

The practical work

The blood sampling of the diabetics and the measurements on Precision Xceed under standardised and optimal conditions in the first user-evaluation, were done in Kristiansand by Signe Røynås, Bente Knudsen and Margarita Milan, biomedical laboratory scientists and laboratory consultants, SKUP/NOKLUS. The blood sampling of the diabetics and the measurements on Precision Xceed in the supplementary user-evaluation, were done by Signe Røynås and Bente Knudsen. 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 and Camilla Eide Jacobsen, SKUP/NOKLUS Centre in Bergen.

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. Precision Xtra Plus/Precision Xceed are 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 Precision Xtra Plus/Precision Xceed 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 made by trained laboratory staff. Ideally, the same quality requirements should apply to measurements done by the diabetics. Previous investigations under the direction of the NOKLUS-project "Diabetes-Self-measurements" in 1997 [5,7] showed that few of the self-monitoring glucose meters tested at the time met the ISO-requirements. Subsequent SKUP-evaluations confirmed these findings. As a consequence, the results by the diabetics have been discussed towards a *modified* goal suggested by NOKLUS, with a total error of ± 25 %. This modified goal has wide, and not ideal, limits. The intention was to tighten up the modified requirements for the diabetics over time, as the meters would hopefully improve due to technological development. More recent evaluations performed by SKUP [8] clearly show that the quality goals set by ISO 15197 now can be achieved also by the diabetics. But for the time being, the quality demands, adjusted to the diabetics' self-measurements, still apply.

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. Precision is descriptive in general terms as "good", "acceptable" and "poor", whereas imprecision is expressed by means of the standard deviation (SD) or coefficient of variation (CV). SD is reported in the same unit as the analytical result and CV is usually reported in percent. 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. Precision Xtra Plus (G3c)/Precision Xceed

Precision Xtra Plus/Precision Xceed is a blood glucose monitoring system based on biosensor technology. Precision Xtra Plus (G3c) is a 3rd generation test strip with "True Measure Technology" from Abbott. Precision Xtra Plus test strips are calibrated to the Yellow Springs Instrument (YSI) 2300 STAT analyser with plasma equivalent results. The evaluated system consists of the Precision Xceed meter and the dry reagent test strips Precision Xtra Plus designed for capillary blood glucose testing by people with diabetes or by health care professionals. The test strips used in this evaluation are calibrated to report plasma glucose values. The meter is turned on by insertion of the Precision Xtra Plus test strip. The system requires calibration by the user. 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 strips. The test principle of Precision Xtra Plus utilises the enzyme glucose dehydrogenase (GDH) and the co-factor NAD^+, linked with an electrochemical mediator 1,10-phenanthroline quinone (PQ) to produce the current measured by the sensor in the meter.

Precision Xtra Plus test strips are individually wrapped in sealed aluminium foil packets. The test strip requires a blood volume of 0,6 µL. The system provides a result in 5 seconds. The sample application zone is at the end of the strip and has top fill. If the test strip window is not completely filled, more blood can be applied within 5 seconds. Easy Touch adjustable lancet pen is used to form a drop of blood on the fingertip. Precision Xtra Plus is cleared for multiple site testing. The device can be used on less sensitive testing sites like the forearm, upper arm or the base of the thumbs. Abbott recommends to consult Healthcare Professional if use of multiple sampling sites. In this evaluation the glucose samples are taken in a finger capillary. The Precision Xceed meter has the capacity of storing 450 results in memory. It is also possible to analyze Precision Xtra β-ketone test strips at Precision Xceed.
Technical data from the manufacturer is shown in table 1.

Table 1. Technical data from the manufacturer.

TECHNICAL DATA FOR PRECISION XTRA PLUS/PRECISION XCEED	
Working temperature	15 – 40 °C (test strips), 10 – 50°C (meter)
Relative humidity	10 – 90 %
Sample volume	0,6 µL
Measuring time	5 seconds
Measuring range	1,1 – 27,8 mmol/L
Hematocrit	30 – 60 %
Memory	450 tests
Power supply	1×3V lithium battery supply (CR 2032)
Operating time	Approximately 1000 tests
Dimension	W= 74,7 mm, H= 53,3 and 4,32 mm, D= 16,3 mm
Weight	42 g

4.2.1. Product information, Precision Xtra Plus/Precision Xceed

Precision Xtra Plus/Precision Xceed blood glucose meter system
Manufactured by: Abbott Laboratories, Abbott Diabetes Care, USA

Suppliers of Precision Xtra Plus/Precision Xceed in the Scandinavian countries:

Sweden:	Norway:	Denmark:
MediSense Sverige AB	Abbott Norge AS Diagnostics Division	Abbott Diabetes Care Danmark A/S
Box 509	P.O.Box 1	Postboks 1102
SE-169 29 Solna	N-1330 Fornebu	7752 Snedsted
Sweden	Norway	Denmark
Phone: (46 8) 5465 6700	Phone: (47) 815 59920	Phone: (45 979) 34 822
Facsimile: (46 8) 5465 6800	Facsimile: (47) 671 13110	Facsimile: (45 979) 34 847
www.abbott.se	www.abbott.no	www.abbott.dk

The first user-evaluation:
81 Precision Xceed blood glucose meters were used in the main user-evaluation.
Serial no. XC1021-3183 (called meter A), XC1021-0171 (called meter B), XC1144-3002 (called meter C) and XC1021-3068 (called meter D) were used by the biomedical laboratory scientists under the standardised and optimal conditions. Attachment 1 gives serial numbers for the 77 meters used by the diabetics.

Precision Xtra Plus Test Strips:

Lot-no. 40109	Expiry 2007/01/31	(called lot a)
Lot-no. 40126	Expiry 2007/01/31	(called lot b)
Lot-no. 40135	Expiry 2007/01/31	(called lot c)

MediSense Glucose Control Solution (level M56733, level H16838)
Lot-no. 29773Q100 Expiry 2006/07/21

The supplementary user-evaluation:
Three Precision Xceed blood glucose meters were used in the supplementary user-evaluation. Serial no. XC1473-3183 (called meter A) and XC1473-1200 (called meter C) were used by the biomedical laboratory scientists under standardised and optimal conditions. Serial no. XC1473-3178 (called meter B) was used by all the diabetics at the consultations.

Precision Xtra Plus Test Strips:

Lot-no. 40638	Expiry 2007/06/30
Lot-no. 40713	Expiry 2007/07/31
Lot-no. 40783	Expiry 2007/08/31

MediSense Glucose Control Solution (level M57522, level H17527)
Lot-no 34194Q100 Expiry 2007/01/14

Easy Touch lancet pen

4.3. Designated comparison method

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

Verifying of trueness
The results from self-monitoring of blood glucose devices (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 both evaluations. In addition, freshly frozen, human serum controls from NOKLUS with glucose concentrations at two levels were analysed in the first user-evaluation. 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 [9]. The trueness of the comparison method in both user-evaluations is presented 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 (e.g. lithium heparin), urine and cerebrospinal fluid (CSF) 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, utilising hexokinase and glucose-6-phosphate dehydrogenase enzymes. The method is implemented on the Architect *ci*8200 System from Abbott Laboratories, with reagents and calibrators from Abbott Laboratories. The measuring principle in the Architect *ci*8200 is as follows: Glucose is phosphorylated by hexokinase in the presence of ATP and magnesium ions. The glucose-6-phosphate that is formed is oxidised in the presence of glucose-6-phosphate dehydrogenase causing the reduction of NADP to NADPH. The NADPH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance.

Internal quality assurance of the Architect ci8200 comparison method during the evaluation periods
The Autonorm Human Liquid Control Solutions at two levels from Sero AS were part of all the measuring series in both user-evaluations. The controls were measured in duplicate as the first and the last samples in all the series. The results are summarised in table 6.

4.3.1. Product information, the comparison method

Designated comparison method Architect ci8200
Manufactured by: Abbott Laboratories
Serial no. C800890

Reagents
Glucose Reagent Kit, List No. 7D66
Lot-no. 32024HW00 Expiry 2006-06-23

Calibrator
Multiconstituent Calibrator. List No. 1E65
Lot-no. 19906M200 Expiry 2006-02-28 Reference value, cal 1 = 5,55 mmol/L
Reference value, cal 2 = 24,31 mmol/L

Internal controls
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 controls
(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 012
Accu-Chek Softclix Pro lancets: Lot-no. WIP 45 G 5 Expiry 2008-12-31

Tubes used for sampling for the designated comparison method
Microvette CB 300 LH (lithium-heparin) manufactured by Sarstedt AS
Lot-no. 5070201 Expiry 2008-01

Centrifuge used for samples for the designated comparison method
Eppendorf Centrifuge 5415D Serial no. 0057100
Sigma 203 Serial no. 30361

Changes in product information for the supplementary user-evaluation:

Reagents
Glucose Reagent Kit, List No. 7D66
Lot-no. 38075HW00 Expiry 2007-02-09

Calibrator
Multiconstituent Calibrator. List No. 1E65
Lot-no. 3718M100 Expiry 2006-10-31 Reference value, cal 1 = 5,66 mmol/L
Reference value, cal 2 = 24,70 mmol/L

Internal controls
Seronorm Autonorm Human Liquid 1 and 2, Sero AS
Liquid 1: Value = 4,62 ± 0,36 mmol/L Lot-no. 501002 Expiry 2007-02
Liquid 2: Value = 16,0 ± 1,12 mmol/L Lot-no. 509415 Expiry 2007-10

4.4. Evaluation procedure for the first user-evaluation

4.4.1. Model for the evaluation

The best part of the practical work with the evaluation was carried out during 8 weeks from October to December 2005 (from week number 41 to week number 48) at Sørlandet Hospital, Kristiansand, in Norway. The last diabetic turned up in second week, 2006. The practical work was done by the biomedical laboratory scientists Signe Røynås, Margarita Milan and Bente Knudsen.

The evaluation consisted of two parallel evaluations. One part of the evaluation was done by the biomedical laboratory scientists under standardised and optimal conditions. This part of the evaluation was 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 were tried kept at a minimum. The evaluation under standardised and optimal conditions documents the quality of the system under as good conditions as possible. The other part of the evaluation was done by diabetics. In order to determine the analytical quality of Precision Xtra Plus/Precision Xceed by the users, 77 diabetics tested their blood glucose using this system. The diabetics were divided into two groups (random distribution). 40 diabetics were called in and received personal training in how to use the blood glucose meter, here called the "training group". 37 diabetics received the blood glucose meter and instructions through the post, here called the "mail group".
The reason for dividing the diabetics into a "training group and a "mail 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.

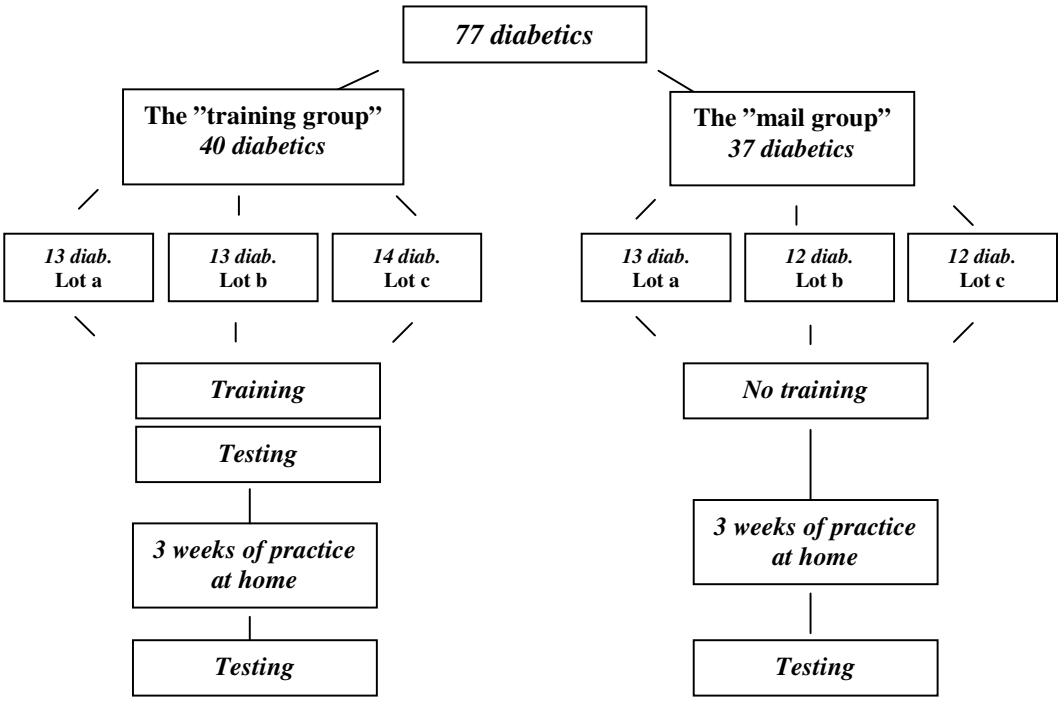

Figure 1. Model for the evaluation

The biomedical laboratory scientists had capacity to receive approximately 25-30 diabetics a week. Therefore, all the diabetics could not participate in the user evaluation during the same weeks. 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 diabetics were recruited through advertisement in the daily press, the local radio station and by mail inquiry sent to members of the local branch of the Norwegian Diabetes Association. 152 diabetics wanted to participate. 29 were excluded because they already used Precision instruments as their own device. From the 123 diabetics that were left, the evaluation started with 84 diabetics of whom seven did not have the opportunity to participate after all or didn't show up. Precision Xtra Plus/Precision Xceed was therefore tested in use by 77 diabetics. This 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 Precision Xceed as their own device. Characteristics of the diabetics in the group are shown in table 2.

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

		Number of diabetics
Total		77
Sex	Men	42
	Women	35
Age (years), mean and range		55 (19 - 75)
Diabetes	Type 1	29
	Type 2	46
	Don't know	2
Treatment	Insulin	42
	Tablets	26
	Insulin and tablets	3
	Diet	6
Frequency of SMBG	1 – 3 per month	3
	1 – 3 per week	12
	4 – 6 per week	5
	7 – 10 per week	9
	> 10 per week	43
	Do not measure	5

The SMBG-devices that the diabetics used regularly were:
Accu-Chek (model not specified) (3), Accu-Chek Aviva/Compact/Compact Plus/Sensor (27), Accutrend Sensor (2), Ascensia Breeze/Contour (8), Freestyle/Freestyle Mini (8), Glucometer Dex/Elite (3), MediSense Precision QID/Xtra (3), One Touch/OneTouch GlucoTouch (2) and OneTouch Ultra (14). Some of the diabetics used more than one SMBG-device at home, but only one device is registered here.

4.4.3. The training group at the first consultation

The 40 diabetics selected to participate in a training programme were called in two and two or four and four at the time. They received the Precision Xceed device along with Precision Xtra Plus test strips, lancet pen, lancets, user manual, and an instruction letter with explanations regarding what to do 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. Two biomedical laboratory scientists were in charge of the training of the diabetics, after having been trained themselves by a representative from Abbott.

Training programme

The training programme covered a simple demonstration of how to use Precision Xtra Plus/Precision Xceed system 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 40 diabetics made duplicate blood glucose tests on Precision Xceed. These results were registered for the evaluation. The biomedical laboratory scientist also collected samples for the evaluation under standardised and optimal conditions. Afterwards the diabetics took the Precision Xceed blood glucose meter home to use it over a three-week period. After this period, they attended a final consultation (see chapter 4.4.6.).

4.4.4. The mail group

The 37 diabetics in the "mail group" received the Precision Xceed device through the post, along with Precision Xtra Plus test strips, lancet pen, lancets, user manual and an instruction letter with explanations regarding what to do 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 (see chapter 4.4.6.).

4.4.5. Use of Precision Xtra Plus/Precision Xceed by the diabetics at home

The diabetics used Precision Xtra Plus/Precision Xceed 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 Precision Xtra Plus/Precision Xceed 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 Precision Xtra Plus/Precision Xceed. They could choose when to do the measurements themselves. Fasting was not necessary. If more convenient to them, they could perform the measurements at the same time as they measured their blood glucose with their own meter.

The third week
During the third week the diabetics performed duplicate measurements at Precision Xtra Plus/Precision Xceed on five 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 Precision Xtra Plus/Precision Xceed in the evaluation. To document correct functioning on the Precision Xtra Plus/Precision Xceed used by the diabetics during the test period, the biomedical laboratory scientists in charge of the practical work checked the meters with control solution 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 Precision Xceed meter and the remaining Precision Xtra Plus test strips to this consultation. They made duplicate blood glucose tests on Precision Xtra Plus test strips at Precision Xceed. These results were registered for the evaluation. The biomedical laboratory scientists also collected samples for the evaluation under standardised and optimal conditions. Finally, a venous sample for hematocrit was taken.

The questionnaires
After all the blood samples were collected and the measurements on Precision Xtra Plus test strips at Precision Xceed were done, the diabetics filled in two questionnaires. The first questionnaire was about the user-friendliness of Precision Xtra Plus test strips at Precision Xceed, the second about the user-manual for Precision Xceed. The questionnaires (in Norwegian) are attached to the report (see attachment 10 and 11). After the evaluation, the diabetics could choose whether to keep Precision Xceed or return it to the project.

4.4.7. Evaluation under standardised and optimal conditions
The biomedical laboratory scientists used four Precision Xceed blood glucose meters in the evaluation (meter A, B, C and D). Meter A and C were used for one lot of test strips for all measurements on all the diabetics. Meter B and D were used for the same three lots as distributed among the diabetics. In this way 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 Precision Xtra Plus test strips measured under standardised and optimal conditions in the first user-evaluation.

Precision Xtra Plus		Lot 40109 (n)	Lot 40126(n)	Lot 40135 (n)
Meter A/C	1st consultation	40 x 2		
	2nd consultation	77 x 2		
Meter B/D	1st consultation	32 x 2	8 x 2	
	2nd consultation		43 x 2	34 x 2
Total		149 x 2	51 x 2	34 x 2

Blood sampling
Meter A/C and B/D 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 (finger prick made by the diabetic)
3. The biomedical laboratory scientist took samples and analysed on meter A, B, A, and B or meter C, D, C and D (finger prick made by the biomedical laboratory scientist)
4. The biomedical scientist took a new sample for the comparison method
5. The biomedical laboratory scientist measured internal quality control at the diabetics' meter

The duration of the sampling should not exceed 10 minutes.

The order of meter A and B or meter C and D 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 used correct cleaning, drying and skin puncture procedures, 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 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 Precision Xtra Plus test strips at Precision Xceed. In the package insert hematocrits from 30 – 60 % are given as acceptable values.

Handling of the samples for the comparison method
The samples for the comparison method were taken from a finger capillary using a Microvette Li-heparin tube from Sarstedt. The samples were centrifuged immediately for three minutes at 10000 g (Eppendorf 5415D) or for ten minutes at 2000g (Sigma 203), and plasma was separated into sample vials. The plasmas were frozen directly and stored at minus 80°C (-81 to -85 degrees). The samples were transported under cold storage (minus 18 °C to minus 24 °C) to NOKLUS Centre where they were kept at minus 80 °C until the analysis took place.

Analysing the samples for the comparison method
The samples were analysed at Architect ci8200. Recommended minimum volume for analysis of glucose on Architect in this evaluation was 120 µL plasma. 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. When the paired measurements give agreeable glucose concentrations at the comparison method, the mean of the two results is looked upon as the estimate of the true value of the sample. Basically, the difference between the first and the second comparative reading must not 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 results 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 were excluded. As a consequence of this, the matching Precision Xtra Plus/Precision Xceed results were excluded for accuracy and trueness calculations. Differences between 4 and 10 % are discussed and included in the calculations (see chapter 6.1.3.). 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.

The questionnaires
The biomedical laboratory scientists evaluated the user-friendliness of Precision Xtra Plus test strips at Precision Xceed and the user-manual. The biomedical laboratory scientists provided a description in 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 40 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 Precision Xtra Plus test strips at Precision Xceed at home for three weeks
3. Results from 37 diabetics in the "mail group" who had not participated in the training programme, but who had practised using Precision Xtra Plus test strips at Precision Xceed at home for three weeks
4. Results from 117 measurements under standardised and optimal conditions
5. Results from 117 measurements from the comparison method

The results from the group with and without training were compared (item number 2 and 3) and the results from the group with and without practise at home (item number 1 and 2) were also compared. All the diabetic measurements were evaluated against the results achieved under standardised and optimal conditions. All the measurements were compared with the results from the comparison method. 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).

4.5. Evaluation procedure for the supplementary user-evaluation

The practical work with the supplementary user-evaluation was carried out during three weeks in June 2006 at Sørlandet Hospital, Kristiansand, in Norway. The practical work was done by the biomedical laboratory scientists Signe Røynås and Bente Knudsen.

The evaluation consisted of two parallel evaluations. One part of the evaluation was done by the biomedical laboratory scientists under standardised and optimal conditions. The other part of the evaluation was done by diabetics. In order to determine if the analytical quality of Precision Xtra Plus/Precision Xceed was improved, 48 of the 77 diabetics that had participated in the first user-evaluation agreed to test their blood glucose by using the system with new lots of test strips. This group of diabetics had either received training in the first user-evaluation or got the instruction through the post. The diabetics were called in, one by one, to a consultation. They received a Precision device (meter B) along with one of the three lots of Precision Xtra Plus test strips, lancet pen and lancet. There was no use for training or user manual since all the diabetics had participated in the first user-evaluation. The diabetics made duplicate blood glucose tests on the Precision device and the results were registered for the evaluation. The biomedical laboratory scientists also collected samples for the evaluation under standardised and optimal conditions. In addition to the 48 diabetics from the first user-evaluation, the biomedical laboratory scientists recruited 33 diabetics from "diabetes poliklinikk", Sørlandet Hospital. These 33 diabetics did not do any glucose measurements themselves, only the biomedical laboratory scientists collected samples for the evaluation under standardised and optimal conditions.

The biomedical laboratory scientists used two Precision Xceed blood glucose meters in the evaluation (meter A and C). Meter A was used for measurements of the 48 diabetics that were recruited from the first user-evaluation. Meter C was used for measurements of the 33 diabetics recruited from Sørlandet Hospital. Both meters were used for the same three lots as distributed among the diabetics. The number of samples for each lot of test strips measured under standardised and optimal conditions is shown in table 4.

Table 4. The number of samples (n) for each lot of Precision Xtra Plus test strips measured under standardised and optimal conditions in the supplementary evaluation.

Precision Xtra Plus	Lot 40638 (n)	Lot 40713 (n)	Lot 40783 (n)
Meter A/C	30 x 2	16 x 2	34 x 2
Meter B	18 x 2	15 x 2	15 x 2
Total	48 x 2	31 x 2	49 x 2

The blood sampling followed the instructions given in the first user-evaluation, but a venous sample for hematocrit was not taken (see chapter 4.4.7. under "*Blood sampling"*).
See chapter 4.4.7 for information about "*Handling of the samples for the comparison method"* and *"Analysing the samples for the comparison method"*.

5. Statistical calculations

5.1. Number of samples

77 diabetics completed the first user-evaluation. The 40 diabetics in the "training group" met at two consultations and the 37 diabetics in the "mail group" met at one consultation. Blood samples were taken at each consultation. 81 diabetics completed the supplementary user-evaluation, 48 of these diabetics were recruited from the first evaluation and 33 diabetics were recruited through Sørlandet Hospital. The diabetics in the supplementary user-evaluation had only one consultation.

5.2. Statistical outliers

All results are checked for outliers according to Burnett [10], 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. Results concerning the supplementary user-evaluation are summarized and explained here:

- ID 147, ID 182 and ID 320 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, these results are excluded when Precision Xtra Plus/Precision Xceed are compared with the comparison method (accuracy and trueness). The results are included in the calculations regarding the imprecision at Precision Xtra Plus/Precision Xceed because each set of duplicate measurements on the device is completed in less then a minute.
- ID 97 did not have any measurements on meter A or C, and is therefore missing in the calculation regarding trueness and accuracy.
- ID 328 had only one result on the comparison method. In the calculation of trueness this single result will represent an estimation of the sample and is not excluded.

Missing or excluded results concerning the first user-evaluation are described in attachment 12.

5.4. Calculations of imprecision based on duplicate results

Two samples from a finger capillary were taken of each diabetic to meter A or C, to meter B or D, to the diabetic's meter and to the comparison method at each consultation in the first user-evaluation. 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

Even if this formula is based on the differences between the paired measurements, the SD is still a measure of the imprecision of single values, and completely comparable with the more commonly used calculation based on repeated measurements of only one sample. The assumption for using this formula is that no systematic difference between the 1st and the 2nd measurement is acceptable. The provided proof of agreement in table 5 is based on the results achieved at the final consultation in the first user-evaluation, and table 5 shows that there is no systematic difference in glucose concentration between the paired measurements on Precision Xtra Plus test strips at Precision Xceed. The conclusion is in accordance with corresponding results in previous user-evaluations under the direction of SKUP, and is confirmed in the supplementary evaluation as well (results not shown).

Table 5. Comparison of the 1st and the 2nd measurement at the final consultation. T-test for paired values. Results from the first user-evaluation.

		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
Precision Xtra Plus test strips at Precision Xceed	Meter A/C	< 7	5,5	5,5	0,04	-0,12 – 0,19	27
		7 – 10	8,5	8,7	0,22	-0,02 – 0,46	28
		> 10	12,4	12,5	0,06	-0,52 – 0,64	22
	Meter B/D	< 7	5,5	5,5	0,09	-0,06 – 0,24	24
		7 – 10	8,2	8,5	0,28	-0,15 – 0,71	24
		> 10	13,0	12,9	-0,16	-0,66 – 0,35	29

5.5. Calculation of trueness

To measure the trueness of the measurements on Precision Xtra Plus test strips at Precision Xceed, 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 of the duplicate values at Precision Xceed meter A/C.

5.6. Calculation of accuracy

To evaluate the accuracy of the results at Precision Xtra Plus test strips at Precision Xceed, the agreement between the Precision Xceed 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 Precision Xtra Plus test strips at Precision Xceed 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 best estimate of the repeatability of a method is achieved by using patient samples. By doing so, the matrix effects in artificially produced materials are avoided. In this evaluation, though, the patient samples can not be used for this purpose. The blood sampling for the comparison method was certainly done in duplicate, but with small blood volumes and with a time gap between the first and the second sample for each patient. Because of the small blood volumes each sample was analysed only once. Because of the time gap, the paired measurements reflect the stability of the glucose concentration during sampling, and not the precision of the method (see 6.1.3).
To get a good estimate of the repeatability of the comparison method in this evaluation, the results from the documentation of the trueness were used. Both the NIST-standards and the NOKLUS controls are genuine patient materials with no additives, and the standards and controls have been analysed repeatedly.

The repeatability of the comparison method is shown in table 7 and 9 for the first user-evaluation and in table 8 for the supplementary user-evaluation. 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 in the two user-evaluations is shown in table 6. 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 6 only the first result in each series is included. All results were inside the limits of the target values for the controls.

The results are shown in attachment 3 and 13.

Table 6. 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 First evaluation	5,2 ± 0,36	5,0	46	0	1,5 (1,2 – 1,9)
Autonorm 2 First evaluation	15,0 ± 1,05	14,7	46	0	1,3 (1,1 – 1,6)
Autonorm 1 Supplementary evaluation	4,6 ± 0,36	4,7	22	0	1,2 (0,9 – 1,7)
Autonorm 2 Supplementary evaluation	16,0 ± 1,12	16,0	22	0	0,7 (0,6 – 1,0)

Discussion
The precision of the comparison method is good. The repeatability is in general < 1,0 CV % (see table 7, 8 and 9) and the reproducibility is between 1,0 and 1,5 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 several times in both the first and the supplementary 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 in the first user-evaluation is shown in table 7.
The agreement between the comparison method and the NIST-standards in the supplementary user-evaluation is shown in table 8.

Table 7. The comparison method – Standard Reference Material (SRM 965a) measured on the comparison method during the first 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	30.11.05	**1,918** (1,898 - 1,938)	1,9	5	0,0 *	0
	05.01.06		1,9	5		0
	25.01.06		1,9	5		0
	Total		**1,9**	**15**		**0**
Level 2	30.11.05	**4,357** (4,309 - 4,405)	4,38	5	0,8 (0,6 – 1,3)	0,5
	05.01.06		4,38	5		0,5
	25.01.06		4,40	5		1,0
	Total		**4,39**	**15**		**0,7**
Level 3	30.11.05	**6,777** (6,704 - 6,850)	6,82	5	0,5 (0,4 – 0,9)	0,6
	06.01.06		6,78	5		0,0
	25.01.06		6,80	5		0,3
	Total		**6,80**	**15**		**0,3**
Level 4	30.11.05	**16,24** (16,05 - 16,43)	16,24	5	0,5 (0,4 – 0,8)	0,0
	06.01.06		16,34	5		0,6
	25.01.06		16,26	5		0,1
	Total		**16,28**	**15**		**0,2**

*The comparison method gives values with only one decimal. All the measurements at level 1 gave the result 1,9 mmol/L, and thereby there is no variation pointed out at this level.

Table 8. The comparison method – Standard Reference Material (SRM 965a) measured on the comparison method during the supplementary 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	08.08.06	**1,918** (1,898 - 1,938)	1,94	5	2,3 (1,8 – 3,9)	1,1
	11.08.06		1,96	5		2,2
	08.09.06		2,00	5		4,3
	Total		**1,97**	**15**		**2,5**
Level 2	08.08.06	**4,357** (4,309 - 4,405)	4,42	5	1,1 (0,9 – 1,8)	1,4
	11.08.06		4,44	5		1,9
	08.09.06		4,48	5		2,8
	Total		**4,45**	**15**		**2,1**
Level 3	08.08.06	**6,777** (6,704 - 6,850)	6,90	5	0,7 (0,5 – 1,0)	1,8
	11.08.06		6,88	5		1,5
	08.09.06		6,90	5		1,8
	Total		**6,89**	**15**		**1,7**
Level 4	08.08.06	**16,24** (16,05 - 16,43)	16,38	5	0,5 (0,4 – 0,8)	0,9
	11.08.06		16,46	5		1,4
	08.09.06		16,44	5		1,2
	Total		**16,43**	**15**		**1,1**

Table 8 reveals that glucose results at Architect ci8200 at the supplementary user-evaluation are slightly higher than the target values from NIST. Even though the obtained results hardly are outside the given uncertainty limits for the Reference Material, it was decided that all results from Architect should be adjusted according to the finds presented in table 8. The adjustment was done by means of the following regression equation ($R^2 = 1,0$):

$$\mathbf{y = 0,991x – 0,0433}$$

Further on in this report, whenever any result from Architect in the supplementary user-evaluation is presented, the result has already been adjusted according to this equation.

In the first user-evaluation, the trueness of the comparison method in addition was verified with freshly frozen, human serum controls from NOKLUS with glucose concentrations at two levels. 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 [9]. Unfortunately, these NOKLUS-controls were not available in the period of the supplementary user-evaluation.

The agreement with target values from the reference laboratory in Belgium is shown in table 9.

Table 9. The comparison method – Control samples from NOKLUS's External Quality Assessment program, measured on the comparison method during the first evaluation 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 control 1	14.12.05	3,20	3,20	6		1,2 (0,9 – 2,1)	0,0
	11.01.06		3,15	6			-1,6
	Total		**3,18**	**12**	**0**		**-0,8**
NOKLUS control 2	14.12.05	7,78	7,73	6		0,8 (0,5 – 1,3)	-0,6
	11.01.06		7,80	6			+0,3
	Total		**7,77**	**12**	**0**		**-0,2**

Discussion
The trueness of the comparison method is very satisfactory.

6.1.3. Stability of the glucose concentration during sampling in the supplementary evaluation

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 (see chapter 4.4.7). Deviations > 10 % are regarded as not acceptable and such results are excluded without further discussion. This applies for ID 147, ID 182 and ID 320. For further explanation, see chapter 5.3. 12 of 80 paired results at the comparison method gave deviations between 4 and 10 %. One sample with a low glucose concentration (below 5,5 mmol/L) had a difference just over the limit at 0,22 mmol/L. This result is still included in the calculations. For 5 of the 11 samples the deviation was less than 6 %. After a general evaluation of all the results, the paired measurements with differences between 4 and 10 % are included in the calculations in this evaluation. The summing up in table 13 has been done with and without these 12 results. The percentage number of results that falls within the different quality limits is not dependent on keeping or excluding these results.

6.2. Precision, trueness and accuracy of Precision Xtra Plus test strips at Precision Xceed in the supplementary user-evaluation

6.2.1. Internal quality control of Precision Xtra Plus test strips at Precision Xceed

Precision Xtra Plus test strips at Precision Xceed meter B 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 controls. The biomedical laboratory scientists' measurements at meter A and C with the manufacturer's control solution were also inside the limits of the controls.

The control results are shown in attachment 7 and 16.

6.2.2. The precision of Precision Xtra Plus test strips at Precision Xceed

Repeatability under standardised and optimal measuring conditions

The repeatability obtained under standardised and optimal conditions with blood samples from the diabetics finger capillaries, is shown in table 10. The table gives the results from the biomedical laboratory scientists' measurements at meter A and C.

Raw data from the biomedical laboratory scientists' measurements at NOKLUS is shown in attachment 14.

Table 10. Precision Xtra Plus/Precision Xceed – Repeatability (results with blood samples from the diabetics) measured under standardised and optimal conditions, n = 80 (meter A/C, three lot of test strips).

Precision Xtra Plus/ Precision Xceed	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A/C	< 7	5,1	15	0	6,7 (4,9–10,5)
Meter A/C	7 – 10	8,6	29	0	6,1 (4,8-8,2)
Meter A/C	> 10	13,4	36	0	5,4 (4,4-7,0)

Repeatability obtained by the diabetics

The repeatability obtained by the diabetics with blood samples from a finger capillary is shown in table 11. The table gives the results from the measurements performed by the diabetics at their consultation at NOKLUS.

Raw data from the diabetics' measurements at NOKLUS is shown in attachment 15.

Table 11. Precision Xtra Plus/Precision Xceed – repeatability (results with diabetic samples) measured by the diabetics at NOKLUS, n = 48 (meter B, three lot of test strips).

Precision Xtra Plus /Precision Xceed	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Diabetics' measurements at NOKLUS	< 7	5,1	7	0	7,4 (4,8-16,4)
Diabetics' measurements at NOKLUS	7 – 10	8,6	14	0	4,5 (3,2-7,2)
Diabetics' measurements at NOKLUS	> 10	12,9	27	0	5,0 (3,9-6,8)

Discussion
Under standardised and optimal conditions, the repeatability of Precision Xtra Plus at Precision Xceed is approximately 6 %. The imprecision is a little higher for glucose concentrations below 7 mmol/L. When measured by the diabetic patients, the precision is acceptable for glucose concentrations above 7 mmol/L. As a whole the imprecision is not significantly more then 5 %.

6.2.3. The trueness of Precision Xtra Plus test strips at Precision Xceed

The trueness of Precision Xtra Plus test strips at Precision Xceed is calculated from the results achieved by the biomedical laboratory scientists. The calculations are based on measurements at meter A and C with three lots of test strips (no. 40683, 40713 and 40783). The result of the calculations is shown in table 12.

Raw data from the samples at the comparison method is shown in attachment 17.

Table 12. Mean difference between Precision Xtra Plus/Precision Xceed and the comparison method, based on the mean of each duplicate at both methods. Results under standardised and optimal conditions, n = 77.

	< 7 mmol/L		**7 – 10 mmol/L**		**≥ 10 mmol/L**	
	The comparison method	**Meter A/C**	**The comparison method**	**Meter A/C**	**The comparison method**	**Meter A/C**
Mean glucose, mmol/L	5,2	5,4	8,4	8,8	13,1	13,4
% deviation from the comparison method (95 % CI)	4,9 (0,3 – 9,4)		4,4 (1,6 – 7,2)		2,3 (-0,7 – 5,2)	
n	14		29		34	
Outliers	0		0		0	

ID 147, ID 182 and ID 320 had a difference > 10% between the paired results on the comparison method and are excluded from the calculations of trueness. ID 97 did not have any measurement on meter A and is therefore not included in the calculations.

Discussion
In the supplementary evaluation the Precision Xtra Plus at Precision Xceed gives slightly higher glucose results than the comparison method, which has demonstrated reliable and true glucose values. The positive bias is approximately 4 to 5 % for glucose values < 10 mmol/L. The bias is statistical significant at this concentration level of glucose, but the deviation from the comparison method is hardly of any importance.
The shift in bias between the test strips in the first and the supplementary evaluation is between 14 and 20 percentage points. This is more than expected based on the stated difference between YSI and hexokinase methods. The negative bias that was pointed out in the first user-evaluation is more than compensated. Even a possible method bias is counterbalanced.

6.2.4. The accuracy of Precision Xtra Plus test strips at Precision Xceed

To evaluate the accuracy of the results at Precision Xtra Plus test strips at Precision Xceed, the agreement between Precision Xtra Plus/Precision Xceed and the comparison method is illustrated in two difference plots. The plots show the deviation of single measurement results at Precision Xtra Plus/Precision Xceed from the true value. The plots give a picture of both random and systematic deviation and reflect the total measuring error. The total error is demonstrated for the first measurements of the paired results, only. At meter A and C 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 chapter 3 in 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, Precision Xtra Plus test strips at Precision Xceed meter A and C under standardised and optimal measuring conditions, with three lot of test strips is shown in figure 2.

The accuracy, Precision Xtra Plus test strips at Precision Xceed, as measured by the diabetics at meter B with three lots of test strips is shown in figure 3.

The accuracy is summarised in table 13 and discussed afterwards.

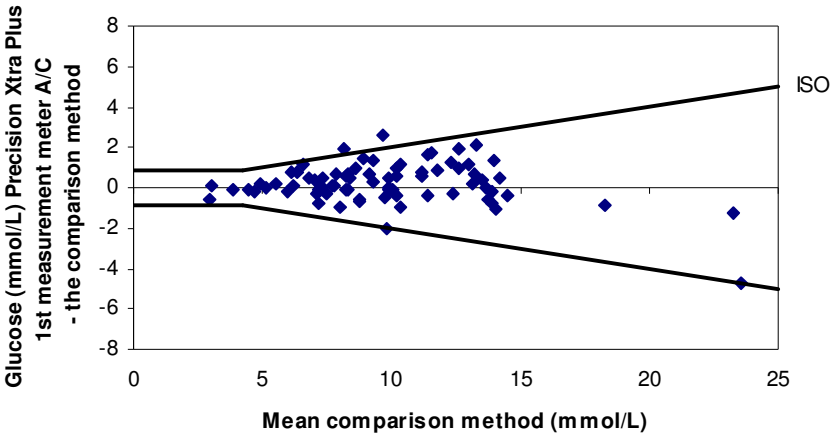

Figure 2. Accuracy. Precision Xtra Plus/Precision Xceed meter A and C under standardised and optimal measuring conditions in the supplementary user-evaluation. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at Precision Xtra Plus/Precision Xceed and the mean value of the duplicate results at the comparison method, n = 76.

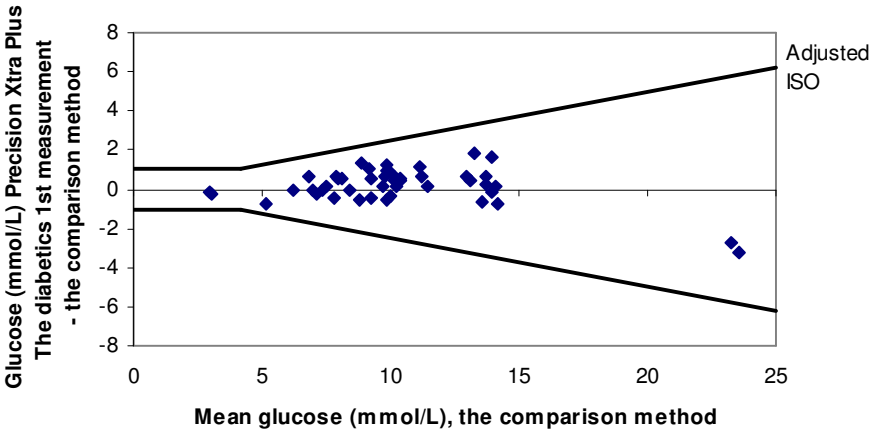

Figure 3. Accuracy. The diabetics' self-measurements at meter B in the supplementary user-evaluation. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at Precision Xtra Plus/Precision Xceed and the mean value of the duplicate results at the comparison method, n = 46.

Table 13. Total error of Precision Xtra Plus/Precision Xceed results compared to the comparison method. Percent Precision Xtra Plus/Precision Xceed results within the quality limits.

Measurements done by	Meter	n	Number of results (%)			Shown in figure
			< ADA (< ±10 %)	**< ISO** < ±20 % or < ±0,83 mmol/L at consentrations ≤ 4,2	**< "adjusted ISO"** < ±25 % or < ±1,0 mmol/L at consentrations ≤ 4,2	
Biomedical laboratory scientists	A/C, 1st measurement	76*	76	96	99	2
Diabetics at NOKLUS	B, 1st measurement	46	80	100	100	3

*ID 147, ID 182 and ID 320 had a difference > 10% between the paired results at the comparison method and are excluded from the calculations of accuracy. ID 328 had only one result on the comparison method and is not included in the calculations. ID 97 did not have any measurement on meter A and is not included in the calculations.

Discussion

Figure 2 shows that the Precision-results tend to be higher than the comparison method. The tendency is still not very pronounced. As a whole the results obtained under standardised and optimal measuring conditions at meter A/C with three lots of test strips are within the ISO-limits.

Figure 3 shows that the diabetics' measurements at meter B with three lots of test strips fulfil the "adjusted ISO-goal". The summing up in table 13 shows that these measurements also fulfil the quality goal set in ISO 15197.

The agreement between the three lots of test strips and the comparison method is discussed in chapter 6.3.

Assessment of accuracy

The Precision Xtra Plus test strips at Precision Xceed fulfil the quality goal set in 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 and C were performed with three different lots of test strips. 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 of the paired results at Precision Xtra Plus test strips at Precision Xceed obtained under standardised and optimal conditions at meter A and C 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 A/C and the comparison method under standardised and optimal conditions, n = 77.

	The comparison method	**Meter A/C Lot 40638**	**The comparison method**	**Meter A/C Lot 40713**	**The comparison method**	**Meter A/C Lot 40783**
Mean glucose, mmol/L	9,7	10,2	11,9	11,9	9,1	9,4
% deviation from the comparison method (95 % CI)	4,9 (1,8 – 8,0)		0,07 (-5,9 – 6,0)		3,4 (1,10 – 5,7)	
n	30		15		32	
Outliers	0		0		0	

ID 147, ID 182 and ID 320 had a difference > 10 % between the paired results at the comparison method at the final consultation and are excluded. ID 97 did not have any measurements on meter A/C and can therefore not be included in the calculations.

Discussion

Two of the three lots of Precision Xtra Plus test strips used in the evaluation gave significantly higher values than the comparison method. The results still fulfil the quality goal set in ISO 15197.

6.4. Effect of hematocrit from the first user-evaluation

The package insert of the Precision Xtra Plus test strips states that the glucose concentrations are not affected by hematocrit values between 30 – 60 %. To measure the effect of hematocrit at Precision Xtra Plus test strips, a hematocrit sample was taken of the diabetics (voluntary) at the final consultation. One of the 77 diabetic patients was not willing to have a sample for hematocrit taken.

The investigation of the effect of hematocrit is based on the measurements at Precision Xtra Plus test strips under standardised and optimal measuring conditions. The glucose concentration range in the samples was from 3,2 to 26,5 mmol/L. The hematocrit range was 35 – 49 %.

The effect of hematocrit is shown in figure 4. The x-axis in the plot shows the hematocrit value and the y-axis shows the difference in glucose concentration between Precision Xtra Plus test strips at Precision Xceed and the comparison method in % (Precision Xceed - the comparison method). Raw data is shown in attachment 9.

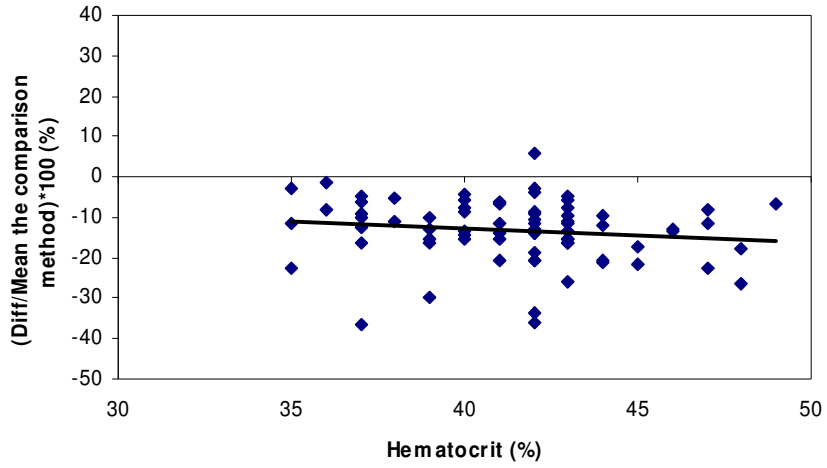

Figure 4. The effect of hematocrit at glucose measurements on Precision Xtra Plus test strips at Precision Xceed under standardised and optimal conditions. The x-axis shows the hematocrit value in %. The y-axis shows the difference in glucose concentration between Precision Xceed and the comparison method (Precision Xceed – the comparison method) in %, n=74

ID 144 and ID 191 had a difference > 10 % between the paired results on the comparison method and are excluded. ID 198 did not have a sample for hematocrit taken

Discussion

Glucose measurements at Precision Xtra Plus test strips at Precision Xceed do not seem to be particularly affected by hematocrit values between 35 and 49 %. Hematocrit values outside this range have not been tested.

7. Practical points of view

Questionnaires (first user-evaluation)

Each diabetic filled in a questionnaire about the user-friendliness of Precision Xtra Plus test strips at Precision Xceed and a questionnaire about the user manual of Precision Xceed when they attended the final consultation (n = 77) at the first user-evaluation. Some diabetics needed assistance in filling in the questionnaires.

The questionnaire about the user-friendliness and the questionnaire about the user manual are attached to the report (in Norwegian), see attachment 10 and 11.

7.1. Evaluation of user-friendliness of Precision Xtra Plus test strips at Precision Xceed

The questionnaire about the user-friendliness had nine questions concerning Precision Xtra Plus test strips at Precision Xceed and one question concerning the Easy Touch lancet pen. Table 17 summarizes seven 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, 5,5 and 5,5 on the questions about calibrating the meter, inserting a test strip into the meter and filling the test strip with blood, respectively. This indicates that the diabetics find it simple to use the test strips and that it was simple to calibrate the meter. The mean is 5,8 and 5,1 on the questions about reading the figures in the display and recognizing the meters' sound signal. The diabetics also find it simple to operate the meter, all in all. The mean is 5,2. Regarding Easy Touch lancet pen the mean is 4,9 which indicates that the diabetics were satisfied with the lancet pen too. The average score of the seven questions was 5,3. This indicates that overall the diabetics found the system simple to use.

Table 17. Questions about Precision Xtra Plus test strips at Precision Xceed (first user-evaluation)

Questions about Precision Xtra Plus test strips at Precision Xceed		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 code the meter	5,3	1-6	0	77
	2. To insert a strip into the meter	5,5	2-6	0	77
	3. To fill the strip with blood	5,5	2-6	0	77
	4. To read the figures in the display	5,8	3-6	0	77
	5. To recognize the meters' sound signal	5,1	1-6	0	77
	6. All in all, to operate the meter	5,2	2-6	0	77
	7. To operate Easy Touch lancet pen	4,9	1-6	5	77

Table 18 shows the answers to the last question about Precision Xceed. 34 % of the diabetics reported that they had technical problems with the meter during the testing period. For 16 of these patients the written comments indicated problems with the meter not turning on at all (8 diabetics) or turning off too quickly (8 diabetics). Some of these problems were solved by replacing the battery. Three patients had other battery-problems. Six patients had problems connected to setting correct date and time. One patient could not calibrate his meter and he therefore got a new device.

Table 18. Precision Xceed – Questions about the meter.

Question about Precision Xceed	Yes	No	Not answered (%)	Total number
Did you have any technical problems with the meter during the testing period?	26	50	1%	77

The diabetics were asked if they had any positive and/or negative comments about the Precision-system.

Positive comments
65 diabetics reported one or more advantages with Precision Xtra Plus/Precision Xceed. The most often advantages reported are distinctly grouped as follows:

1. The size of the meter (34)
2. The meter has short measuring time (30)
3. Simple operating of the meter (15)
4. To read the figures in the display/good display (13)
5. The meter/strip needs little blood sample volume (11)

Negative comments
36 diabetics reported one or more disadvantages with Precision Xtra Plus/Precision Xceed. The most often disadvantages reported are distinctly grouped as follows:

1. The test strips are individually packed; difficult to open (21)
2. Disadvantages with the lancet pen; sticks too deep, difficult to replace the needle (19)
3. The test strips need too much blood (7)
4. Not satisfied with the meters adjustment possibilities (5)

7.2. Evaluation of the user manual for Precision Xceed

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

Table 19 shows that 86 % of the diabetics had used the user manual, i.e. 66 of the 77 diabetics that participated in the study. Most of them answered that they were satisfied with the description of how to perform a blood glucose measurement with this meter. Most of them were quite satisfied with the user manual. Some of them thought the manual had essential shortcomings; the manual was not simple enough, difficult to understand the setting of the date. Three diabetics meant the user manual was too comprehensive and complicated.

Table 19. Precision Xceed – Questions about the user manual (first user-evaluation).

Questions about the user manual	Yes (%)	No (%)	Not answered (%)	Number
Have you been reading in the user manual?	86%	14%	0	77
If yes, did you read the entire user manual?	45%	44%	11%	66
And/or did you consult the user manual when needed?	70%	7%	23%	66
1. Are you satisfied with the description of how to perform a blood glucose measurement with this meter?	94%	5%	1%	66
2. Do you think the user manual has essential shortcomings?	8%	91%	1%	66
3. All in all, are you satisfied with the user manual?	91%	5%	4%	66

7.3. The biomedical laboratory scientists' evaluation

The biomedical laboratory scientists thought Precision Xceed was easy to use. They agreed with the diabetics that it was difficult to open the test strips package and it was difficult to replace the needle in the lancet pen. Regarding the user manual one of the biomedical laboratory scientists pointed out that it is necessary to set correct date (yy/mm/dy) to get the meter to function. This is not mentioned in the user manual. Some of the diabetic patients misunderstood the setting of date because the setting of year comes first.

The biomedical laboratory scientist had some problems with meter "A" which did not function properly all the time. The meter did not turn on at all or turned off too quickly. She got phone calls from diabetics with the same problem. The problem was solved by replacing the battery.

It was reported that one of the diabetics in the training group had problems filling the test strips with blood and getting enough blood to start a measurement. Several measurements gave different results when blood was applied and when he/she tried to apply more blood within 5 seconds. This occurred during the training session, and these results are not part of the evaluation.

8. References

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2. Skeie, S., et al., *Instruments for self-monitoring of blood glucose: comparisons of testing quality achieved by patients and a technician.* Clin Chem, 2002. **48**(7): p. 994-1003.
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5. Skeie S, Thue G, Sandberg S, "Patient-derived Quality Specifications for Instruments Used in Self-Monitoring of Blood Glucose". *Clinical Chemistry* 2001; **47** (1): 67 – 73.
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10. Burnett RW, "Accurate Estimation of Standard Deviations for Quantitive Methods Used in Clinical Chemistry". *Clinical Chemistry* 1975; **21** (13): 1935 – 1938.

9. Attachments

1. Serial numbers, Precision Xceed meters (first user-evaluation)
2. Information letter to the diabetics (in Norwegian) (first user-evaluation)
3. Raw data, internal quality control, Architect ci8200 (first user-evaluation)
4. Raw data, Precision Xtra Plus/Precision Xceed results under standardised conditions, (first user-evaluation)
5. Raw data, Precision Xtra Plus/Precision Xceed results, the diabetics measurements at NOKLUS (first user-evaluation)
6. Raw data, Precision Xtra Plus/Precision Xceed results, the diabetics measurements at home (first user-evaluation)
7. Raw data, internal quality control, Precision Xtra Plus/Precision Xceed (first user-evaluation)
8. Raw data, Architect ci8200 results, diabetic blood samples (first user-evaluation)
9. Raw data, hematocrit (first user-evaluation)
10. Questionnaire, user-friendliness (in Norwegian)
11. Questionnaire, user manual (in Norwegian)
12. Results from the first user-evaluation
13. Raw data, internal quality control, Architect ci8200 (supplementary user-evaluation)
14. Raw data, Precision Xtra Plus/Precision Xceed results under standardised conditions, (supplementary user-evaluation)
15. Raw data, Precision Xtra Plus/Precision Xceed results, the diabetics measurements at NOKLUS (supplementary user-evaluation)
16. Raw data, internal quality control, Precision Xtra Plus/Precision Xceed (supplementary user-evaluation)
17. Raw data, Architect ci8200 results, diabetic blood samples (supplementary user-evaluation)
18. SKUP evaluations
19. Response from Abbott Diabetes Care

Attachments with raw data are included only in the report to Abbott Norge as.

Attachment 1

Serial numbers, Precision Xceed instruments used by biomedical laboratory scientists

Instrument	Serialnumber
A	XC1021-3183
B	XC1021-0171
C	XC1144-3002
D	XC1021-3068

Serial numbers, Precision Xceed instruments used by diabetics

ID	Serialnumber
1	XC1144-2168
2	XC1144-0117
6	XC1021-3195
7	XC1144-2124
8	XC1021-3191
13	XC1021-1128
14	XC1144-3007
15	XC1144-0148
16	XC1021-2133
20	XC1021-2036
22	XC1021-2211
26	XC1021-1039
58	XC1144-1100
59	XC1144-1142
60	XC1021-2131
61	XC1021-1057
64	XC1021-1056
67	XC1021-1111
69	XC1144-0097
70	XC1144-2139
71	XC1021-0023
73	XC1021-2069
80	XC1144-3099
81	XC1144-2109
82	XC1021-3182
92	XC1021-2017
94	XC1021-1126
97	XC1144-2118
99	XC1144-2094
101	XC1144-3091
102	XC1144-0153
112	XC1021-3174
113	XC1021-0147
121	XC1021-2204
123	XC1144-2003
124	XC1144-3077
125	XC1144-2110
130	XC1144-2131
133	XC1144-0056

ID	Serialnumber
136	XC1144-3031
138	XC1021-2170
139	XC1144-3142
142	XC1021-0184
143	XC1021-0182
144	XC1021-3175
147	XC1144-0147
150	XC1021-0119
158	XC1021-2046
159	XC1144-2014
164	XC1021-3103
166	XC1021-0151
167	XC1144-0105
168	XC1021-3066
170	XC1021-3126
171	XC1021-3020
172	XC1021-1004
175	XC1021-0075
176	XC1021-0039
178	XC1144-3095
181	XC1144-3008
182	XC1144-1120
183	XC1021-3076
184	XC1021-2210
185	XC1021-1096
187	XC1144-3041
188	XC1021-1110
190	XC1144-3120
191	XC1021-0196
193	XC1144-1054
198	XC1144-2116
199	XC1144-0083
204	XC1144-2167
207	XC1021-3207
210	XC1144-0219
211	XC1144-3025
213	XC1144-3097
216	XC1021-0260

NORSK KVALITETSFORBEDRING AV
LABORATORIEVIRKSOMHET UTENFOR SYKEHUS

NOKLUS

«Navn»
«Adresse»
«Postadresse»

«ID-nr.»

Oktober 2005.

Utprøving av blodsukkerapparat

Du har fått utlevert en eske med:

- 1 ***Precision Xceed*** blodsukkerapparat i etui
- 1 pakke ***Precision Xtra Plus*** teststrimler for glukose (*50* stk.)
- 1 ***Easy To****uch* prøvetakingspenn
- ***50*** lansetter
- Brukerveiledning

Du skal bruke utprøvingsapparatet hjemme i en periode på ca. 3 uker. I denne prøveperioden skal du bruke dette apparatet **i tillegg** til ditt eget apparat. Det betyr at du skal utføre blodsukkermålingene med ditt vanlige apparat så ofte som du ellers ville ha gjort. **Når du skal vurdere ditt eget blodsukker, skal du bruke resultatene fra ditt vanlige apparat.** Utprøvingsapparatet skal du bruke slik det står beskrevet nedenfor:

1. og 2. uke:
De to første ukene skal benyttes til å bli kjent med apparatet. I løpet av disse to ukene skal du bruke ca. 25 strimler til å måle ditt eget blodsukker med utprøvingsapparatet.

Du kan selv velge når på dagen du vil gjøre disse målingene (du trenger ikke å være fastende). Passer det best slik, kan du utføre blodsukkermålingen med utprøvingsapparatet samtidig som du måler med ditt vanlige apparat. Dersom du ønsker det, kan du benytte ditt eget utstyr for prøvetaking i stedet for *Easy Touch* prøvetakingspenn.

3. uke:
Etter at du har brukt de 25 første strimlene, skal du i løpet av den tredje uken måle blodsukkeret med utprøvingsapparatet på 5 forskjellige dager. Du kan selv velge når på dagen du vil gjøre disse målingene (du trenger ikke være fastende). Hver av disse 5 dagene skal du: Stikke deg i fingeren og **måle blodsukkeret to ganger rett etter hverandre** med blod fra samme stikk. Dersom du ikke får nok blod til å utføre begge målingene, kan du stikke deg på nytt til andre måling. Resultatene føres i skjemaet på baksiden.

«ID-nr.»
«Lot-num. teststrimler»
«Serie-nummer apparat»

Dato	***Precision Xceed*** **Svar 1 (mmol/L)**	***Precision Xceed*** **Svar 2 (mmol/L)**	**Er målingene gjort med blod fra samme/forskjellige stikk? Stryk det som ikke passer.**
Dag 1:			Samme / forskjellige
Dag 2:			Samme / forskjellige
Dag 3:			Samme / forskjellige
Dag 4:			Samme / forskjellige
Dag 5:			Samme / forskjellige

Har du brukt ***Easy Touch*** prøvetakingspenn til prøvetakingen?

☐Ja ☐Nei ☐Noen ganger

Av de *50* strimlene du fikk sammen med apparatet, skal du nå ha ca. 15 strimler igjen. Du må spare fem av strimlene til målingene du skal gjøre når du kommer hit til laboratoriet for den avsluttende utprøvingen. Til den **avsluttende utprøvingen skal du ta med *Precision Xceed*, resten av strimlene og** *Easy Touch* prøvetakingspenn med lansetter. Du skal utføre egne målinger med utprøvingsapparatet. I tillegg vil bioingeniøren stikke deg to ganger i fingeren og til slutt ta en blodprøve fra armen. Du vil også bli bedt om å svare på noen spørsmål mht. apparatets brukervennlighet og om brukerveiledningen. Det hele vil ta ca ½ time.

Har du spørsmål, enten før du starter, eller i løpet av prøveperioden, er det bare å ringe:

Signe Røynås, Bente Knudsen eller Margarita Milán på tlf. 38073425 eller 99226232 mandag til fredag fra kl.08-15.30

Lykke til!

Med vennlig hilsen

Sverre Sandberg
Prosjektansvarlig (sign.)

Bente Knudsen og Margarita Milán
Bioingeniør (sign.)

Attachment 3

Raw data, internal quality control (Seronorm Autonorm Human Liquid 1 and 2), Architect ci8200

Date	Res. Autonorm 1 mmol/L	Res. Autonorm 2 mmol/L
06.12.2005	5,0	14,5
06.12.2005	5,0	14,7
07.12.2005	5,0	14,8
07.12.2005	5,1	15,0
07.12.2005	5,0	14,6
07.12.2005	5,1	15,1
08.12.2005	5,1	14,7
08.12.2005	5,1	14,7
08.12.2005	5,1	14,6
09.12.2005	5,0	14,4
09.12.2005	5,1	14,8
09.12.2005	5,0	14,3
12.12.2005	5,0	14,5
12.12.2005	5,1	15,0
12.12.2005	5,1	14,5
12.12.2005	5,1	14,9
14.12.2005	5,1	14,6
14.12.2005	5,1	14,7
14.12.2005	5,0	14,4
14.12.2005	5,0	14,7
21.12.2005	5,1	14,7
21.12.2005	5,1	14,6
02.01.2006	5,0	14,3
02.01.2006	5,0	14,7
05.01.2006	5,1	14,7
05.01.2006	5,1	14,7
05.01.2006	4,9	14,7
05.01.2006	5,1	14,9
06.01.2006	5,0	14,7
06.01.2006	5,0	14,5
06.01.2006	5,1	14,7
06.01.2006	5,2	14,9
09.01.2006	4,9	14,6
09.01.2006	5,1	14,4
09.01.2006	5,0	14,6
09.01.2006	5,0	14,6
10.01.2006	5,0	14,4
10.01.2006	5,0	14,7
10.01.2006	5,1	14,9
10.01.2006	5,0	14,5
11.01.2006	4,8	14,6
11.01.2006	5,1	14,9
11.01.2006	4,9	14,4
11.01.2006	5,0	14,5
24.01.2006	5,1	14,4
25.01.2006	5,1	14,6

Attachment 7

Raw data, internal quality control, Precision Xtra Plus/Precision Xceed

	MediSense Glucose Control Solution
Lot no. / Exp	29773Q100 / 2006/07/21
Glucose level:	
Lot 40109	3,6-6,7 mmol/L (level M), 12,1-20,4 mmol/L (level H)
Lot 40126	3,8-6,9 mmol/L (level M), 12,2-20,5 mmol/L (level H)
Lot 40135	3,8-6,9 mmol/L (level M), 11,8-20,1 mmol/L (level H)

MediSense Glucose Control Solution (level M, level H) analyzed on biomedical laboratory scientist's meter A/C and B/D.

Level M Date	**Meter A/C Lot 40109, mmol/L**	**Meter B/D Lot 40109, mmol/L**	**Meter B/D Lot 40126, mmol/L**	**Meter B/D Lot 40135, mmol/L**
17.okt	4,9	5,1		
19.okt	4,8	5,2		
21.okt			5,3	
26.okt	4,8		5,3	
31.okt	4,9			
01.nov	4,7	4,8		
02.nov	5,3		5,5	
04.nov	4,8		5,6	
07.nov	4,6		5,3	
09.nov	5,1		5,4	
28.nov	4,6		5,2	
Level H Date				
10.okt	13,8	14,4		
11.okt	14,6	14,5		
07.nov	14,2			15,6
08.nov	12,5			14,6
14.nov	14,1			14,7
14.nov	15,2			16,2
16.nov	15,2		15,8	
18.nov	15,0			14,5
21.nov	13,2			15,1
08.des	14,7			12,7
14.des	13,7		15,7	
16.des	14,8		15,8	
12.jan	14,8		15,1	

Training group		**First consultation**		**Final consultation**	
ID	Lot no. teststrips	MediSense Glucose Control Solution Level M, mmol/L	MediSense Glucose Control Solution Level H, mmol/L	MediSense Glucose Control Solution Level M, mmol/L	MediSense Glucose Control Solution Level H, mmol/L
1	40135		15,9	5,2	
2	40109	5,1			13,3
7	40126		14,9	5,3	
8	40135		15,8	5,4	
14	40135	5,1		5,3	
15	40126		14,4	forgotten	
16	40126		15,3	5	
22	40135		15,2	5,3	
26	40135	5,2		5,3	
60	40135		13,2	5,1	
64	40135		13,7	5,2	
67	40109		15	5,1	
69	40126	5,6			14,6
71	40135		12,3	5,2	
80	40109		14,6	5,3	
97	40126	5,3		5,4	
99	40126		15,6	5,1	
101	40109		14,7	5,1	
102	40135	5,4		5,2	
123	40135	4,9		5,2	
125	40109		12,1	4,6	
130	40109	5,1		5,4	
133	40109	5,1		4,8	
136	40109		13,6	4,5	
139	40126	5,2		5	
147	40135	4,9		4,9	
159	40109	5,2			17,9
167	40135	5,8			14,8
175	40135	5,2		5,6	
176	40135	5,4			14,9
181	40109		14,1	5,2	
183	40126	5,2		5,7	
184	40126		15,3	5,8	
188	40126	4,6			14,8
190	40109	5,1		5,2	
198	40109	5,4		5,3	
204	40126	4,7			15,6
210	40126	5,3			15,9
213	40109	5,1		5,1	
216	40126	5,5		4,6	

Attachment 7

Mail group		Final consultation	
ID	Lot no. teststrips	MediSense Glucose Control Solution Level M, mmol/L	MediSense Glucose Control Solution Level H, mmol/L
6	40135		14,6
13	40126		13,9
20	40135		14
58	40126	5,2	
59	40109		12,8
61	40126		17,2
70	40135		13,8
73	40126		15,7
81	40135		14,8
82	40135		14,8
92	40126		17,3
94	40135		13,9
112	40109		13,7
113	40126		14,2
121	40126		14,5
124	40109		16,9
138	40109		15,7
142	40135		14,4
143	40135		forgotten
144	40109	5,3	
150	40109		14,9
158	40126		15,1
164	40109		14,7
166	40109		14,1
168	40109		13,1
170	40135		14,9
171	40126		14,1
172	40135		17,2
178	40135		14,8
182	40135	5,6	
185	40126		16,2
187	40109		15,2
191	40109		
193	40126		15,2
199	40109		14,1
207	40109	4,9	
211	40126		14,2

ID-nummer (diabetiker): _____

Precision Xceed

Spørreskjema om blodsukkerapparatets brukervennlighet

Hvordan vil du rangere følgende på en skala fra 1 til 6, der 1 er *vanskelig* og 6 er *enkelt*:

1. Å kode (kalibrere) apparatet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

2. Å sette strimmel inn i apparatet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

3. Å fylle/påføre blod på strimmelen

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

4. Å lese tallene i displayet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

5. Å oppfatte lydsignal fra apparatet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

6. Å betjene apparatet, totalt sett

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

Snu arket

7. Å betjene Easy Touch blodprøvetakingspenn (skal kun besvares hvis denne er benyttet i utprøvingen)

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

8. Var det tekniske problemer med apparatet i utprøvingsperioden? ☐ **Ja** ☐ **Nei**

Hvis ja, kan du beskrive problemet/ene:_____

_____

_____

9. Synes du det er noen fordeler ved Precision Xceed?

- _____
- _____
- _____

10. Synes du det er noen ulemper ved Precision Xceed?

- _____
- _____
- _____

Evt. andre kommentarer:_____

_____

_____

_____

ID-nummer (diabetiker):_____

Precision Xceed

Spørreskjema om brukerveiledning til apparatet

Har du lest i brukerveiledningen? ☐ **Ja** ☐ **Nei**

Hvis du svarer nei, skal du ikke svare på resten av spørsmålene på dette arket.

Hvis du svarer ja:

- har du lest gjennom hele brukerveiledningen? ☐ **Ja** ☐ **Nei**

- og/eller har du slått opp i den ved behov? ☐ **Ja** ☐ **Nei**

1. **Er du fornøyd med beskrivelsen av hvordan man skal utføre en blodsukkermåling med dette apparatet?** ☐ **Ja** ☐ **Nei**

   Hvis nei, kan du beskrive hva du ikke er fornøyd med: _____

   _____

   _____

2. **Mener du at det er vesentlige mangler i brukerveiledningen?** ☐ **Ja** ☐ **Nei**

   Hvis ja, kan du beskrive hva som mangler: _____

   _____

   _____

3. **Totalt sett, er du fornøyd med brukerveiledningen?** ☐ **Ja** ☐ **Nei**

   Hvis nei, kan du beskrive hva du ikke er fornøyd med: _____

   _____

   _____

   Evt. andre kommentarer:_____

   _____

   _____

   _____

1.1. Missing or excluded results

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

- ID 144 and ID 191 at the final consultation (mail group) 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, these results are excluded when Precision Xtra Plus/Precision Xceed are compared with the comparison method (accuracy and trueness). The results are included in the calculations regarding the imprecision at Precision Xtra Plus/Precision Xceed because each set of duplicate measurements on the device is completed in less then a minute. ID 144 and ID 191 are also excluded from calculation regarding the effect of hematocrit for the same reason.
- In the calculation of repeatability based on the diabetics' measurements at home some measurements are missing. ID 82 did not have any measurements obtained at home. ID 150 and ID 168 had only single measurements. ID 133 had only one duplicate measurement. ID 176 had two duplicate measurements. ID 164 had three duplicate measurements. This means that 24 results are missing from this calculation.
- ID 198 had no hematocrit result and is missing from calculations regarding the effect of hematocrit.
- Note that ID 8 is excluded in two different connections. ID 8 is excluded as an outlier according to Burnett regarding repeatability measured by the diabetics and regarding trueness of Precision Xtra Plus/Precision Xceed (meter A/D versus the comparison method).

1.2. Stability of the glucose concentration during sampling

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. Deviations > 10 % were regarded as not acceptable and such results were excluded without further discussion. This applies for ID 144 and ID 191 (mail group). For further explanation, see chapter 1.1. 23 of 117 paired results at the comparison method gave deviations between 4 and 10 %. Three samples with a low glucose concentration (below 5,5 mmol/L) in the second consultation had a difference just over the limit at 0,22 mmol/L, respectively 0,3 to 0,4 mmol/L. They are still included in the calculations. For 14 of the 23 samples the deviation was less than 6 %. After a general evaluation of all the results, the paired measurements with differences between 4 and 10 % are included in the calculations in this evaluation. The summing up in table 13 has been done with and without these 23 results. The percentage number of results that falls within the different quality limits is not dependent on keeping or excluding these results.

1.3. Precision, trueness and accuracy of Precision Xtra Plus test strips at Precision Xceed

1.3.1. Precision of Precision Xtra Plus test strips at Precision Xceed

The Precision Xtra Plus test strips at Precision Xceed 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 controls.

Repeatability under standardised and optimal measuring conditions

The repeatability obtained under standardised and optimal conditions with capillary blood samples is shown in table 1. 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 1. Precision Xtra Plus/Precision Xceed – Repeatability (results with patient samples) measured under standardised and optimal conditions, n = 117 (meter A/C), n = 115 (meter B/D).

Precision Xtra Plus/Precision Xceed	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A/C	< 7	5,6	38	0	4,7 (3,8-6,1)
Meter B/D	< 7	5,6	34	0	4,4 (3,6-5,8)
Meter A/C	7 – 10	8,5	46	0	5,0 (4,2-6,3)
Meter B/D	7 – 10	8,2	40	2*	5,0 (4,1-6,4)
Meter A/C	> 10	12,3	33	0	6,7 (5,4-8,8)
Meter B/D	> 10	12,6	41	0	6,3 (5,2-8,1)

*ID 178 and ID 211 are excluded as outliers according to Burnett.

Repeatability obtained by the diabetics

The repeatability obtained by the diabetics with capillary blood samples is shown in table 2. The table gives the results from the measurements at the first and second consultation for the "training group", the consultation for the "mail 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 check 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 5.
Raw data from the diabetics' measurements at home is shown in attachment 6.

Table 2. Precision Xtra Plus/Precision Xceed – Repeatability (results with patient samples) measured by the diabetics ("training group" and the "mail group").

Precision Xtra Plus/Precision Xceed	Consultation/ diabetic group	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
NOKLUS	1st /training group	< 7	6,0	12	0	5,9 (4,2-10,0)
	2nd /training group	< 7	5,2	9	0	8,0 (5,4-15,4)
	The mail group	< 7	6,0	16	0	7,4 (5,5-11,5)
Home**		< 7	5,5	125	2	5,9 (5,3-6,8)
NOKLUS	1st /training group	7 – 10	8,3	10	0	4,9 (3,4-9,0)
	2nd /training group	7 – 10	8,4	15	0	9,3 (6,8-14,6)
	The mail group	7 – 10	8,8	7	0	5,8 (3,7-12,8)
Home**		7 – 10	8,2	136	2	5,8 (5,2-6,6)
NOKLUS	1st /training group	> 10	12,1	18	0	4,0 (3,0-6,0)
	2nd /training group	> 10	13,2	15	1*	4,0 (2,9-6,3)
	The mail group	> 10	12,6	14	0	6,8 (5,0-11,0)
Home**		> 10	13,2	91	5	5,7 (5,0-6,7)

* ID 8 is excluded as an outlier according to Burnett (poor agreement between the paired results at Precision).
** 12 measurements are missing, 12 measurements are excluded because of missing duplicates and 9 outliers are excluded, n= 385-24-9=352

Discussion

Under standardised and optimal conditions, the precision of Precision Xtra Plus at Precision Xceed is acceptable for glucose concentrations below10 mmol/L. The CV is between 4 and 5 %. For glucose values > 10 mmol/L the precision is poorer with a CV significantly > 5 %. There is no difference in the imprecision between meter A/C with one lot of test strips and meter B/D where three lots were used.

When measured by the diabetic patients, the precision is not quite acceptable. The CV is between 4 and 9 %. As opposed to the results achieved under optimal conditions, the diabetic patients get the better results when the glucose values are above10 mmol/L. At this concentration level the precision is acceptable, with a CV at approximately 5 %. For glucose concentrations < 10 mmol/L, the results vary more than desirable with a CV between 5 and 9 %.

The CVs for the group with and without a training programme (the training group and the mail group) are not significantly different. The imprecision at the final consultation tends to be poorer than before the practise period, but the differences are not significant. (The same laboratory scientists coordinated the first and final consultations, and the test strips were opened immediately before each measurement.) The results the diabetic patients achieved at home show that they have been practising with the new device according to the instructions, but one should not make a point of the calculated values.

Reproducibility with Internal Quality Control
The results for reproducibility are obtained with the MediSense Glucose Control Solution level M and level H. The measurements are carried out on meter A/C and B/D during the whole evaluation period. The reproducibility of Precision Xtra Plus test strips at Precision Xceed at meter A/C is shown in table 3. The results from meter B/D are included in attachment 7.

Internal Quality Control at the diabetics' meters
The control measurements on the diabetics' meters were done with the MediSense Glucose Control Solution level M and level H. All the control measurements were done by the biomedical laboratory scientists with the test strips that were distributed to each diabetic patient. The control solutions were kept at NOKLUS during the evaluation period. The imprecision at all the meters of the diabetics is shown in table 4. Raw data for all measurements with internal quality control is shown in attachment 7.

Table 3. Precision Xtra Plus – Reproducibility (results with MediSense Glucose Control Solution (level M, level H)) measured by the biomedical laboratory scientists on meter A/C with lot 40109.

Precision Xtra Plus/ Precision Xceed	Lot of strips	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
Meter A/C, level M	40109	3,6 – 6,7	4,9	10	0	4,5 (3,1-8,2)
Meter A/C, level H	40109	12,1 – 20,4	14,3	13	0	5,7 (4,1-9,4)

Table 4. Precision Xtra Plus/Precision Xceed – imprecision (results with MediSense Glucose Control Solution level M, level H) measured by the biomedical laboratory scientist on the diabetic patient's meters, n = 114.

Precision Xtra Plus /Precision Xceed	Lot of strips	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV % (95 % CI)
1st consultation						
The diabetic patient's meters	40109	3,6 – 6,7	5,2	7	0	2,2 (1,4 – 4,8)
	40126	3,8 – 6,9	5,2	8	0	6,8 (4,5 – 13,9)
	40135	3,8 – 6,9	5,2	8	0	5,7 (3,7 – 11,5)
	40109	12,1-20,4	14,0	6	0	7,6 (4,7 – 18,6)
	40126	12,2-20,5	15,1	5	0	3,1 (1,8 – 8,8)
	40135	11,8-20,1	14,4	6	0	10,4 (6,5 – 25,6)
2nd consultation*						
The diabetic patient's meters	40109	3,6 – 6,7	5,1	13	0	5,6 (4,0 – 9,2)
	40126	3,8 – 6,9	5,2	9	0	7,1 (4,8 – 13,6)
	40135	3,8 – 6,9	5,3	13	0	3,6 (2,6 – 5,9)
	40109	12,1-20,4	14,7	12	0	10,5 (7,4 – 17,8)
	40126	12,2-20,5	15,2	15	0	7,1 (5,2 – 11,1)
	40135	11,8-20,1	14,7	12	0	5,9 (4,2 – 10,1)

*The internal quality controls were forgotten at three of the diabetic patients' meters at the second consultation.

Discussion

The reproducibility at Precision Xtra Plus test strips at Precision Xceed is a result from analysing Glucose Control solutions. Artificially produced materials have other matrix effects than whole blood, and may therefore give other results than achieved with blood. The reproducibility obtained under standardised and optimal conditions measured by the biomedical laboratory scientist on meter A/C (one lot) is approximately 5 %. The imprecision obtained at NOKLUS measured by the biomedical laboratory scientist on the diabetics' meters is between 2 and 10 %.

Abbott informs that the MediSense Glucose Control Solutions are primarily designed for performing a QC check on the system operation; however, the precision of the system is optimised for testing with blood samples.

1.3.2. The trueness of Precision Xtra Plus test strips at Precision Xceed

The trueness of Precision Xtra Plus test strips at Precision Xceed is calculated from the results achieved by the biomedical laboratory scientist at the final consultation (the "training group" and the "mail group"). The calculations are based on measurements at meter A/C with lot 40109 and are shown in table 5.

Raw data from the samples at the comparison method is shown in attachment 8.

Table 5. Mean difference between Precision Xtra Plus/Precision Xceed and the comparison method, based on the mean of each duplicate at both methods. Results under standardised and optimal conditions from the final consultation, n = 74.

	< 7 mmol/L		**7 – 10 mmol/L**		**> 10 mmol/L**	
	The comparison method	**Meter A/C**	**The comparison method**	**Meter A/C**	**The comparison method**	**Meter A/C**
Mean glucose, mmol/L	5,5	5,0	8,2	7,5	13,6	11,2
% deviation from the comparison method (95 % CI)	-9,7 (-12,7 – (-6,8))		-8,6 (-10,5 – (-6,7))		-18,0 (-21,4 – (-14,6))	
n	18		22		34	
Outliers	0		0		1*	

ID 144 and ID 191 had a difference > 10% between the paired results on the comparison method and are excluded from the calculations of trueness.
*ID 8 is excluded as an outlier according to Burnett (poor agreement between Precicion and the comparison method).

Discussion

The comparison method has demonstrated very reliable and true glucose values. Precision Xtra Plus at Precision Xceed gives lower glucose results than this method. The glucose results at Precision Xtra Plus are between 8 – 18 % too low, compared with the comparison method. The negative bias comes out most strongly for glucose concentrations > 10 mmol/l, but the bias is significant also for glucose values < 10 mmol/l.

1.3.3. The accuracy of Precision Xtra Plus test strips at Precision Xceed

To evaluate the accuracy of the results at Precision Xtra Plus test strips at Precision Xceed, the agreement between Precision Xtra Plus/Precision Xceed and the comparison method is illustrated in three difference plots. The plots show the deviation of single measurement results at Precision Xtra Plus/Precision Xceed from the true value. The plots give a picture of both random and systematic deviation and reflect the total measuring error. The total error is demonstrated for the first measurements of the paired results, only. At meter A and C only one lot of test strips were used. At meter B and D 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 chapter 3 in the 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, Precision Xtra Plus test strips at Precision Xceed meter A/C, under standardised and optimal measuring conditions, with one lot of test strips (lot 40109) at the final consultation is shown in figure 1.

The accuracy, Precision Xtra Plus test strips at Precision Xceed meter B/D, under standardised and optimal measuring conditions, with two lots of test strips (lot 40126 and 40135) at the final consultation is shown in figure 2.

The accuracy, Precision Xtra Plus test strips at Precision Xceed, as measured by the diabetics with three lots of test strips (lot 40109, 40126 and 40135) at the final consultation is shown in figure 3.

The accuracy is summarised in table 6 and discussed afterwards.

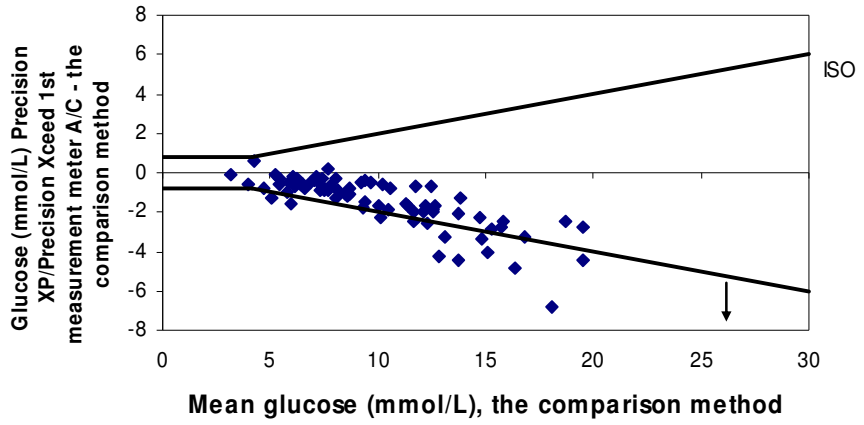

Figure 1. Accuracy. Precision Xtra Plus/Precision Xceed meter A/C (lot 40109) under standardised and optimal measuring conditions at the final consultation. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at Precision Xtra Plus/Precision Xceed and the mean value of the duplicate results at the comparison method, n = 75.
The arrow symbolises ID 8 which was an outlier according to Burnett. This result falls outside the border of the plot.

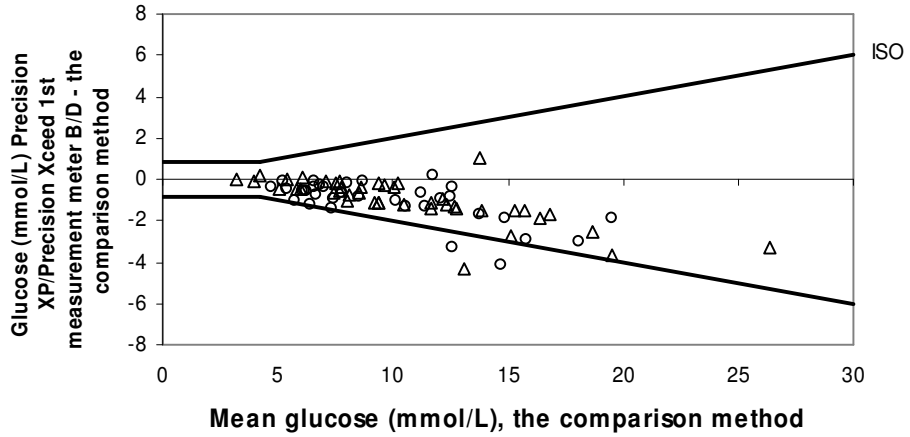

Figure 2. Accuracy. Precision Xtra Plus/Precision Xceed meter B/D (lot 40126 symbolised with Δ and lot 40135 symbolised with o) under standardised and optimal measuring conditions at the final consultation. The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at Precision Xtra Plus/Precision Xceed and the mean value of the duplicate results at the comparison method, n = 75.

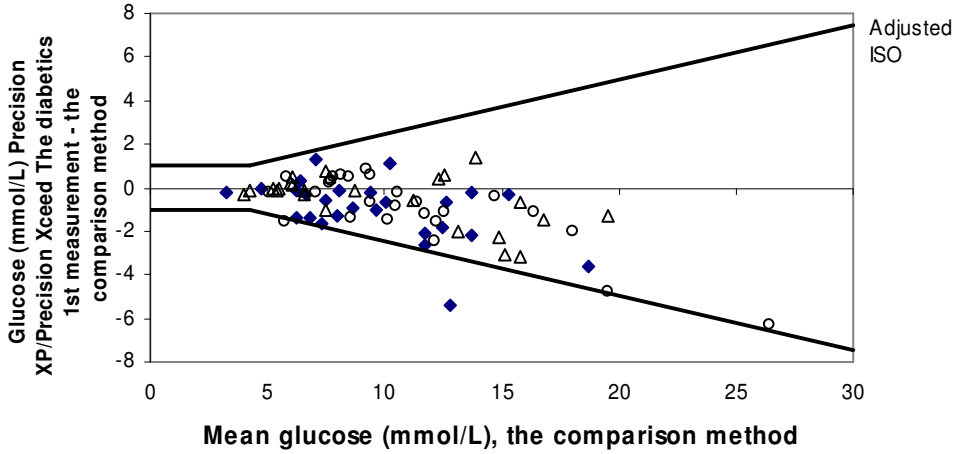

Figure 3. Accuracy. The diabetics' self-measurements at the final consultation (lot 40109 symbolised with ♦, lot 40126 symbolised with Δ and lot 40135 symbolised with o). The x-axis represents the mean value of the duplicate results at the comparison method. The y-axis shows the difference between the first measurement at Precision Xtra Plus/Precision Xceed and the mean value of the duplicate results at the comparison method, n = 75.

Table 6. Total error of Precision Xtra Plus/Precision Xceed results compared to the comparison method. Percentage Precision Xtra Plus/Precision Xceed results within the quality limits.

Measurements done by	Consultation	Meter	n	Number of results (%)			Shown in figure
				< ADA (< ±10 %)	**< ISO** < ±20 % or < ±0,83 mmol/L at consentrations ≤ 4,2	**< "adjusted ISO"** < ±25 % or < ±1,0 mmol/L at consentrations ≤ 4,2	
Biomedical laboratory scientist	1st	A/C 1st measurement	40	35	78		
		B/D 1st measurement	40	45	88		
Biomedical laboratory scientist	2nd *	A/C 1st measurement	75	35	81		2
		B/D 1st measurement	75	63	96		3
Diabetic patients at NOKLUS	1st	1st measurement	40	60	95	98	
	2nd *	1st measurement	75	63	88	97	4

*ID 144 and ID 191 had a difference > 10% between the paired results at the comparison method and are excluded from the calculations of accuracy.

Discussion

Figure 1 shows that the results obtained under standardised and optimal measuring conditions for one lot of Precision Xtra Plus test strips (lot 40109) at Precision Xceed meter A/C are inaccurate. The measurements at Precision give lower glucose values than the comparison method. The difference between the two methods increases with increasing glucose concentration. The measurements do not fulfil the quality goal set in ISO 15197.

Figure 2 shows that the results obtained under standardised and optimal measuring conditions for two lots of test strips (lot 40126 and 40135) at meter B/D are lower than the comparison method. The difference between the two methods increases with increasing glucose concentration, but the results fulfil the ISO-goal.

Figure 3 shows that the diabetic patients' measurements (training group and mail group together) with three lots of Precision Xtra Plus test strips (lot 40109, 40126 and 40135) at the second consultation fulfil the "adjusted ISO-goal". For glucose concentrations > 7 mmol/L the Precision-system gives lower values than the comparison method. The difference between the two methods increases with increasing glucose concentration.

The summing up in table 6 shows that the measurements with Precision Xtra Plus test strips at Precision Xceed performed under standardised and optimal conditions with the training group at the first consultation (40 results) do not fulfil the quality goal set in ISO 15197. The measurements were done with one lot of test strips at meter A/C and with two lots of test strips at

meter B/D (lot 40109 and 40126). These results are not shown in plots. The measurements performed by the 40 diabetic patients themselves at the first consultation fulfil the "adjusted ISO-goal" and are also within the ISO-goal. Nor these results are shown in a plot.

The accuracy seems to be better when lot 40126 and 40135 of test strips are used together compared with using lot number 40109 alone. Lot number 40109 was the "main lot" and was used on all the measurements at meter A and C. Lot number 40109 seems to be the lot that gives the lowest glucose values. This can explain some of the differences in the percent number of results that fall within the ISO-limits in table 6.
In the comparison of all the 1st and 2nd glucose measurements in table chapter 5.4 in the report, the results at meter A/C (one lot of test strips) are lower than the results at meter B/D (two lots of test strips) for glucose concentration above 10 mmol/L.
The agreement between the three lots of test strips and the comparison method is discussed in chapter 1.4. Lot number 40109 shows the largest percent deviation from the comparison method, but the deviation between the three lots and the comparison method is not significantly different.

Assessment of accuracy
Under standardised and optimal conditions, at the final consultation, measurements with Precision Xtra Plus test strips at Precision Xceed fulfil the quality goal set in the ISO 15197 only when lot 40126 and 40135 of test strips are used. The rest of the measurements under standardised and optimal conditions do not fulfil the ISO-goal. Assessed as a whole, approximately 85 % of all the results achieved under standardised and optimal conditions are within the limits in the ISO-standard. The "adjusted ISO-goal" is met by the measurements of the diabetics.

Response from Abbott Diabetes Care, see attachment 19 in this report.

1.4. Variation between three lots of test strips

All the measurements on meter A and C were performed with one lot of test strips. The measurements on meter B and D were performed with three different lots of test strips, in 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 Precision Xtra Plus test strips at Precision Xceed obtained under standardised and optimal conditions at meter B/D were compared with the mean of the paired values from the comparison method (paired t-test). The results are shown in table 7.

Table 7. Variation between three lots of test strips. T-test for paired values between three lots at meter B/D and the comparison method under standardised and optimal conditions (first and final consultation together), n = 115

	The comparison method	**Meter B/D Lot 40109**	**The comparison method**	**Meter B/D Lot 40126**	**The comparison method**	**Meter B/D Lot 40135**
Mean glucose, mmol/L	10,1	8,8	10,4	9,5	9,9	8,8
% deviation from the comparison method (95 % CI)	-12,6 (-16,7 – (-8,6))		-8,5 (-10,9 – (-6,2))		-11,3 (-14,6 – (-8,0))	
n	32		51		32	
Outliers	0		0		0	

ID 144 and ID 191 had a difference > 10 % between the paired results at the comparison method at the final consultation and are excluded.

Discussion

All three lots of Precision Xtra Plus test strips used in the evaluation gave significantly lower values than the comparison method.

Attachment 13

Raw data from the supplementary user-evaluation, internal quality control (Seronorm Autonorm Human Liquid 1 and 2), Architect ci8200

Date	Result Autonorm 1 mmol/L	Result Autonorm 2 mmol/L
80806	4,7	16,1
80806	4,7	16,1
80806	4,6	15,9
80806	4,6	15,9
80806	4,7	16,0
80806	4,6	16,0
80806	4,6	15,9
80806	4,6	16,0
80806	4,6	15,8
80806	4,6	16,1
100806	4,7	16,1
100806	4,7	16,2
100806	4,7	15,9
100806	4,7	15,9
100806	4,7	16,0
100806	4,8	16,1
100806	4,7	15,8
100806	4,7	15,8
110806	4,7	16,1
110806	4,7	16,0
110806	4,7	16,0
110806	4,7	15,9

Attachment 16

Raw data from the supplementary user-evaluation, internal quality control, Precision Xtra Plus/Precision Xceed

	MediSense Glucose Control Solution
Lot no. / Exp	34194Q100 / 2007/01/14

MediSense Glucose Control Solution (level M, level H) analyzed on biomedical laboratory scientist's meter A, meter B and meter C.

Level M Date	Meter A Result mmol/L	Meter A Lot-no	Target range mmol/L
07.06.2006	5,6	40638	3,8 - 6,9
12.06.2006	5,8	40638	3,8 - 6,9
21.06.2006	5,3	40638	3,8 - 6,9
23.06.2006	5,8	40638	3,8 - 6,9
06.06.2006	5,3	40713	3,6 - 6,7
09.06.2006	5,8	40713	3,6 - 6,7
15.06.2006	4,9	40713	3,6 - 6,7
20.06.2006	5,2	40713	3,6 - 6,7
08.06.2006	5,3	40783	3,9 - 7,0
13.06.2006	5,6	40783	3,9 - 7,0
19.06.2006	5,2	40783	3,9 - 7,0
Level M Date	**Meter B Result mmol/L**	**Meter B Lot-no**	**Target range mmol/L**
07.06.2006	5,8	40638	3,8 - 6,9
12.06.2006	5,3	40638	3,8 - 6,9
21.06.2006	5,8	40638	3,8 - 6,9
23.06.2006	5,3	40638	3,8 - 6,9
06.06.2006	5,7	40713	3,6 - 6,7
09.06.2006	6,1	40713	3,6 - 6,7
15.06.2006	4,9	40713	3,6 - 6,7
20.06.2006	5,3	40713	3,6 - 6,7
08.06.2006	5,7	40783	3,9 - 7,0
13.06.2006	5,4	40783	3,9 - 7,0
19.06.2006	5,8	40783	3,9 - 7,0
Level H Date	**Meter C Result mmol/L**	**Meter C Lot-no**	**Target range mmol/L**
16.06.2006	17,9	40638	13,2 - 21,5
19.06.2006	17,6	40638	13,2 - 21,5
20.06.2006	15,2	40638	13,2 - 21,5
21.06.2006	16,1	40638	13,2 - 21,5
22.06.2006	15,4	40638	13,2 - 21,5
07.06.2006	16,5	40783	13,3 - 21,6
09.06.2006	16,3	40783	13,3 - 21,6
12.06.2006	16,7	40783	13,3 - 21,6
13.06.2006	17,0	40783	13,3 - 21,6

List of evaluations organised by SKUP

Summaries and complete reports from the evaluations are found at www.skup.nu

Evaluations performed in 2004 - 2006

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2005/52*	Strep A	Clearview Exact Strep A Dipstick	Applied Biotech, Inc.
SKUP/2005/51*	Glucose[1]	FreeStyle	Abbott Laboratories
SKUP/2006/50	Glucose[1]	Glucocard X-Meter	Arkray, Inc.
SKUP/2006/49	Glucose[1]	Precision Xtra Plus	Abbott Laboratories
SKUP/2006/48	Glucose[1]	Accu-Chek Sensor	Roche Diagnostic
SKUP/2006/47	Haematology	Chempaq XBC	Chempaq
SKUP/2005/46*	PT-INR	*Confidential*	
SKUP/2006/45	Glucose[1]	HemoCue Monitor	HemoCue AB
SKUP/2005/44	Glucose[1]	Accu-Chek Aviva	Roche Diagnostics
SKUP/2005/43	Glucose[1]	Accu-Chek Compact Plus	Roche Diagnostics
SKUP/2005/42*	Strep A	Twister Quick-Check Strep A	ACON laboratories, Inc.
SKUP/2005/41*	HbA1c	*Confidential*	
SKUP/2005/40	Glucose[1]	OneTouch GlucoTouch	LifeScan, Johnson & Johnson
SKUP/2005/39	Glucose[1]	OneTouch Ultra	LifeScan, Johnson & Johnson
SKUP/2004/38*	Glucose	GlucoSure Plus	Apex Biotechnology Corp.
SKUP/2004/37*	u-hCG	Quick response u-hCG	Wondsfo Biotech
SKUP/2004/36*	Strep A	Dtec Strep A testcard	UltiMed
SKUP/2004/35*	u-hCG	QuickVue u-hCG	Quidel Corporation
SKUP/2004/34*	u-hCG	RapidVue u-hCG	Quidel Corporation
SKUP/2004/33	PT-INR	Hemochron Jr. Signature	ITC International Technidyne Corp
SKUP/2004/32*	Strep A	QuickVue In-Line Strep A test	Quidel Corporation
SKUP/2004/31*	PT-INR	*Confidential*	
SKUP/2004/30	Glucose[1]	Ascensia Contour	Bayer Healthcare
SKUP/2004/29	Haemoglobin	Hemo_Control	EKF-diagnostic

*A report code followed by an asterisk, indicates that the evaluation for instance is a pre-marketing evaluation, and thereby confidential. A pre-marketing evaluation can result in a decision by the supplier not to launch the instrument onto the Scandinavian marked. If so, the evaluation remains confidential. The asterisk can also mark evaluations at special request from the supplier or evaluations that are not complete according to SKUP guidelines, e.g. the part performed by the intended users was not included in the protocol.

[1] Including an user-evaluation among diabetic patients.

Evaluations performed in 1999 - 2003

Evaluation no.	Component	Instrument/test kit	Producer
SKUP/2003/28*	Strep A	QuickVue In-Line Strep A test	Quidel Corporation
SKUP/2003/27*	Strep A	QuickVue Dipstick Strep A test	Quidel Corporation
SKUP/2003/26*	HbA1c	*Confidential*	
SKUP/2003/25*	HbA1c	*Confidential*	
SKUP/2003/24*	Strep A	OSOM Strep A test	GenZyme, General Diag.
SKUP/2002/23*	Haematology with CRP	ABX Micros CRP	ABX Diagnostics
SKUP/2002/22	Glucose[1]	GlucoMen Glycó	Menarini Diagnostics
SKUP/2002/21	Glucose[1]	FreeStyle	TheraSense Inc.
SKUP/2002/20	Glucose	HemoCue 201	HemoCue AB
SKUP/2002/19*	PT-INR	Reagents and calibrators	
SKUP/2002/18	Urine–Albumin	HemoCue	HemoCue AB
SKUP/2001/17	Haemoglobin	Biotest Hb	Biotest Medizin-technik GmbH
SKUP/2001/16*	Urine test strip	Aution Sticks and PocketChem UA	Arkray Factory Inc.
SKUP/2001/15*	Glucose	GlucoSure	Apex Biotechnology Corp.
SKUP/2001/14	Glucose	Precision Xtra	Medisense
SKUP/2001/13	SR	Microsed SR-system	ELECTA-LAB
SKUP/2001/12	CRP	QuikRead CRP	Orion
SKUP/2000/11	PT-INR	ProTime	ITC International Technidyne Corp
SKUP/2000/10	PT-INR	AvoSure PT	Avocet Medical Inc.
SKUP/2000/9	PT-INR	Rapidpoint Coag	
SKUP/2000/8*	PT-INR	Thrombotest/Thrombotrack	Axis-Shield
SKUP/2000/7	PT-INR	CoaguChek S	Roche Diagnostics
SKUP/2000/6	Haematology	Sysmex KX-21	Sysmex Medical Electronics Co
SKUP/2000/5	Glucose	Accu-Chek Plus	Roche Diagnostics
SKUP/1999/4	HbA1c	DCA 2000	Bayer
SKUP/1999/3	HbA1c	NycoCard HbA1c	Axis-Shield PoC AS
SKUP/1999/2*	Glucose	Precision QID/Precision Plus Electrode, whole blood calibration	Medisense
SKUP/1999/1	Glucose	Precision G/Precision Plus Electrode, plasma calibration	Medisense

* A report code followed by an asterisk, indicates that the evaluation for instance is a pre-marketing evaluation, and thereby confidential. A pre-marketing evaluation can result in a decision by the supplier not to launch the instrument onto the Scandinavian marked. If so, the evaluation remains confidential. The asterisk can also mark evaluations at special request from the supplier or evaluations that are not complete according to SKUP guidelines, e.g. the part performed by the intended users was not included in the protocol.

[1] Including an user-evaluation among diabetic patients.

Grey area – The instrument is not in the market any more.

Abbott Diabetes Care

Response from Abbot Diabetes Care to SKUP Regarding the Report of Evaluation SKUP/2006/49 of Precision Xtra Plus (G3c) / Precision Xceed

ISO15197 makes reference to several Error Grid analyses, which were considered along with other criteria, in determining the standard's specification for accuracy. Error grid analysis is important in determining the clinical accuracy of blood glucose monitoring system results.

Abbott Diabetes Care (ADC) has taken data from the first user evaluation (attachments 4 & 5 of the SKUP report) to perform a Consensus Error Grid analysis[1] on the results. The data used, therefore, includes all glucose results on patient samples summarised in Table 6, Attachment 12 of the SKUP report. Results from the Precision Xceed meters are shown plotted against results from the comparative method on the Error Grid in the figures below.[2] It can be seen that all results are clinically acceptable, lying within Zones A and B of the Consensus Error Grid. Any clinical action based upon these results would lead to clinically correct treatment decisions or benign treatment decisions. There are no results within Zones C, D or E – hence no incorrect or missed treatment decisions leading to clinically significant errors would be made as a result of testing with these strip lots.

This importantly demonstrates that even the results falling outside the ISO standard requirement (±20% or ±0.83 mmol/L) are clinically acceptable and would not lead to treatment errors.

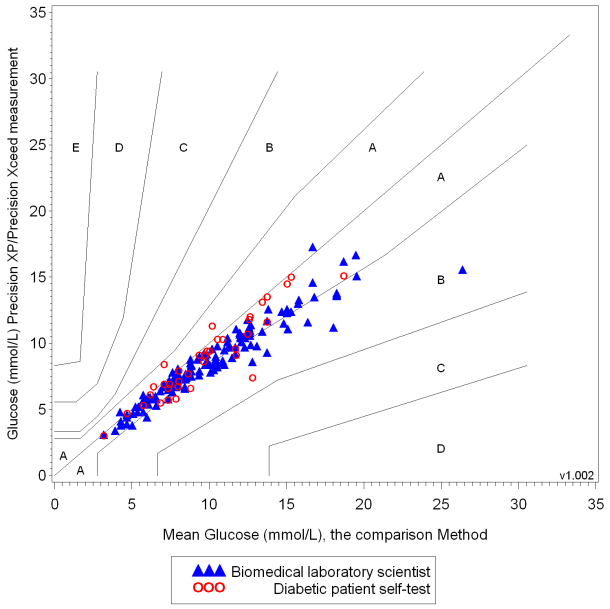

Figure 1. 'Precision Xtra Plus/Precision Xceed' measurements on the Consensus Error Grid – strip lot 40109 (meters A/C & B/D)

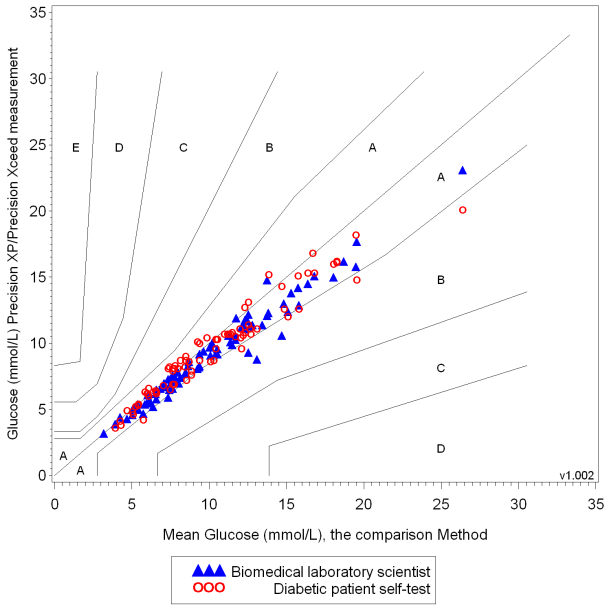

Figure 2. 'Precision Xtra Plus/Precision Xceed' measurements on the Consensus Error Grid – strip lots 40126 & 40135 (meter B/D)

[1] A New Consensus Error Grid to Evaluate the Clinical Significance of Inaccuracies in the Measurement of Blood Glucose; JL Parkes, S Pardo, SL Slatin, BH Ginsberg, *Diabetes Care*, 2000, 23:1143-1148

[2] Report EDMS010743 – held on file at ADC UK.