GlucoMen® LX

Meter and test strips designed for glucose self-measurement manufactured by A. Menarini Diagnostics

Report from an evaluation organised by

SKUP

The evaluation was ordered by A. Menarini Diagnostics, Sweden

SKUP in Norway, NOKLUS, Box 6165, NO-5892 Bergen. Phone +47 55 97 95 02. www.SKUP.nu

SKUP/2009/71

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 BFG"[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 purpose of SKUP is to improve the quality of near patient testing in Scandinavia by providing objective and supplier-independent information on analytical quality and user-friendliness of laboratory equipment. This information is generated by organising SKUP *evaluations*.

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

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

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

SKUP reports are published at www.skup.nu. A detailed list of previous SKUP evaluations is included in this report.

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

[2] "Afdeling for Biokemi, Farmakologi og Genetik" (Afdeling BFG) is the Department for Clinical Chemistry at the University Hospital in Odense, Denmark. Afdeling BFG 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 Läkaresällskapet" (Swedish Society of Medicine) and IBL (Swedish Institute of Biomedical Laboratory Science).

To make contact with SKUP

SKUP secretariat
Grete Monsen
+47 55 97 95 02
grete.monsen@noklus.no

SKUP in Denmark
Esther Jensen
Afdeling BFG
Odense Universitetshospital
DK-5000 Odense C
+45 6541 2865
skup@skup.dk

SKUP in Norway
Grete Monsen
Camilla Eide Jacobsen
Sverre Sandberg
NOKLUS
Boks 6165
NO-5892 Bergen
+47 55 97 95 02
grete.monsen@noklus.no
camilla.jacobsen@noklus.no
sverre.sandberg@isf.uib.no

SKUP in Sweden
Arne Mårtensson
Gunnar Nordin
EQUALIS
Box 977
SE-751 09 Uppsala
+46 18 69 31 64
arne.martensson@equalis.se
gunnar.nordin@equalis.se

www.SKUP.nu

Table of contents

Attachments with raw data are included only in the copy to A. Menarini Diagnostics.

1. Summary

Background
The GlucoMen LX blood glucose meter and the GlucoMen LX Sensor test strips are designed for glucose self-measurements performed by diabetes patients. The meter and the test strips are produced by A. Menarini Diagnostics and supplied in Scandinavia by A. Menarini Diagnostics. In Norway Med-Nett AS will distribute the system on license of A. Menarini Diagnostics. GlucoMen LX and GlucoMen LX Sensor test strips have not yet been launched onto the Norwegian market. In order to give reimbursement for the test strips in Norway, the Norwegian Labour and Welfare Organisation (NAV) requires from the companies to carry out an evaluation that includes a user-evaluation among diabetes patients.
The SKUP-evaluation of GlucoMen LX and GlucoMen LX Sensor test strip was carried out under the direction of SKUP from September to December 2008.

The aim of the evaluation
The aim of the evaluation of GlucoMen LX is to

- reflect the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in a hospital environment
- reflect the analytical quality by the intended users
- compare the analytical quality among trained and un-trained diabetes patients
- examine the variation between three lots of test strips
- examine if hematocrit interferes with the measurements
- evaluate GlucoMen LX regarding user-friendliness
- evaluate the GlucoMen LX user guide

Materials and methods
84 diabetes patients took part in the evaluation. 43 participants had two consultations and the rest had one consultation. The diabetes patients in the "training group" were given a standardised instruction about GlucoMen LX before they did a finger prick and performed two measurements on the meter. The biomedical laboratory scientist also collected capillary samples from the diabetes patients and measured twice on GlucoMen LX. In addition, two capillary samples were taken for measurements with a designated comparison method. The diabetes patients in the "mail group" received GlucoMen LX by mail and no training was given. Both groups of diabetes patients used the equipment for approximately three weeks at home, before they attended 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 answered questionnaires about the user-friendliness and the user guide of GlucoMen LX.

Results

- The overall precision of GlucoMen LX was acceptable. The repeatability CV obtained under standardised and optimal conditions was approximately 4,5%, and approximately 6% when the measurements were performed by the diabetes patients.
- For low glucose concentrations (<7 mmol/L) the results on GlucoMen LX were systematic higher than the results from the comparison method. The mean deviation from the comparison method at this concentration level was +0,45 mmol/L. For glucose concentrations between 7 and 10 mmol/L GlucoMen LX gave results in agreement with the comparison method. For high glucose concentrations (≥10 mmol/L) GlucoMen LX gave lower results than the comparison method. The bias at this concentration level was -0,40 mmol/L.
- The accuracy of GlucoMen LX was good. The results fulfilled the quality goal proposed in ISO 15197. More than 95% of the results achieved under standardised and optimal conditions were within the limits described in ISO 15197. The "adjusted ISO-goal" was met by the measurements of the diabetes patients, and >95% of the results achieved by the diabetes patients also fulfilled the ISO-goal.
- There was no provable difference between the results achieved with three different lots of test strips.
- The glucose results on GlucoMen LX were not affected by hematocrit values from 30 – 49%.
- The diabetes patients thought that the GlucoMen LX device was easy to operate. Most of them were pleased with the device. The diabetes patients that had used the user guide were satisfied with the guide.

Conclusion

The precision of GlucoMen LX was acceptable. The repeatability CV was between 4 and 7%. The accuracy of GlucoMen LX was good, and the results fulfilled the quality goal based on ISO 15197. Glucose measurements on GlucoMen LX were not affected by hematocrit in this study. Most of the users found the GlucoMen LX device easy to use.

Comments from A. Menarini Diagnostics

There is no additional information from producer attached to the report.

2. 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. GlucoMen LX is designed for monitoring blood glucose, and the quality goals must be set according to this.

Precision
For glucose meters designed for monitoring blood glucose one should point out the need of a method with good precision [1]. According to the American Diabetes Association (ADA) the imprecision (CV) of new glucose devices must be less than 5% [2]. Other authors also recommend an imprecision of 5% or less [3].

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 GlucoMen LX is based on ISO 15197, *In vitro diagnostic test systems – Requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus* [4]. The ISO-guide is an international protocol for evaluating meters designed for glucose monitoring.

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 performed by the diabetes patients. Previous investigations under the direction of the NOKLUS-project "Diabetes-Self-measurements" in 1997 [3, 5] 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 achieved by the diabetes patients 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 diabetes patients over time, as the meters would hopefully improve due to technological development. More recent evaluations performed by SKUP [6] clearly show that the quality goals set by ISO 15197 now can be achieved also by the diabetes patients. But for the time being, the quality demands adjusted to the diabetes patients' self-measurements, still apply.

Quality demands, adjusted to the diabetes patients 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.

3. Materials and methods

3.1. GlucoMen LX

GlucoMen LX is a blood glucose monitoring system based on biosensor technology. The system consists of a meter, GlucoMen LX, and dry reagent test strips, GlucoMen LX Sensor. The system is designed for capillary blood glucose testing performed by persons with diabetes or by health care professionals. GlucoMen LX reports plasma glucose values. The system requires no calibration.

The test principle of GlucoMen LX is as follows. Glucose reacts with the oxidised form of glucose oxidase (GOD_{ox}) to produce gluconolactone. This reaction results in the reduction of GOD_{ox} into GOD_{red}. GOD_{ox} is then regenerated *via* interaction with the potassium ferricyanide mediator, which is in turn reduced to ferrocyanide. The applied polarisation voltage of +350 mV finally allows electrochemical re-oxidation of ferrocyanide to ferricyanide. The latter process generates electrons that are measured as an electrical current by the meter. This current is directly proportional to the concentration of glucose into the sample.

$$\text{Glucose} + GOD_{ox} \longrightarrow \text{Gluconolactone} + GOD_{red}$$

$$GOD_{red} + [Fe(CN)_6]^{3-} \longrightarrow GOD_{ox} + [Fe(CN)_6]^{4-}$$

$$[Fe(CN)_6]^{4-} \xrightarrow{\text{Electrode, +350 mV}} [Fe(CN)_6]^{3-} + e^-$$

The test strips are packed in a plastic bottle with flip-top closure. The system requires a blood volume of 0,3 µL. According to the package insert the measurement starts only when the correct amount of blood is applied to the test strip. The result is shown within 4 seconds. It is possible to test with blood from alternate test sites as the palm and forearm. 400 results are automatically stored in the memory with date and time, offering the possibility of taking an average over 1, 7, 14 or 30 days. Results can be downloaded to a PC using the GlucoLog software. Technical data from the manufacturer is shown in table 1.

3.1.1. Product information, GlucoMen LX

GlucoMen LX blood glucose meter system

Manufactured by:
A. Menarini Diagnostics S.r.l.
Via Sette Santi 3
50131 Firenze
Italy

Table 1. Technical data from the manufacturer

Technical data for GlucoMen LX	
Optimal operating temperature	5 – 45 °C
Sample volume	0,3 µL
Measuring time	4 seconds
Measuring range	1,1 – 33,3 mmol/L
Hematocrit	25-60%
Memory	400 test results
Power source	One 3-volt lithium battery (CR2450)
Operating time	Approximately 1000 tests
Humidity	10 – 90 % RH
Dimensions	96 mm x 51mm x 20 mm
Weight	Approximately 75 g

88 GlucoMen LX blood glucose meters were used in this evaluation. The evaluation took place in Lillehammer and Gjøvik. In Lillehammer serial no. D080910052XL (called meter A) and serial no. D080909052XL (called meter B) were used by the biomedical laboratory scientist. In Gjøvik serial no. D080907052XL (called meter A) and serial no. D080911052XL (called meter B) were used by the biomedical laboratory scientist. Attachment 1 gives serial numbers for the 84 meters used by the diabetes patients.

GlucoMen LX test strips:

Lot 3208010249	Expiry 2010-01-31
Lot 3208037249	Expiry 2010-02-28
Lot 3208011249	Expiry 3010-01-31

GlucoMen LX Control N:

D-glucose in 99% non-reactive ingredients

Control Normal	Lot 3308158302	Expiry 2010-12
Control Normal	Lot 3308123302	Expiry 2010-11-30

Suppliers of GlucoMen LX in the Scandinavian countries:

Denmark:	Norway:	Sweden:
Menarini has no supplier in Denmark	Med-Nett AS Gamle Snarøyvei 49 D 1367 Snarøya	A. Menarini Diagnostics Medeon Science Park Per Albin Hansson väg 41 214 32 Malmø
	Phone: +47 67 82 90 00 Fax: +47 67 82 90 02 mednett@online.no www.mednett.no	Phone: +46 40 32 12 70 Fax: +46 40 32 12 71 info@menarinidiagnostics.se

The 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.

The designated comparison method in this evaluation
In a SKUP evaluation the designated comparison method is usually a well established routine method in a hospital laboratory. The trueness of the comparison method is usually documented with reference materials and/or by comparison with external quality controls from an external quality assurance programme. A glucose comparison method should be a plasma method, hexokinase by preference.

In this evaluation, the routine method for quantitative determination of glucose in human serum and plasma (e.g. lithium heparin) on the Laboratory at Haraldsplass Diaconal Hospital (HDH) 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 used on Architect *ci*8200 System from Abbott Laboratories, with reagents and calibrators from Abbott Laboratories. The measuring principle 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 NAD to NADH. The NADH produced absorbs light at 340 nm and can be detected spectrophotometrically as an increased absorbance.

Verifying of trueness
The comparison 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 [7] consists of ampoules with human serum with certified concentrations of glucose (and their given uncertainties) at four levels. The uncertainty is defined as an interval estimated to have a level of confidence of at least 95%. The SRM 965a materials cover a glucose concentration range from 1,9 to 16,2 mmol/L, and were used in this evaluation to verify the trueness. In addition, freshly frozen, human serum controls, produced by SERO AS, with glucose concentrations at two levels were analysed. These controls have target values determined with an isotope-dilution gas chromatography/mass spectrometry method in a Reference laboratory in Belgium; Laboratory for Analytical Chemistry, University of Gent, Belgium [8]. The controls are included in NOKLUS's External Quality Assessment program. The results are summarized in chapter 5.1.2.

Internal quality assurance of the comparison method during the evaluation period
The Autonorm Human Liquid Control Solutions at two levels from SERO AS were included in all the measuring series in this evaluation. The results are summarised in table 5.

3.2.1. Product information, the comparison method

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

Reagents
Glucose Reagent Kit, Ref. 3L82-20 and 3L82-40
Lot 61052HW00 Expiry 2008-11-30

Glucose Reagent Kit, Ref. 30-3635/R2
Lot 62002HW00 Expiry 2009-01-31

Calibrator
Multiconstituent Calibrator, List No. 1E65
Lot 61387M100 Expiry 2009-06-30 Reference value, cal 1 = 5,33 mmol/L
Reference value, cal 2 = 24,03 mmol/L

Internal quality controls
Autonorm Human Liquid 1 and 2, SERO AS
Liquid 1: Value = 3,37 ±0,20 mmol/L Lot 609470 Expiry 2008-11-30
Liquid 2: Value = 15,97 ±0,83 mmol/L Lot 611674 Expiry 2009-01-31

External Quality controls, SERO AS
Reference value from Laboratory for Analytical Chemistry, University of Gent, Belgium; ID-GCMS method
Serum TM Gluc L-1 Value = 4,78 ±0,09 mmol/L Lot 0809361
Serum TM Gluc L-2 Value = 11,80 ±0,16 mmol/L Lot 0809362

NIST standards
Standard Reference Material® 965a, National Institute of Standards & Technology
Expiry 2008-12-31
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 WIR 028
Accu-Chek Softclix Pro lancets: Lot WIT 44 H 2 Expiry 2011-10-31

Tubes used for sampling for the designated comparison method
Microvette CB 300 LH (lithium-heparin) manufactured by Sarstedt AS
Lot 7070301 Expiry 2009-12

Centrifuge used for samples for the designated comparison method
Eppendorf Centrifuge 5415D Serial no. 0057100
Biofuge pico (Heraeus) Fabr.nr: 291323

3.2. Planning of the evaluation

Background for the evaluation
GlucoMen LX is a blood glucose monitoring system designed for capillary blood testing performed by diabetes patients or by health care professionals. The GlucoMen LX-system is produced by A. Menarini Diagnostics and supplied in Scandinavia by A. Menarini Diagnostics, Sweden. In Norway Med-Nett will distribute the system on license of A. Menarini Diagnostics. The system is marketed in Sweden, but has not been launched onto the Danish or Norwegian market yet.

Inquiry about an evaluation
Johan Vikner, Menarini Diagnostics, applied to SKUP in October 2007 for an evaluation of GlucoMen LX glucose meter with GlucoMen LX Sensor. At the time, the meter and test strips were still under development and not ready for being launched onto the market. The expected time for delivery of equipment for an evaluation was February 2008. SKUP accepted to organise this evaluation for Menarini.

Protocol, agreements and contract
The protocol for the evaluation was approved in January 2008. The laboratory at Haraldsplass Diaconale Hospital (HDH) in Bergen agreed to carry out the analytical part of the evaluation concerning analysing the samples for the comparison method. Menarini and SKUP signed a contract about the evaluation in February.

Preparations and training program
The preparations for the evaluation started in January 2008. SKUP took on two biomedical laboratory scientists for the practical work with the evaluation. They were educated in the evaluation procedures by SKUP in January. There after, Sabina Sjöberg, Menarini Diagnostics, trained them for the practical work with GlucoMen LX. The meters and test strips for the evaluation were received in the end of February, and the equipment was directly unpacked and prepared for distribution among the diabetes patient.

Recruitment of the diabetes patients
The diabetes patients were recruited in February through advertisements in three local newspapers and in "Diabetes" (2008/1), a magazine for the members of The Norwegian Diabetes Association. Diabetes patients were also recruited by mail inquiry sent to the members of the local branch of The Norwegian Diabetes Association.

Delay
In March, Johan Vikner, Menarini, reported of a deplorable change of planes. The producer had announced that the LX Sensor and meter had to undergo additional improvements and production changes. Assumed delivery of new equipment was within a month. The arrangements with the first group of diabetes patients had to be cancelled. The delivery of the new equipment was even further delayed, and during April it became clear that the new equipment was expected at the earliest in the end of Mai. The decision had to be made to postpone the evaluation until August.

Clearing up and new preparations
The equipment that already was received was repacked and returned to the supplier in Sweden in May. All the diabetes patients got a letter from SKUP with an apology for the delay, and a request for participation in the evaluation in the autumn. The new equipment for the postponed evaluation was delivered in July. New appointments with the diabetes patients were made in August, and the practical work with the evaluation could finally start in September 2008.

The SKUP evaluation
SKUP evaluations are based upon the fundamental guidelines in the book "*Evaluation of analytical instruments. A guide particularly designed for evaluations of instruments in primary health care*" [9]. The evaluation of a self-monitoring blood glucose device in principle follows the guidelines in the book, but the evaluation in primary health care is replaced by a user-evaluation conducted among diabetes patients, based on the model worked out by the NOKLUS-project "*Diabetes-Self-measurements*" [10]. This model has become basis for the quality specifications used when The Norwegian Labour and Welfare Organisation (NAV) decides whether or not to give reimbursement for glucose test strips [11]. The evaluation model has been used by SKUP since 2002, and has recently been evaluated and discussed in an article presenting the results from nine of the SKUP evaluations [12].

The evaluation comprises the following studies:
- An examination of the analytical quality under standardised and optimal conditions, performed by a biomedical laboratory scientist in a hospital environment
- An examination of the analytical quality among approximately 80 diabetes patients
- The agreement between GlucoMen LX and a designated comparison method
- A comparison of the analytical quality among diabetes patients with and without a training programme
- An examination of the variation between three lots of test strips
- An examination to see if hematocrit interferes with the measurements
- An evaluation of the user-friendliness of GlucoMen LX
- An evaluation of the user guide of GlucoMen LX

After the evaluation, the diabetes patients returned the GlucoMen LX device to the project.

3.3.1. Evaluation sites and persons involved
The blood sampling of the diabetes patients and the measurements on GlucoMen LX under standardised and optimal conditions, were carried out by Sonja Jørgensen and Helen Skoglund, biomedical laboratory scientist, SKUP/NOKLUS at the Hospital Innlandet HF in Lillehammer and Gjøvik, Norway. Three biomedical laboratory scientists, Grethe Kalleklev, Kjersti Østrem and Grete H. Solsvik, 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 Ann Kristin Fagerbakke and Grete Monsen, SKUP/NOKLUS in Bergen.

3.3. The evaluation procedure

3.4.1. The model for the evaluation

The practical work with the evaluation was carried out during 10 weeks from September to December. The evaluation consisted of two parallel parts. One part of the evaluation was carried out under standardised and optimal conditions in a hospital laboratory. This part of the evaluation was done by laboratory educated personnel, in exact accordance with the protocol and the user guide and after having received thorough 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 conditions as favourable as possible for achieving good analytical quality. The other part of the evaluation was performed by diabetes patients. In order to determine the analytical quality of GlucoMen LX by the users, 84 diabetes patients tested their blood glucose using GlucoMen LX. The diabetes patients were divided into two groups (random distribution). 43 diabetes patients received personal training in how to use the blood glucose meter, here called the "training group". The other group received the blood glucose meter and instructions by mail, here called the "mail group". Dividing the diabetes patients into a "training group" and a "mail group" reflects the actual market situation regarding training when diabetes patients acquire blood glucose meters [10]. The model for the evaluation is shown in figure 1.

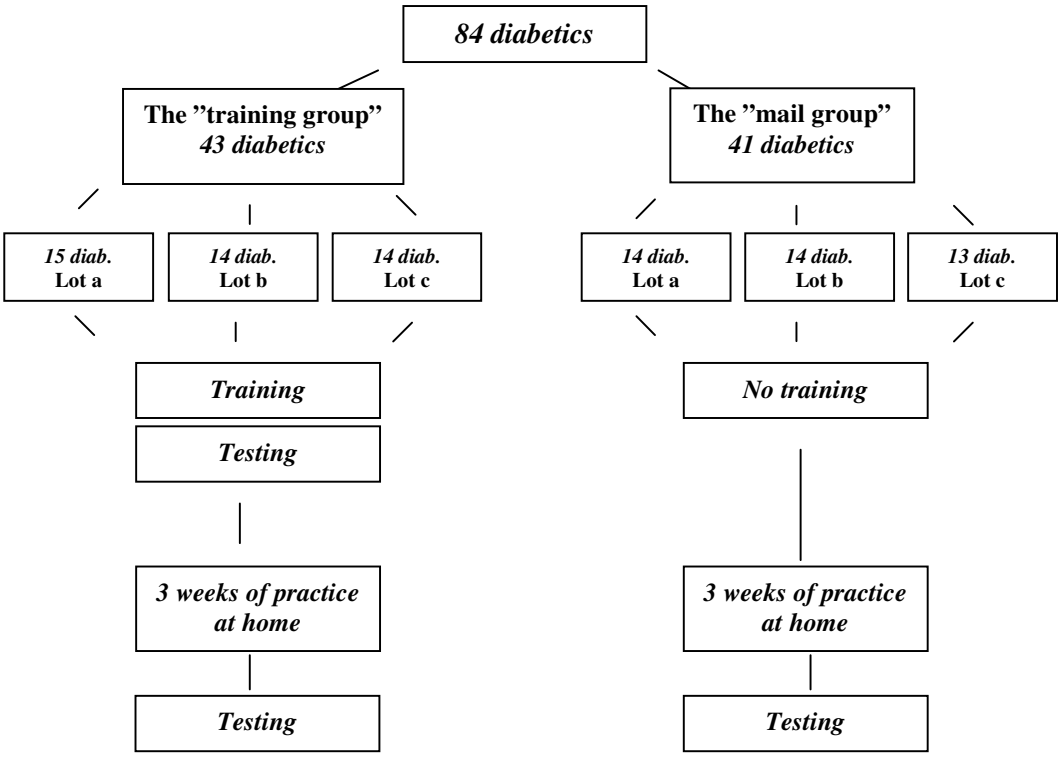

Figure 1. Model for the evaluation

3.4.2. Selection of diabetes patients

The GlucoMen LX glucose meter was tested in use by 84 diabetes patients. The group of diabetes patients was representative for diabetes patients who carry out self-monitoring of blood glucose (SMBG). The group included diabetes patients from across a range of self-monitoring frequencies, i.e. diabetes patients who perform self-monitoring often (once or more a day) and those who perform self-monitoring less frequently (once a week).
Characteristics of the diabetes patients are shown in table 2.

Table 2. Characteristics of the diabetes patients (n=84)

		Number of diabetes patients
Total		84
Sex	Men	55
	Women	29
Age, median in years (range)		60 (19-76)
Diabetes	Type 1	20
	Type 2	63
	Missing	1
Treatment	Insulin	40
	Insulin and tablets	10
	Tablets	25
	Diet	5
	Missing	4
Frequency of SMBG	Less than weekly	1
	1 – 3 per week	13
	4 – 6 per week	11
	7 – 10 per week	10
	>10 per week	45
	Missing	4

The SMBG-devices that the diabetes patients used regularly were: Accu-Chek (model not specified) (12), Accu-Chek Aviva (10), Accu-Chek Compact/Compact Plus (13), Accu-Chek Sensor (1), Ascensia Breeze/Breeze 2 (3), Ascensia Contour (11), FreeStyle/FreeStyle Fredom/Freestyle Lite/FreeStyle Mini (10), Medisense (model not specified) (2), OneTouch (model not specified)/Ultra/Ultra 2/Ultra Smart (15), Precision/Precision Xtra (3) and unregistered (1).

Some of the diabetes patients used more than one SMBG-device at home, but only one device is registered here.

3.4.3. The "training group" at the first consultation

The 43 diabetes patients who were selected to participate in a training programme were invited in pairs for training. They received the GlucoMen LX device along with test strips, lancet pen, lancets, user guide (in Norwegian), and an information letter with explanations regarding what to do with the GlucoMen LX device during the period at home. The information letter is attached to the report (in Norwegian), see attachment 2. The responsibility for the training programme was undertaken by SKUP. Sonja Jørgensen and Helen Skoglund were in charge of the training of the diabetes patients, after having been trained themselves by a representative from Menarini.

The training programme

The training programme covered a simple demonstration of how to use GlucoMen LX, with an explanation of the display and error messages, insertion of the test strips, blood sampling and drawing of the 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 diabetes patients received the same instruction.

Blood sampling

After having been trained, the 43 diabetes patients made duplicate blood glucose tests on GlucoMen LX. These results were registered for the evaluation. The biomedical laboratory scientist collected samples for the evaluation under standardised and optimal conditions (see chapter 3.4.7.). Afterwards the diabetes patients brought the GlucoMen LX home to use it over a three-week period. After this period they attended a final consultation (see chapter 3.4.6).

3.4.4. The "mail group"

The 41 diabetes patients in the "mail group" received the GlucoMen LX device by mail, along with test strips, lancet pen, lancets, user guide (in Norwegian) and an information letter with explanations regarding what to do with the GlucoMen LX device during the period at home. No training was given. They used the meter over a three-week period at home. After this period they attended a final consultation (see chapter 3.4.6).

3.4.5. Use of GlucoMen LX by the diabetes patients at home

The diabetes patients used GlucoMen LX 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 guide at once when they receive the meter. As the diabetes patients should evaluate the user guide at the final consultation, it would be unfortunate if the practice period at home was too long. During the practice period the diabetes patients used GlucoMen LX 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 diabetes patients familiarised themselves with the new device during the first two weeks. Each diabetes patient used approximately 25 test strips to measure his/her blood glucose with GlucoMen LX. 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 performed measurements with their own meter.

The third week
During the third week the diabetes patients performed duplicate measurements on GlucoMen LX 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 diabetes patients are not familiar with control solutions for glucose self-measurements. Therefore they were not instructed to use the control solution on GlucoMen LX in the evaluation. To document correct functioning of the GlucoMen LX meters used by the diabetes patients during the test period, the biomedical laboratory scientist in charge of the practical work checked the meters with the control solution when the diabetes patients met at the consultations.

3.4.6. The final consultation

Blood sampling
After the three-week practice period at home, 84 diabetes patients met, one by one, for a consultation. Each diabetes patient brought their assigned GlucoMen LX and the remaining test strips to the consultation. Before the samples were collected, the GlucoMen LX device was equilibrated to room temperature while the diabetes patients filled in the questionnaires. Then the diabetes patients made duplicate blood glucose tests on their assigned meter. These results were registered for the evaluation. The biomedical laboratory scientist collected samples for the evaluation under standardised and optimal conditions. Finally, a venous sample for hematocrit was taken.

Evaluation of the user-friendliness and the user guide
Before the blood samples were collected and the measurements on GlucoMen LX were performed, the diabetes patients filled in two questionnaires. The first questionnaire deals with the user-friendliness of GlucoMen LX; the second covers the user guide. The questionnaires (in Norwegian) are attached to the report.

3.4.7. Evaluation under standardised and optimal conditions

The biomedical laboratory scientist used two GlucoMen LX blood glucose meters for the evaluation (meter A and B). On meter A one lot of test strips was used for all the measurements. Meter B was used for the same three lots as distributed among the diabetes patients. The agreement of the three lots to the comparison method was assessed. The number of samples for each lot of test strips measured under standardised and optimal conditions is shown in table 3.

Table 3. The number of samples for each lot of test strips measured under standardised and optimal conditions

GlucoMen LX		Lot 320801249	Lot 3208037249	Lot 3208011249
Meter A	1st consultation	43 x 2		
	2nd consultation	84 x 2		
Meter B	1st consultation	14 x 2	18 x 2	11 x 2
	2nd consultation	32 x 2	29 x 2	23 x 2
Total		173 x 2	47 x 2	34 x 2

Blood sampling
Meter A and B were checked by means of the manufacturer's control solution every day they were used. The biomedical laboratory scientist measured the internal quality control (GlucoMen LX Control N) on the diabetes patient's meter at each consultation.

All the samples for GlucoMen LX, as well as the samples for the comparison method, were collected from finger capillaries.

The blood sampling and analysis were carried out in the following order:

1. The biomedical laboratory scientist took a first sample for the comparison method
2. The biomedical laboratory scientist took samples and analysed on meter A, B, A and B
3. The diabetes patient took duplicate samples for his/her assigned meter
4. The biomedical laboratory scientist took a second sample for the comparison method

In order to reduce the possibility for a change in the glucose concentration during the sampling sequence, the sampling time ought not to exceed 10 minutes. The stability of the glucose concentration during the sampling in the evaluation is supervised. A more detailed explanation of the matter is found in the paragraph "*Analysing the samples for the comparison method*" and in section 5.1.3.

The order of meter A and B was changed between each diabetes patient, but the blood samples for the comparison method were always taken at the start and in the end of each sampling sequence in accordance with ISO 15197. The biomedical laboratory scientist registered whether the diabetes patients used correct cleaning, drying and skin puncture procedures, applied the blood sample correctly to the test strip, and otherwise followed the manufacturer's instructions for performing a blood glucose test. At the final consultation a venous sample for hematocrit determination was taken. Hematocrit may influence on blood glucose readings, especially in meters designed for self-monitoring. The product insert of GlucoMen LX Sensor test strips states that the glucose measurements are not influenced by hematocrit values from 25 to 60%.

Handling of the samples for the comparison method
The samples for the comparison method were taken from a finger capillary using Microvette Li-heparin tubes from Sarstedt. The samples were centrifuged immediately for three minutes at 10.000g, and plasma was separated into sample vials. The plasma samples were frozen directly and stored at minus 80° C. The samples were transported under cold storage to NOKLUS where they were kept at minus 80° C until the analysis took place [7].

Analysing the samples for the comparison method
The samples were analysed on an Architect instrument in December - January. Recommended minimum volume for analysis of glucose on Architect in this evaluation was 120 µL plasma. The samples were thawed at NOKLUS just before they were analysed. For each sampling sequence, two samples for the comparison method were collected. These pairs of samples, taken at the start and at the end of each blood sampling sequence, reflect the stability of the glucose concentration during the sampling time. When the paired measurements give agreeable glucose concentrations on 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 exceeds these limits, the samples are re-analysed. If the results from the re-run confirm the difference, the difference is looked upon as a real difference in the glucose concentration in the two samples. If the deviation between the two results is not confirmed by the re-run, the result from the re-run is used as the accepted result.
Deviations >10% are regarded as not acceptable. Such results will be excluded, and the matching meter results removed before assessment of accuracy and calculation of trueness. No paired results from the comparison method in this evaluation showed deviations >10%. Differences between 4 and 10% are discussed and will be included in the calculations if not affecting the outcome and assessment of accuracy and bias (see chapter 5.1.3.).

Evaluation of the user-friendliness and the user guide
The biomedical laboratory scientist evaluated the user-friendliness of GlucoMen LX and the user guide. The biomedical laboratory scientist provided a description in form of key words and looked for any defects and deficiencies or whether there was anything with the system that did not function optimally.

3.4.8. Evaluation of analytical quality

The following sets of data give the basis for the evaluation of the analytical quality (for missing or excluded results, see 4.2.3.):

1. Results from 43 diabetes patients in the “training group” who had participated in the training programme, but not practiced using the blood glucose meter at home
2. Results from 43 of the same diabetes patients after they had practiced using GlucoMen LX at home for three weeks
3. Results from 41 diabetes patients in the “mail group” who had not participated in the training programme, but had practiced using GlucoMen LX at home for three weeks
4. Results from 127 measurements in duplicate under standardised and optimal conditions
5. Results from 127 measurements in duplicate from the comparison method

All the diabetes patients’ measurements were evaluated against the results achieved under standardised and optimal conditions. All the measurements were compared with the results from the comparison method.
The three lots of test strips were distributed evenly between the diabetes patients in the group with and without training (random distribution in each group). Each lot was used by approximately 14 diabetes patients in each group (see figure 1).

4. Statistical expressions and calculations

4.1. Statistical terms and expressions

The definitions in this section come from the International Vocabulary of Metrology, VIM [13].

4.1.1. Precision

Definition: Precision is the closeness of agreement between measured quantity values obtained by replicate measurements on the same or similar objects under stated specified conditions.

Precision is descriptive in general terms (good, acceptable, poor e.g.) and measured as imprecision. 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.

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.

To be able to interpret an assessment of precision, the precision conditions must be defined. The "specified conditions" can be, for example, repeatability, intermediate precision or reproducibility conditions of measurement. The precision conditions in this evaluation are close to the defined *repeatability* and *reproducibility* conditions, and the imprecision is expressed as repeatability CV and reproducibility CV. The imprecision is summarised in tables.

4.1.2. Accuracy

Definition: Accuracy is the closeness of agreement between a measured quantity value and the true quantity value of a measurand.

Inaccuracy is a measure of the deviation of a single measurement from the 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 is illustrated by difference-plots with quality goals for the total error shown as deviation limits in percent.

4.1.3. Trueness

Definition: Trueness is the closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value.

Trueness is 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 percent. The bias at different glucose concentration levels is summarised in tables.

4.2. Statistical calculations

4.2.1. Number of samples

84 diabetes patients completed the evaluation. 43 of the diabetes patients in the "training group" met at two consultations. The 41 diabetes patients in the "mail group" met at one consultation. Blood samples were taken at each consultation. The total number of samples is:
[(43 x 2 (duplicates)) + (43 x 2) + (41 x 2)] x 4 (meter A, meter B, diabetes patient's meter, comparison method) = 1016 samples.

4.2.2. Statistical outliers

The criterion promoted by Burnett [14] was used for the detection of outliers. The model takes into consideration the number of observations together with the statistical significance level for the test. The significance level is often set to 5%, so also in this evaluation. The segregation of outliers was made with repeated truncations. All the results were checked. 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 the calculations. Possible outliers will be commented on under each table.

4.2.3. Missing or excluded results

Besides the statistical outliers, no result is missing or excluded for other reasons.

4.2.4. Calculations of imprecision based on duplicate results

Two capillary samples were taken of each diabetes patient for meter A, meter B, the diabetes patient's meter and for the comparison method at each consultation. The imprecision was calculated by use of paired measurements [15, 16], 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 two parallel measurements of every duplicate, the calculated standard deviation is 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 of the duplicate is acceptable. Table 4 shows that no systematic difference was pointed out between the paired measurements. This conclusion is also supported by observations in previous user-evaluations carried out by SKUP.

Table 4. Comparison of the 1st and the 2nd measurement. T-test for paired values

GlucoMen LX	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
Meter A	< 7	6,10	6,13	0,03	(-0,09) — 0,15	32
	7 – 10	8,08	8,18	0,10	(-0,06) — 0,26	46
	≥ 10	13,54	13,76	0,22	(-0,03) — 0,48	49
Meter B	< 7	6,05	6,00	-0,05	(-0,16) — 0,06	35
	7 – 10	8,26	8,18	-0,08	(-0,24) — 0,08	45
	≥ 10	13,68	13,75	0,07	(-0,19) — 0,34	47

4.2.5. Calculation of trueness

To assess the trueness of the results on GlucoMen LX, the mean deviation 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 on the comparison method and the mean values on GlucoMen LX meter A. The mean difference is shown with a 95% confidence interval.

4.2.6. Calculation of accuracy

To evaluate the accuracy of the results on GlucoMen LX, the agreement between GlucoMen LX and the comparison method is illustrated in difference-plots. In the plots the x-axis represents the mean value of the duplicate results on the comparison method. The y-axis shows the difference between the first measurement on GlucoMen LX with three lots and the mean value of the duplicate results on the comparison method.

5. Results and discussion

5.1. Analytical quality of the designated comparison method

5.1.1. 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 diabetes patient samples for the comparison method 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 a time gap between the first and the second sample for each diabetes 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 the sampling time, and not the precision of the method (see 5.1.3). To get a good estimate of the repeatability of the comparison method, the results from the documentation of trueness were used. The NIST-standards and the external quality controls are genuine patient materials with no additives, and the standards and the controls have been analysed repeatedly.

The repeatability of the comparison method is shown in table 6 and table 7. The results are obtained with the NIST-standards SRM 965a and freshly frozen, human serum controls produced by SERO AS.

The reproducibility of the comparison method is shown in table 5. The results are obtained with internal quality control solution at two levels of glucose concentrations. All the results were inside the limits of the target values for the controls.

The internal quality control raw data is shown in attachment 3.

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

Control Solution	Target value glucose (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV% (95% CI)
Autonorm 1	3,37 ± 0,20	3,34	6	0	0,6 (0,4 — 1,6)
Autonorm 2	15,97 ± 0,83	15,85	6	0	0,8 (0,5 — 1,9)

Discussion

The precision of the comparison method is good. The repeatability CV (see table 6 and 7) as well as the reproducibility CV (table 5) is below 1,0%.

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

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

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	02.12.08	**1,918** (1,898 — 1,938)	1,91	5	0,9 (0,6 — 1,4)	-0,6
	12.12.08		1,92	5		+0,2
	16.01.09		1,92	5		-0,1
	Total		**1,91**	**15**		
Level 2	02.12.08	**4,357** (4,309 - 4,405)	4,41	5	0,5 (0,4 —0,8)	+1,2
	12.12.08		4,37	5		+0,3
	16.01.09		4,40	5		+1,0
	Total		**4,39**	**15**		
Level 3	02.12.08	**6,777** (6,704 — 6,850)	6,86	5	0,7 (0,5 —1,2)	+1,3
	12.12.08		6,83	5		+0,8
	16.01.09		6,88	5		+1,5
	Total		**6,86**	**15**		
Level 4	02.12.08	**16,24** (16,05 — 16,43)	16,45	5	0,6 (0,4 —1,0)	+1,3
	12.12.08		16,48	5		+1,5
	16.01.09		16,65	5		+2,5
	Total		**16,53**	**15**		

Table 6 shows that the glucose results of the NIST-standards at level 3 and 4 at Architect ci8200 were slightly higher than the certified target values. The achieved results were just outside the uncertainty limits. All results from Architect are therefore adjusted according to the certified NIST-targets. The adjustment was carried out by means of inverse calibration [17, 18] by the following regression equation: **y = 0,9798x + 0,0495.**

Further on in the report, whenever any result from the comparison method is presented, the result has already been adjusted according to this equation.

To verify the trueness of the comparison method, freshly frozen, human serum controls, produced by SERO AS, with glucose concentrations at two levels were analysed. The agreement with target values from the Reference laboratory in Belgium is shown in table 7.

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

Control	Date	Target value glucose (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	Combined CV% (95% CI)	% deviation from target value
TM Gluc L-1	02.12.08	4,78	4,78	5	0	0,7 (0,5 — 1,1)	0,0
	12.12.08		4,83	5	0		0,9
	16.01.09		4,82	5	0		0,8
	Total		4,80	15			
TM Gluc L-2	02.12.08	11,8	11,88	5	0	0,7 (0,5 — 1,1)	0,7
	12.12.08		11,86	5	0		0,5
	16.01.09		11,88	5	0		0,6
	Total		11,87	15			

Discussion
The trueness of the comparison method is good.

5.1.3. Stability of the glucose concentration during the sampling time

The first and the second sample for the comparison method, taken at the start and at the end of each blood sampling sequence, reflect the stability of the glucose concentration during the sampling time (see chapter 3.4.7. *Analysing the samples for the comparison method*). No paired results from the comparison method in this evaluation showed deviations > 10%.

30 of 127 paired results on the comparison method gave deviations between 4 and 10%. For 20 of these 30 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 carried out with and without these 30 results. The percentage number of results that falls within the quality limits is not dependent on keeping or excluding these results.

5.2. Analytical quality of GlucoMen LX

5.2.1. The precision of GlucoMen LX

The GlucoMen LX-meters in the user evaluation were checked with the manufacturer's control solutions by the biomedical laboratory scientist. All results from the calculation of the precision are discussed at the end of this chapter.

Repeatability under standardised and optimal measuring conditions

The repeatability obtained under standardised and optimal conditions with capillary blood samples from the diabetes patients, is shown in table 8. The table gives the results from the biomedical laboratory scientist's measurements at the first and the final consultation together.

The raw data is shown in attachment 4.

Table 8. GlucoMen LX – Repeatability. Results achieved with blood samples from the diabetes patients, measured under standardised and optimal conditions

GlucoMen LX	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV% (95% CI)
Meter A	< 7	6,2	35	0	3,8 (3,1 — 5,0)
Meter B	< 7	6,1	36	0	4,1 (3,3 —5,3)
Meter A	7 – 10	8,2	43	0	4,7 (3,9 — 6,0)
Meter B	7 – 10	8,2	44	0	4,5 (3,7 —5,7)
Meter A	≥ 10	13,7	49	0	4,7 (3,9 — 5,9)
Meter B	≥ 10	13,7	47	0	4,6 (3,8 —5,8)

Comments:

The results in table 8 are achieved under standardised and optimal conditions. No results were segregated as outliers according to Burnett. The repeatability CV is < 5%. The precision is good.

Repeatability obtained by the diabetes patients
The repeatability obtained by the diabetes patients with capillary blood samples is shown in table 9. The table gives the results from the measurements at the first and the second consultation for the "training group" and the results from the measurements at the consultation for the "mail group". The results obtained at home have a higher degree of uncertainty since it is impossible to check what has actually been done. The reporting of these home-values revealed that some of the diabetes patients did not quite understand the instruction on how to perform and report the five duplicate measurements they were supposed to carry out. The results obtained by the diabetes patients at home document their training efforts, but repeatability is not calculated on the basis of these results.

The raw data from the diabetes patients' measurements at NOKLUS is shown in attachment 5.
The raw data from the diabetes patients' measurements at home is shown in attachment 6.

Table 9. GlucoMen LX – Repeatability. Results achieved by the "training group" and the "mail group

GlucoMen LX	Consultation/ diabetic group	Glucose level (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV% (95% CI)
At NOKLUS	1st/training group	< 7	6,13	19	0	4,9 (3,7 — 7,2)
	2nd/training group	< 7	6,22	7	0	6,8 (4,4 —14,9)
	The mail group	< 7	6,05	10	1*	6,2 (4,3 — 11,4)
At NOKLUS	1st/training group	7 – 10	8,63	12	0	5,7 (4,0 —9,6)
	2nd/training group	7 – 10	7,88	21	0	6,8 (5,2 — 9,8)
	The mail group	7 – 10	8,59	11	0	5,4 (3,8 — 9,5)
At NOKLUS	1st/training group	≥ 10	13,43	12	0	5,3 (3,8 —9,1)
	2nd/training group	≥ 10	14,72	15	0	5,5 (4,0 — 8,6)
	The mail group	≥ 10	13,42	19	0	4,2 (3,2 — 6,2)

* One outlier (ID91) according to Burnett

Comments
The results in table 9 are achieved by the diabetes patients. One result was segregated as outliers according to Burnett. The measuring procedure was carried out without any obvious or visible mistakes, and there were no error messages related to the measurements. The repeatability CV is between 4,2 and 6,8. The precision is acceptable.

Reproducibility with Internal Quality Control Solution
The reproducibility is assessed with GlucoMen LX Control Normal. Artificially produced control materials have other matrix effects than whole blood, and may therefore give other results than results achieved with blood. The measurements are carried out on meter A and meter B during the whole evaluation period. The reproducibility of GlucoMen LX on meter A and meter B is shown in table 10.

Table 10. GlucoMen LX – Reproducibility (results with GlucoMen LX Control N) measured by the biomedical laboratory scientist on meter A (one lot) and meter B (three lots)

GlucoMen LX	QC	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV% (95% CI)
Meter A	N	6,0 – 8,2	7,3	36	0	5,1 (4,2 — 6,7)
Meter B	N	6,0 – 8,2	7,4	39	0	4,4 (3,6 — 5,7)

Internal Quality Control on the diabetes patients' meters
The control measurements on the diabetes patients' meters (totally 84 meters) were performed with GlucoMen LX Control Normal. The control was used every morning on meter A and meter B, and the same bottle of control solution was used the rest of the day on the diabetes patients' meters. All the control measurements are performed by the biomedical laboratory scientist with the test strips that were distributed to each diabetes patient (three different lots of test strips). The control solutions were kept according to the instructions in the product insert through out the evaluation period.

The raw data from the measurements with the internal quality control is shown in attachment 7.

Table 11. GlucoMen LX – Reproducibility. Results achieved with GlucoMen LX Control N, measured by the biomedical laboratory scientist on the diabetes patients' meters

GlucoMen LX Control N	Target value (mmol/L)	Mean value glucose (mmol/L)	n	Outliers	CV% (95% CI)
1st consultation					
The diabetes patients' meters	6,0 — 8,2	7,3	43	0	3,8 (3,2 — 4,9)
2nd consultation					
The diabetes patients' meters	6,0 — 8,2	7,5	84	0	4,9 (4,2 — 5,7)

Comments
The results of the internal quality control GlucoMen LX Control N were inside the limits of the control.

Discussion, repeatability and reproducibility
The precision obtained under standardised and optimal conditions was good. The repeatability CV was <5%. A recommended quality goal for precision is obtained.
The precision achieved when the measurements were performed by the diabetes patients, was acceptable. The repeatability CV was between 4 and 7%. The CV was not significantly more than 5%, with exception of the CV achieved by the training group at the second consultation at the glucose level 7–10 mmol/L.

The reproducibility on GlucoMen LX under standardised and optimal conditions was good when measured with GlucoMen LX Control N. The CV was between 4–5%. The reproducibility CV obtained with measurements on the diabetes patients' meters was approximately 4% at the first consultation and approximately 5% at the second consultation.

For the diabetes patients in the training group, the CV appears to increase at the second consultation. The quality control results at the second consultation achieved with the patients' meters and test strips support this observation. The difference between the CV achieved at the first and second consultation is small, but statistical significant (F-test). It seems that the performance of the test strips has been slightly affected by having been stored and used by the diabetes patients for three weeks at home.

5.2.2. The trueness of GlucoMen LX

The trueness of GlucoMen LX 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 on meter A and are shown in table 12. All the measurements on meter A are performed with lot 320801249.

The raw data from the comparison method is shown in attachment 8.

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

	< 7 mmol/L		**7 – 10 mmol/L**		**≥ 10 mmol/L**	
	The comparison method	**Meter A**	**The comparison method**	**Meter A**	**The comparison method**	**Meter A**
Mean glucose (mmol/L)	5,9	6,3	8,2	8,3	14,3	13,9
Mean deviation from the comparison method, mmol/L (95% CI)	0,45 ((+0,23) — (+0,67))		0,10 ((-0,07) — (+0,28))		(-0,40) ((-0,66) — (-0,14))	
n	23		27		34	
Outliers	0		0		0	

Discussion
Table 12 shows a small, but significant bias between GlucoMen LX and the comparison method at two of the three concentrations levels. For glucose levels <7 mmol/L, GlucoMen LX gives significantly higher values than the comparison method. The bias is +0,45 mmol/L. For glucose levels ≥10 mmol/L, GlucoMen LX gives significant lower values than the comparison method. The bias is -0,40 mmol/L.

5.2.3. The accuracy of GlucoMen LX

To evaluate the accuracy of the results on GlucoMen LX, the agreement between GlucoMen LX and the comparison method is illustrated in two difference-plots. The plots show the deviation of single measurement results on GlucoMen LX from the true value, and give a picture of both random and systematic deviation, reflecting the total measuring error on GlucoMen LX. The total error is demonstrated for the first measurements of the paired results, only. On meter A only one lot of test strips were used. On meter B three different lots were used. The same three lots were randomly distributed between the diabetes patients. The limits in the plots are based upon the quality goals discussed in chapter 2 in this report. Under standardised and optimal measuring conditions the ISO-goal at ±20% is used. For the diabetes patients' self-measurements the "adjusted ISO-goal" at ±25% is used.

The accuracy, GlucoMen LX meter B, with three lots of test strips, under standardised and optimal measuring conditions, at the final consultation is shown in figure 2.

The accuracy, GlucoMen LX, as measured by all the diabetes patients at the final consultation (the "training group" and the "mail group") is shown in figure 3.

The accuracy is summarised in table 13 and discussed afterwards.

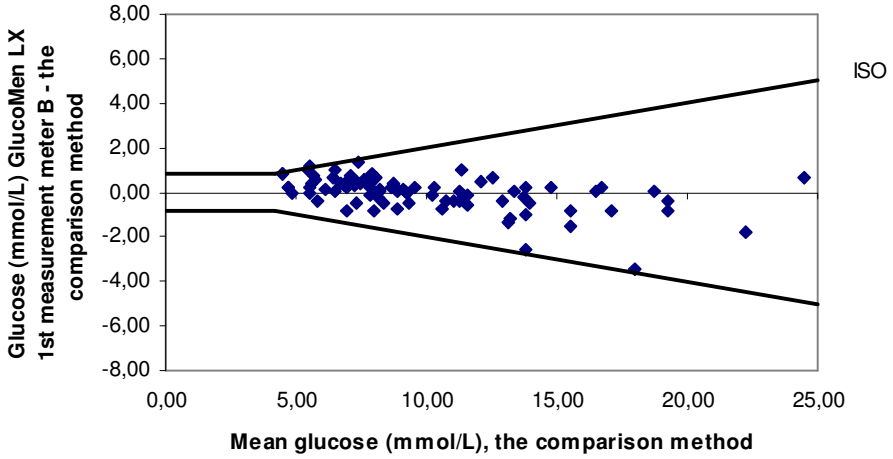

Figure 2. Accuracy. GlucoMen LX meter B and three lots of test strips under standardised and optimal measuring conditions at the final consultation. The x-axis represents the mean value of the duplicate results on the comparison method. The y-axis shows the difference between the first measurement on GlucoMen LX and the mean value of the duplicate results on the comparison method. Lines represent limits suggested in ISO 15197 [±20%], n = 84

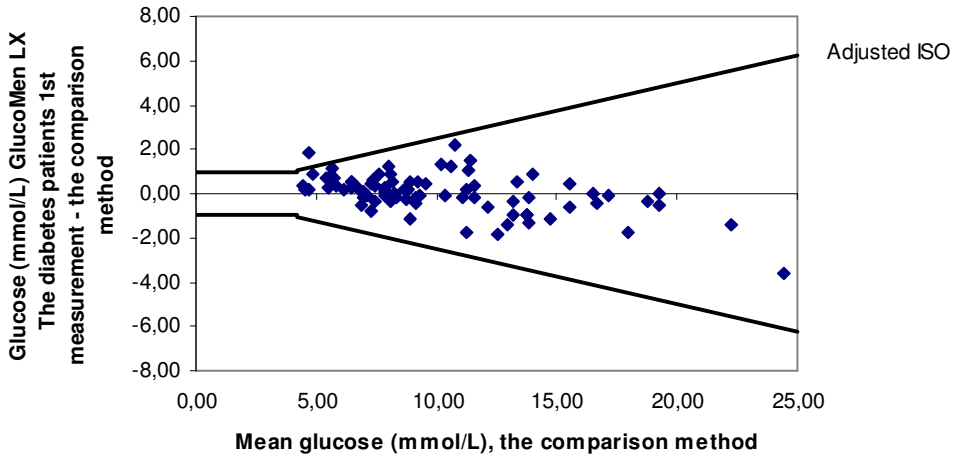

Figure 3. Accuracy. The diabetes patients' self-measurements at the final consultation. Three lots of test strips. The x-axis represents the mean value of the duplicate results on the comparison method. The y-axis shows the difference between the first measurement on GlucoMen LX and the mean value of the duplicate results on the comparison method. Lines represent modified ISO limits suggested by NOKLUS [±25%], n = 84

Table 13. Total error of GlucoMen LX results compared to the comparison method. Percentage GlucoMen LX results within the limits

Measurements performed by	Consultation	Meter	n	Number of results within the limits (%)			Shown in figure
				ADA <±10%	**ISO** <±20% and <±0,83 mmol/L at conc. ≤4,2	**"adjusted ISO"** <± 25% and <±1,0 mmol/L at conc. ≤4,2	
Biomedical laboratory scientist	1st	A 1st measurement	43	74	100		
		B 1st measurement	43	81	100		
Biomedical laboratory scientist	2nd	A 1st measurement	84	75	98		
		B 1st measurement	84	81	99		2
Diabetes patients at NOKLUS	1st	1st measurement	43	74	98	98	
	2nd	1st measurement	84	75	96	99	3

Discussion

Figure 2 and 3 show that the GlucoMen LX-results are lower than the comparison method for glucose concentration ≥10 mmol/L. The results still seem to be within the quality limits.

The summing up in table 13 shows that more than 95% of the results achieved under optimal measuring conditions, as well as by the diabetes patients are within the quality limits proposed in ISO 15197. The accuracy is good and the quality goal is attained.

5.3. Variation between three lots of test strips

The measurements on meter B were performed with three different lots of test strips. The three lots were distributed randomly among the patients. Only test strips from one lot was used per patient. The deviation from the comparison method for each of the three lots was calculated (paired t-test), as an indirect measure of the lot variation. Obviously, the mean glucose concentration in different groups of diabetes patients is not identical, and therefore the results achieved with the three different lots can not be used directly as a measure of the inter-lot-variation.

The results are shown in table 14.

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

	The comparison method	**Meter B Lot 320801249**	**The comparison method**	**Meter B Lot 3208037249**	**The comparison method**	**Meter B Lot 3208011249**
Mean glucose (mmol/L)	9,9	10,0	9,7	9,6	9,7	9,8
Mean deviation from the comparison method, mmol/L (95% CI)	+0,04 ((-0,18) — (+0,25))		(-0,04) ((-0,25) — (+0,18))		+0,07 ((-0,12) — (+0,25))	
n	32		28		22	
Outliers	0		1*		1**	

* One outlier (ID 47) according to Burnett.
** One outlier (ID58) according to Burnett.

Discussion
There was no provable difference between the glucose results achieved with three different lots of test strips. All three lots gave glucose results in agreement with the comparison method.
This result can be surprising in the light of the bias that was pointed out for lot 320801249 with meter A at the low and high glucose concentration level in table 12, but can be explained by how the sorting of results was carried out ahead of the calculations. For the calculation of bias, the 84 results were sorted according to the glucose concentration, and the bias was calculated for three different concentration levels separately. For the calculation of lot variation, the 84 results were sorted according to the lot of test strips. To keep a sufficient number of results in each group, the deviation of each lot must then be calculated for the whole concentration range as a whole.

5.4. Effect of hematocrit

The product insert of GlucoMen LX Sensor test strips states that glucose measurements are not influenced by hematocrit values from 25 to 60%. To measure the effect of hematocrit on GlucoMen LX, a hematocrit sample was taken of the diabetes patients at the second consultation. The investigation of the effect of hematocrit is based on the measurements on GlucoMen LX (meter A with one lot of test strips) under standardised and optimal measuring conditions. The glucose concentration range in the samples was 4,5 – 19,2 mmol/L. The hematocrit range was 30 – 49%.

The effect of hematocrit is shown in figure 4. The x-axis in the plot shows the hematocrit value in percentage and the y-axis shows the difference in glucose concentration between GlucoMen LX and the comparison method (GlucoMen LX - the comparison method) in mmol/L. The trend-line is shown in the figure.

The raw data is shown in attachment 9.

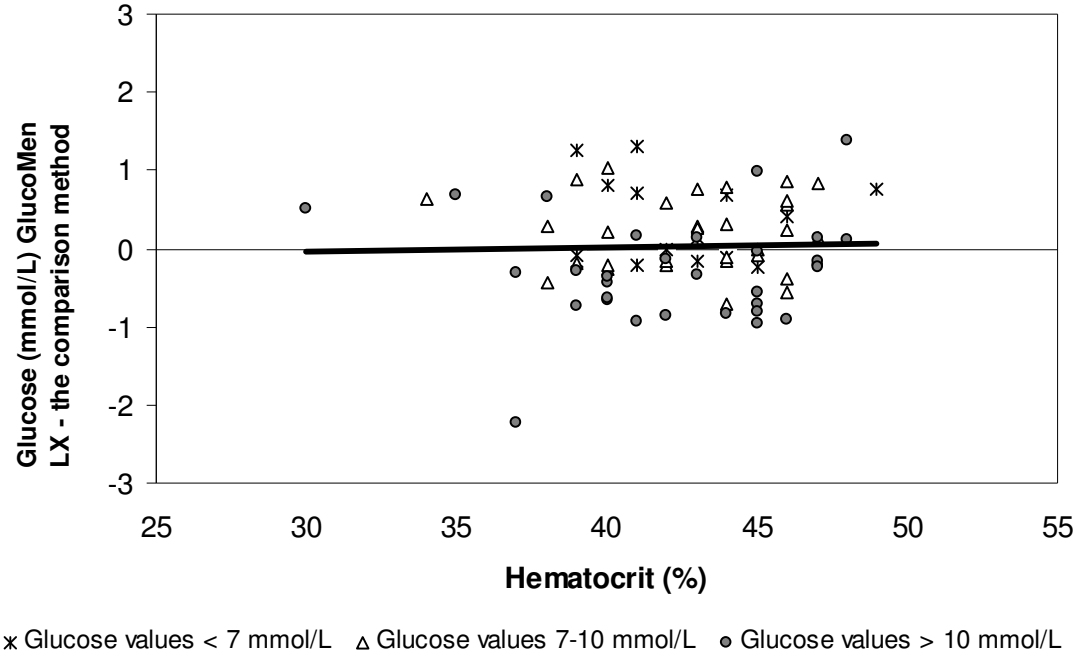

Figure 4. The effect of hematocrit on glucose measurements on GlucoMen LX measured under standardised and optimal conditions. The x-axis shows the hematocrit value in percent. The y-axis shows the difference in glucose concentration between GlucoMen LX and the comparison method (GlucoMen LX – the comparison method) in mmol/L, n= 77.

Discussion

Glucose measurements on GlucoMen LX were not affected by the hematocrit values of the samples. Hematocrit outside the range 30 – 49% has not been tested.

5.5. Practical points of view

The most important response regarding user-friendliness comes from the users themselves. The end-users often emphasize other aspects than those pointed out by more extensively trained laboratory personnel.

Questionnaires
Each diabetes patient filled in a questionnaire about the user-friendliness and a questionnaire about the user guide of GlucoMen LX when they attended the final consultation. The biomedical laboratory scientist was available for clarifying questions, and there was room for free comments. The questionnaires about the user-friendliness and user guide are attached to the report (in Norwegian), see attachment 11 and 12.

5.5.1. Evaluation of the user-friendliness of GlucoMen LX

The questionnaire about the user-friendliness was made up of nine questions concerning GlucoMen LX. Table 15 summarizes six questions where the diabetes patients were asked to rank the answers on a scale from 1 to 6, where 1 is difficult and 6 is simple.

The mean score is 4,7, 5,9 and 5,1 on the questions about inserting a strip into the meter, filling the strip with blood and hearing the sound signal, respectively. This indicates that the diabetes patients seemed satisfied with the procedure for filling the strip with blood, and that they were satisfied with the sound signal, but that they thought it was a bit difficult to insert the strip into the meter. Verbally a few of the diabetes patients commented that it was not convenient to have the insertion opening on the top of the instrument, and that it was difficult to be sure that the strip was placed far enough into the meter. Some commented that the test strip was too flexible. The mean score is 5,9 on the question about reading the figures in the display. The diabetes patients also seemed satisfied with operating the meter, all in all. The mean score is 5,5. Regarding Glucoject Dual lancet pen the mean score is 4,9, which indicates that some of the diabetes patients found it a bit difficult to use the lancet pen.

Table 15. GlucoMen LX - Questions about the meter

Questions about GlucoMen LX		Total number	No answer (% of total)	Range	Mean score
How will you rank the following questions on a scale from 1 to 6, where 1 is difficult and 6 is simple	To insert a strip into the meter	84	1	1 – 6	4,7
	To fill the strip with blood	84	2	3 – 6	5,9
	To hear the sound signal	84	5	1 – 6	5,1
	To read the figures in the display	84	2	5 – 6	5,9
	All in all, to operate the meter	84	2	1 – 6	5,5
	To operate Glucoject Dual lancet pen	84	12	1 - 6	4,9

The diabetes patients were asked if they had any positive and/or negative comments about GlucoMen LX.

Positive comments
60 diabetes patients reported one or more advantages with GlucoMen LX. The most often reported advantages are distinctly grouped as follows:

1. The meter has short measuring time (20)
2. Easy to use (14)
3. The meter/test strip requires a small blood sample volume (7)
4. The small size of the meter (6)
5. The instrument calculates average glucose values (4)
6. No coding (4)

Negative comments
62 diabetes patients reported one or more disadvantages with GlucoMen LX. The most often reported disadvantages are distinctly grouped as follows:

1. Different problems with the test strips (25); for instance the test strip is difficult to insert (13), not in a disc (3), too weak (to easy to bend by mistake) (2), too short (2), some test strips did not work (1), too long and weak test strip (1), the test strips are mixed both ways in the box (1), difficult to get out of the test box (1)
2. The etui was not well fitted, the instrument could easily fall out of the etui (7)
3. The instrument is too big (3)
4. It is not convenient to have the insertion opening on the top of the instrument (2)

Table 16 shows the answers regarding technical problems with GlucoMen LX. Some of the diabetes patients (5%) answered that they had technical problems with the meter during the testing period. One meter stopped functioning and it was replaced by a new one. Written comments from some of them indicate that their problems were not technical ones after all, but were problems related to the test strips and batteries.

Table 16. GlucoMen LX – Questions about the meter

Question about GlucoMen LX	Total number	Yes (%)	No (%)	No answer (%)
Did you have any technical problems with the meter during the testing period?	84	5	84	11

5.5.2. Evaluation of the GlucoMen LX user guide

In the questionnaire about the user guide each diabetes patient was first asked whether he/she had used the guide. If the answer was no, they were to ignore the rest of the questionnaire.

Table 17 shows that 67% of the diabetes patients had used the guide. None of the diabetes patients who had used the guide answered that he/she was not satisfied with the description of how to perform a blood glucose measurement with the meter. Four of the diabetes patients thought the guide had essential shortcomings; but he/she didn't write what was missing. In general, the diabetes patients were satisfied with the user guide.

Table 17. GlucoMen LC – Questions about the user guide

Questions about the user guide	Number	Yes (%)	No (%)	No answer (%)
Have you been reading in the user guide?	83	67	32	1
If yes, did you read the entire user guide?	53	33	30	37
And/or did you consult the user guide when needed?	41	42	7	51
Are you satisfied with the description of how to perform a blood glucose measurement with the meter?	57	68	0	32
Do you think the user guide has essential shortcomings?	59	5	65	30
All in all, are you satisfied with the user guide?	59	70	0	30

5.5.3. The biomedical laboratory scientists' evaluation

Positive comments:

- The meter is easy to operate
- No coding
- The figures is easy to read
- Few keys
- Short measuring time
- The test strips requires a small blood sample volume

Negative comments:

- Difficult to get a single test strip out of the box, it could be hard to separate the test strips from each other.
- The test strips are weak and flexible
- The insertion slit blended in with the instrument and was difficult to locate, especially for diabetes patients with bad eyesight. Some diabetes patients expected the slit to be on the opposite site of the instrument.
- It was hard to see whether the test strip was inserted far enough into the instrument.

- Occasionally the instrument was not automatically turned on when the test strip was inserted.
- The Glucoject Dual lancet pen was difficult to recharge, the spring was too firm.
- The etui was not well fitted. It was difficult to get room enough for all the equipment. The instrument could easily fall out of the etui.

6. References

1. Stöckl D, Baadenhuijsen H, Fraser CG, Libeer JC, Petersen PH, Ricos C, "*Desirable Routine Analytical Goals for Quantities Assayed in serum*". Eur J Clin Biochem 1995; **33** (3): 157 – 169.
2. American Diabetes Association. *Self-monitoring of blood glucose*. Diabetes Care 1996; **19** (suppl 1): 62 – 66.
3. 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.
4. *In vitro diagnostic test systems - Requirements for blood-glucose monitoring systems for self- testing in managing diabetes mellitus*, ed. ISO. 2003.
5. Kristensen, G.B, et al., *Standardized evaluation of instruments for self-monitoring of blood glucose by patients and a technologist.* Clin Chem, 2004. **50** (6): p. 1068-71.
6. www.skup.nu: Reports and summaries from evaluations under the direction of SKUP.
7. National Institute of Standards and Technology, Certificate of Analysis, Standard Reference Material® 965a, Glucose in Frozen Human Serum
8. Thienpont, L.M., et al., *Determination of reference method values by isotope dilution-gas chromatography/mass spectrometry: a five years' experience of two European Reference Laboratories.* Eur J Clin Chem Clin Biochem, 1996. **34** (10): p. 853-60.
9. Christensen, N.G, Monsen G, Sandberg S, *Utprøving av analyseinstrumenter*. 1997: Alma Mater Forlag.
10. 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.
11. Quality specifications for glucose test strips reimbursement from NAV http://www.uib.no/isf/noklus/diabetes/kravspes.pdf.
12. Kristensen G.B.B, Monsen G, Skeie S, Sandberg S, "*Standardized Evaluation of Nine Instruments for Self-Monitoring of Blood Glucose*". Diabetes Technology & Therapeutics, 2008; **10** (6), p. 467-77.
13. International vocabulary of metrology – Basic and general concepts and associated terms, VIM, 3rd edition, JCGM 200:2008.
14. Burnett RW, "*Accurate Estimation of Standard Deviations for Quantitative Methods Used in Clinical Chemistry*". Clinical Chemistry 1975; **21** (13): 1935 – 1938.
15. Saunders, E. Tietz textbook of clinical chemistry and molecular diagnostics. 2006. Chapter 14, Linnet, K., Boyd, J. "*Selection and analytical evaluation of methods – with statistical techniques*", ISBN 0-7216-0189-8.
16. Fraser, C.G, Biological variation: *From principles to practice*. 2006. Chapter 1 "*The Nature of Biological Variation*". AACC Press. ISBN 1-890883-49-2.
17. Krutchkoff, R. G, *Classical and inverse Regression Methods of Calibration*. Technometrics, Vol. 9, No. 3: 425-439
18. Tellinghuisen, J, *Inverse vs. classical calibration for small data sets*. Fresenius J. Anal. Chem. (2000) 368:585-588.

Attachments

1. Serial numbers, GlucoMen LX blood glucose meters used by the diabetes patients
2. Information letter to the diabetes patients (in Norwegian)
3. Raw data glucose, internal quality control (Autonorm), the comparison method
4. Raw data glucose, GlucoMen LX results under standardised and optimal conditions
5. Raw data glucose, GlucoMen LX results, the diabetes patients' measurements at NOKLUS
6. Raw data glucose, GlucoMen LX results, the diabetes patients' measurements at home
7. Raw data glucose, internal quality control, GlucoMen LX
8. Raw data glucose, results from the comparison method
9. Raw data hematocrit
10. Questionnaire, user-friendliness (in Norwegian)
11. Questionnaire, user guide (in Norwegian)
12. "SKUP-info". Summary for primary health care (in Norwegian)
13. List of evaluations organised by SKUP

Attachments with raw data are included only in the report to A. Menarini Diagnostics.

Attachment 1

Serial numbers, GlucoMen LX blood glucose meters used by the diabetes patients

ID	Serial number
1	D080876052XL
2	D080928052XL
3	D080929052XL
5	D080871052XL
6	D080893052XL
7	D080891052XL
8	D0808925052XL
9	D080888052XL
10	D080923052XL
11	D080922052XL
12	D080877052XL
13	D080920052XL
14	D080889052XL
15	D080890052XL
17	D080873052XL
18	D080886052XL
19	D080879052XL
21	D080868052XL
22	D080874052XL
23	D080887052XL
24	D080882052XL
25	D080872052XL
27	D080845052XL
29	D080898052XL
30	D080934052XL
31	D080933052XL
32	D080883052XL
33	D080884052XL
34	D080885052XL
35	D080936052XL
36	D080935052XL
39	D080895052XL
40	D080867052XL
41	D080866052XL
42	D080894052XL
44	D080904052XL
45	D080865052XL
46	D080864052XL
47	D080927052XL
48	D080899052XL
49	D080863052XL
50	D080862052XL

ID	Serial number
51	D080860052XL
52	D080861052XL
55	D08091052XL
56	D080896052XL
57	D080859052XL
58	D080905052XL
60	D080855052XL
62	D080900052XL
63	D080903052XL
64	D080854052XL
66	D080897052XL
68	D080857052XL
69	D080914052XL
70	D080913052XL
71	D080856052XL
72	D080853052XL
73	D080906052XL
74	D080847052XL
75	D080852052XL
76	D080849052XL
79	D080912052XL
80	D080917052XL
82	D080851052XL
85	D080850052XL
86	D080844052XL
89	D080846052XL
91	D080918052XL
92	D080843052XL
94	D080919052XL
95	D080908052XL
96	D080842052XL
97	D080930052XL
99	D080915052XL
100	D080932052XL
101	D080924052XL
103	D080878052XL
104	D080931052XL
105	D080875052XL
107	D080925052XL
110	D080926052XL
111	D080870052XL
114	D080858052XL

ID 27 got a new meter because the first meter stopped functioning.

NORSK KVALITETSFORBEDRING AV LABORATORIEVIRKSOMHET UTENFOR SYKEHUS

NOKLUS

«Navn»
«Adresse»
«Postadresse»

«ID-nr.»

Oktober 2008

Utprøving av blodsukkerapparat

Du har fått utlevert:

- 1 GlucoMen LX blodsukkerapparat i etui
- 1 pakke GlucoMen LX Sensor teststrimler for glukose (50stk.)
- 1 Glucoject Dual prøvetakingspenn
- 25 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 blodsukkermålinger 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 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 Glucoject Dual 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.

Helen Skoglund Laboratoriekonsulent NOKLUS Avd. for laboratoriemedisin SI- Lillehammer, Anders Sandvigsgt.17 2609 Lillehammer

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

Dato	GlucoMen LX Svar 1 (mmol/L)	GlucoMen LX 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 Glucoject Dual 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 sykehuset for den avsluttende utprøvingen. Til den avsluttende utprøvingen skal du ta med dette skjemaet, GlucoMen LX, resten av strimlene og Glucoject Dual 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:

Helen Skoglund Tlf.nr: 61272382 / 99641710

Lykke til!

Med vennlig hilsen

Sverre Sandberg (sign.)
Leder i NOKLUS/prof.dr.med.

Helen Skoglund (sign.)
Labratoriekonsulent/bioingeniør

Attachment 3

Raw data glucose, internal quality control (Autonorm), the comparison method

Date	Res. Autonorm 1 glucose, mmol/L	Res. Autonorm 2 glucose, mmol/L
02.12.2008	3,34	15,98
02.12.2008	3,36	16,00
08.01.2009	3,30	15,71
08.01.2009	3,35	15,87
09.01.2009	3,33	15,72
09.01.2009	3,35	15,81

Attachment 7

Raw data glucose, internal quality control, GlucoMen LX

ClucoMen LX Control N	Lot-no	Expiry	Glucose level mmol/L
Control N	3308158302	2010 - 12	6,0 – 8,2

FreeStyle Control analysed on the biomedical laboratory scientists' meter A and B

Date	GlucoMen LX Control N Glucose mmol/L	
	Meter A	Meter B
15.09.2008	7,7	7,4
16.09.2008	7,9	6,9
17.09.2008	7,2	7,8
18.09.2008	7,2	7,5
18.09.2008		7,3
18.09.2008		7,2
19.09.2008	6,9	6,8
22.09.2008	7,6	7,5
22.09.2008	7,0	7,2
26.09.2008	7,0	7,4
06.10.2008	7,4	7,3
07.10.2008	7,1	7,5
08.10.2008	7,7	8,0
08.10.2008		8,2
08.10.2008		7,5
13.10.2008	7,1	7,3
13.10.2008	7,7	
14.10.2008	7,5	7,4
15.10.2008	7,5	7,0
17.10.2008	7,3	7,7
17.10.2008	8,0	7,1

Date	GlucoMen LX Control N	
	Meter A	Meter B
17.10.2008	7,3	
21.10.2008	7,8	7,8
22.10.2008	6,8	7,4
22.10.2008	7,6	
23.10.2008	6,8	7,4
23.10.2008	6,8	7,3
24.10.2008	6,7	7,5
24.10.2008	7,9	7,2
27.10.2008	6,8	6,9
27.10.2008		7,4
28.10.2008	7,2	7,0
29.10.2008	7,1	7,0
30.10.2008	7,0	7,5
30.10.2008	7,8	7,3
31.10.2008	6,9	7,2
10.11.2008	7,0	7,3
10.11.2008		7,6
18.11.2008	6,9	6,7
20.11.2008	7,1	7,8
25.11.2008	7,2	7,0
28.11.2008	7,5	7,8

GlucoMen LX Control N analysed on the diabetes patients' meters

Trained group

ID	Lot-no test strips	GlucoMen LX Control N Glucose mmol/L	
		1'st consultation	Final consultation
6	3208011249	7,3	7,4
7	320801249	7,4	7,4
8	3208037249	7,0	7,9
9	3208011249	7,3	7,6
14	3208011249	7,2	7,0
15	320801249	7,4	7,5
18	320801249	7,5	7,4
23	3208037249	7,9	7,5
24	3208011249	7,6	7,3
32	3208011249	7,4	7,8
33	320801249	7,2	7,1
34	3208011249	7,3	7,4
40	320801249	7,5	7,9
41	3208037249	7,2	7,8
45	3208037249	7,1	7,3
46	3208037249	7,3	7,7
47	3208011249	7,3	7,5
49	3208037249	6,9	7,2
50	3208011249	7,4	7,6
51	3208011249	7,7	7,5
52	3208037249	7,0	7,2
57	3208011249	6,8	7,4
60	3208037249	7,3	6,8
64	3208037249	7,4	7,8
68	320801249	7,0	6,9
71	3208011249	7,7	7,8
72	3208037249	7,0	7,6
74	3208011249	7,0	7,2
75	320801249	7,5	7,9
76	3208037249	7,3	7,2
82	320801249	7,2	7,4
85	3208037249	7,4	8,0
86	320801249	7,3	7,7
89	320801249	7,4	6,7
92	3208011249	7,1	6,9
94	3208037249	7,9	8,1
96	3208037249	6,9	7,2
97	320801249	7,2	7,5
100	320801249	7,1	7,5
104	3208011249	7,1	7,3
107	320801249	7,6	8,0
110	320801249	6,9	7,5
114	320801249	8,0	7,6

Attachment 7

Mail group

ID	Lot-no test strips	GlucoMen LX Control N Glucose mmol/L Final consultation
1	3208011249	7,3
2	320801249	7,3
3	3208037249	7,0
5	3208011249	7,9
10	320801249	7,1
11	320801249	7,2
12	3208037249	7,4
13	3208011249	7,4
17	3208011249	7,7
19	3208011249	7,7
21	320801249	7,4
22	3208011249	6,7
25	320801249	7,7
27	3208037249	7,4
29	3208037249	6,5
30	3208037249	7,2
31	320801249	7,9
35	3208037249	7,7
36	3208011249	7,5
39	3208011249	7,8
42	3208037249	7,4
44	320801249	8,0
48	3208011249	7,9
55	3208037249	6,9
56	3208037249	7,5
58	3208037249	8,1
62	320801249	7,7
63	3208011249	7,5
66	320801249	7,8
69	3208011249	7,7
70	320801249	7,2
73	3208011249	8,4
79	320801249	7,7
80	3208037249	7,5
91	3208037249	7,4
95	320801249	7,5
99	3208037249	6,8
101	3208037249	7,2
103	320801249	7,3
105	3208011249	7,9
111	320801249	6,9

Attachment 9

Raw data hematocrit

ID	Hematocrit
1	0,42
2	0,43
3	0,44
5	
6	0,47
7	0,45
8	0,47
9	0,46
10	0,44
11	0,45
12	0,46
13	0,43
14	0,38
15	0,49
17	0,46
18	
19	0,45
21	0,45
22	0,44
23	0,39
24	0,40
25	0,46
27	0,42
29	0,39
30	
31	0,43
32	0,46
33	0,40
34	0,34
35	0,40
36	0,40
39	0,45
40	0,42
41	0,43
42	0,40
44	0,42
45	0,38
46	0,47
47	
48	0,44
49	0,35
50	0,39

ID	Hematocrit
51	0,46
52	
55	0,42
56	
57	0,46
58	0,37
60	0,45
62	0,42
63	0,44
64	0,41
66	0,37
68	0,41
69	0,41
70	0,47
71	0,45
72	0,40
73	0,46
74	0,30
75	0,40
76	
79	0,45
80	0,44
82	0,40
85	0,39
86	0,44
89	0,47
91	0,41
92	0,45
94	0,41
95	0,43
96	0,43
97	0,43
99	0,39
100	0,39
101	0,48
103	0,48
104	0,44
105	0,42
107	0,39
110	0,47
111	0,40
114	0,38

ID-nummer (diabetiker):_____

GlucoMen LX

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 sette strimmel inn i apparatet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

2. Å fylle strimmelen med blod

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

3. Å oppfatte lydsignalet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

4. Å lese tallene i displayet

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

5. Å betjene apparatet, totalt sett

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

6. Å betjene Glucoject Dual lansettpenn (skal kun besvares hvis Glucoject Dual lansettpenn er benyttet i utprøvingen)

Vanskelig *Enkelt*

1	2	3	4	5	6
☐	☐	☐	☐	☐	☐

Snu arket

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

Hvis ja, kan du beskrive problemet/ene:_____

_____

_____

8. Synes du det er noen fordeler med GlucoMen LX?

- _____
- _____
- _____

9. Synes du det er noen ulemper med GlucoMen LX?

- _____
- _____
- _____

Evt. andre kommentarer:_____

_____

_____

_____

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:_____

   _____

   _____

   _____

.....

SKUP-info

GlucoMen LX blodsukkerapparat fra A. Menarini Diagnostics
Sammendrag fra en utprøving i regi av SKUP

Konklusjon
Presisjonen på GlucoMen LX er akseptabel. CV er rundt 4,5 % når målingene utføres av laboratorieutdannet personale og rundt 6 % når målingene utføres av diabetikere. Målingene i denne utprøvingen oppfyller internasjonale kvalitetskrav (ISO 15197) med et avvik på mindre enn ± 20 % fra en anerkjent glukosemetode. Dette gjelder både for målinger utført av laboratorieutdannet personale og for målinger utført av diabetikere. Hematokrit ser ikke ut til å påvirke glukosemålinger på GlucoMen LX.

GlucoMen LX er beregnet til egenmåling av glukose. Målesystemet består av apparatet GlucoMen LX og GlucoMen LX Sensor teststrimler. Apparatet trenger ikke kodes. Måling av glukose starter kun når korrekt mengde blod er tilført strimmelen. Det kreves 0,3 µL blod til hver måling. Målingen tar 4 sekunder. GlucoMen LX har minnekapasitet til å lagre 400 målinger med dato og klokkeslett. Resultatene kan overføres til PC ved bruk av GlucoLog programvare.

Utprøvingen er utført under optimale betingelser av laboratorieutdannet personale og blant de brukere apparatet er beregnet for. I utprøvingen deltok 84 diabetikere. Diabetikerne i "opplæringsgruppen" fikk opplæring i bruken av apparatet før det ble utført målinger med apparatet. Diabetikerne i "postgruppen" fikk apparat og instruksjon tilsendt pr. post og fikk ingen opplæring. Alle diabetikerne brukte apparatet hjemme i tre uker og møtte deretter til en avsluttende konsultasjon.

Resultater
Presisjonen er akseptabel. CV er rundt 4,5 % når målingene er utført av laboratorieutdannet personale. Når målingene er utført av diabetikere, er upresisheten rundt 6 %. Ved glukoseverdier under 7 mmol/L ga GlucoMen LX ca. 0,5 mmol/L for høye verdier, for glukoseverdier over 10 mmol/L ga GlucoMen LX ca. 0,4 mmol/L for lave resultater. Målingene på GlucoMen LX gir nøyaktige resultater. Den totale målefeil var innenfor kvalitetsmålet (ISO 15197), som tillater avvik opp til ± 20 % fra en anerkjent metode for måling av glukose, både når det gjelder målinger utført av laboratorieutdannet personale og målinger utført av diabetikere. Hematokrit (30 — 49 %) ser ikke ut til å påvirke glukosemålinger på GlucoMen LX.

Brukervennlighet
Diabetikerne som deltok i utprøvingen syntes at GlucoMen LX var enkelt å bruke, og de fleste var fornøyde med apparatet. De fleste av diabetikerne som hadde lest i brukermanualen, var fornøyde med denne.

Tilleggsinformasjon
Den fullstendige rapporten fra utprøvingen av GlucoMen LX, SKUP/2009/71, finnes på SKUPs nettside, www.skup.nu. Opplysninger om pris fåes ved å kontakte leverandør.
Laboratoriekonsulentene kan gi nyttige råd om analysering av glukose på legekontor. De kan også orientere om det som finnes av alternative metoder/utstyr.

List of previous SKUP evaluations

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

Evaluations performed in 2004 – 2009

Evaluation no.	Component	Instrument/testkit	Producer
SKUP/2008/72	Glucose[1]	*Confidential*	
SKUP/2009/71	Glucose[1]	GlucoMen LX	A. Menarini Diagnostics
SKUP/2008/69*	Strep A	Diaquick Strep A test	Dialab GmbH
SKUP/2008/66	Glucose[1]	DANA DiabeCare IISG	SOOIL Developement co. Ltd
SKUP/2008/65	HbA1c	Afinion HbA1c	Axis-Shield PoC AS
SKUP/2007/64	Glucose[1]	FreeStyle Lite	Abbott Laboratories
SKUP/2007/63	Glucose[1]	*Confidential*	
SKUP/2007/62*	Strep A	QuikRead	Orion Diagnostica Oy
SKUP/2008/61	CRP	i-CHROMA	BodiTech Med. Inc.
SKUP/2007/60	Glucose[1]	*Confidential*	
SKUP/2007/59	Glucose[1]	Ascensia BREEZE2	Bayer HealthCare
SKUP/2006/58	HbA1c	*Confidential*	
SKUP/2007/57*	PT (INR)	Simple Simon PT	Zafena AB
SKUP/2007/56*	PT (INR)	*Confidential*	
SKUP/2007/55	PT (INR)	CoaguChek XS	Roche Diagnostics
SKUP/2007/54*	Mononucleosis	*Confidential*	
SKUP/2006/53*	Strep A	*Confidential*	
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/2006/41*	HbA1c	*Confidential*	
SKUP/2005/40	Glucose[1]	OneTouch GlucoTouch	LifeScan, Johnson & Johnson
SKUP/2005/39	Glucose[1]	OneTouch Ultra	LifeScan, Johnson & Johnson

*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 a user-evaluation among diabetes patients

Evaluations performed in 1999 – 2004

Evaluation no.	Component	Instrument/test kit	Producer
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
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 a user-evaluation among diabetes patients

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